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Research Progress on the Chemical Components and Pharmacological Activities of Gesneriaceae

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Abstract: The chemical components of the family Gesneriaceae are complex and diverse. The compounds isolated from the plants of this family mainly include flavonoids, phenylethanoid glycosides, terpenoids, anthraquinones, organic carboxylic acids, and steroids. Gesneriaceae have a wide range of pharmacological activities, including antioxidant, antibacterial, anti-tumor, enzyme inhibition and activation, cytotoxicity, and anti-Alzheimer activities. In this study, the chemical components and pharmacological activities of Gesneriaceae in recent years were summarized to provide a reference for future studies.

Keywords: Gesneriaceae; chemical components; flavonoids; phenylethanosides; pharmacological activity. © 2022 ACG Publications. All rights reserved.

1. Introduction

Gesneriaceae are distributed in eastern and southern Asia, Africa, southern Europe, Oceania, South America, and tropical to temperate areas of Mexico. The plants of the Gesneriaceae family are widely distributed in China [1]. There are 805 known plants (including infraspecies) found in China as of December 31, 2021. They belong to 45 genera and are mainly distributed in southwest to south China, and endemic and narrowly distributed species are abundant [2]. At present, Gesneriaceae plants are widely used for ornamental planting because of their simple reproduction and good flowering. In addition, a variety of chemical constituents and pharmacological activities of the plants from the Gesneriaceae family have been discovered and extensively studied. Liu et al. [3] for the first time isolated two flavonoids, 7-hydroxy-6,8,4'-trimethoxy-5-O- β -D-glucoflavone glycoside (9) and 7-hydroxy-6,8,4'-trimethoxy-5-O- β -D-glucose flavonoid glycoside (10), from Lysionotus pauciflorus Maxim (L. pauciflorus), from the family Gesneriaceae. A survey of the literature has identified more than 200 compounds from Gesneriaceae over the past few decades. However, few reviews have systematically evaluated the chemical constituents and pharmacological

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activities of this family. In this review, we discuss the research progress on Gesneriaceae in terms of chemistry and pharmacology by collecting and reviewing the related literature both in China and abroad. This review provides a comprehensive and in-depth perspective for the further investigation of the Gesneriaceae family.

2. Traditional uses

Plants of the Gesneriaceae family are widely distributed and often used in folk medicine to treat a variety of diseases. In China, some ethnic minorities mostly use the whole plant as medicine and analyze its taste, meridian, and efficacy in combination with the theory of traditional Chinese medicine. For example, *L. pauciflorus* whole plants are used in medicine to clear lung phlegm, stop bleeding, and remove dampness stagnation, and the Miao folk have utilized this for the treatment of lymphatic tuberculosis [4, 5]. *Chirita longgangensis* W. T. Wang var. hongyao S. Z. Huang (*C. longgangensis* var. *hongyao*) is sweet, astringent, flat, and has been used to nourish the blood, relieve pain due to swelling, and improve blood circulation, and detoxify and has been commonly used in Zhuang medicine [6, 7]. It is recorded in *Yunnan Chinese Herbal Medicine* and *Commonly Used Herbs in Kunming* as bitter, pungent, and cold. Table 1 summarizes the scientific names, aliases, geographical distribution and traditional uses of eight well-studied genera from the Gesneriaceae family.

Table 1. Traditional uses of eight species of Gesneriaceae

Scientific Name	Common Name	Distribution	Traditional Uses
L. pauciflorus	Cherhnexjenlvie eb, Shi diaolan, Yan gang dou (Chinese)	China Vietnam Japan	Treatment of chronic bronchitis, fall injury, and lung heat cough [8], Miao folk treatment for lymphatic tuberculosis [4, 5]
C. longgangensis var. hongyao	Shao yao, Mo guhua (Chinese)	China Vietnam Japan Mongolia Siberia	Treatment of early cold upper respiratory tract infection and irregular menstruation [7], treatment of physical weakness, anemia, and fracture [9]
Hemiboea subcapitata Clarke (H. subcapitata)	Hu shanye, Si taihua (Chinese)	China	Treatment of poisoning and boils [10]
Corallodiscus kingianus (C. kingianus)	Shi lianhua (Chinese)	China Sikkim Bhutan	Treatment of hot diarrhea [11]
Boea hygrometrica (Bge.) R. Br (B. hygrometrica)	Niu ercao, Mao erduo (Chinese)	China	Treatment of traumatic injuries, low back pain, traumatic hemorrhage, and otitis media [12]
Corallodiscus flabellatus (Craib) Burtt (C. flabellatus)	Shi hua, Yan zhijia (Chinese)	Southwest China	Treatment of irregular menstruation, palpitations, sore carbuncle, and intractable tinea [13, 14]
Oreocharis acericula (S.Moore) Clarke (O. acericula)	Yan baicai (Chinese)	Southern China	Treatment of traumatic injuries, carbuncles, boils, and various bleeding [15]
Chirita eburnea Hance (C. eburnea)	Shi sanqi, Shi huer (Chinese)	Southern China	To treat tuberculosis and hypertension in Guangxi folk [16]

3. Chemical Constituents

3.1. Flavonoids and Their Glycosides

Flavonoids and their glycosides have been widely studied in Gesneriaceae plants. The flavonoid skeleton of Gesneriaceae plants mainly includes flavonoids, flavonois, dihydroflavonoids, and dihydroflavonoids often exist in the form of glycosides, aerobic glycosides, and carbon glycosides, and most of the glycosides consist of glucose units.

Flavonoids and their glycosides are derived from 10 species of Gesneriaceae. Apigenin (6) and 5,7,4'-trihydroxy-6-methoxy-flavone (7) were isolated from *A. superbus* for the first time[17]. Moreover, 5,7,3',4'-tetrahydroxy-6-C-β-D-gluco dihydro flavone carboglycoside (26) has been isolated and elucidated from ethyl acetate and n-butanol fractions of *Chirita linearifolia* W. T. Wang (*C. linearifolia*) [18]. Figure 1 shows the structure of flavonoids and their glycosides. Table 2 summarizes the names, sources, and references of flavonoids and their glycosides.

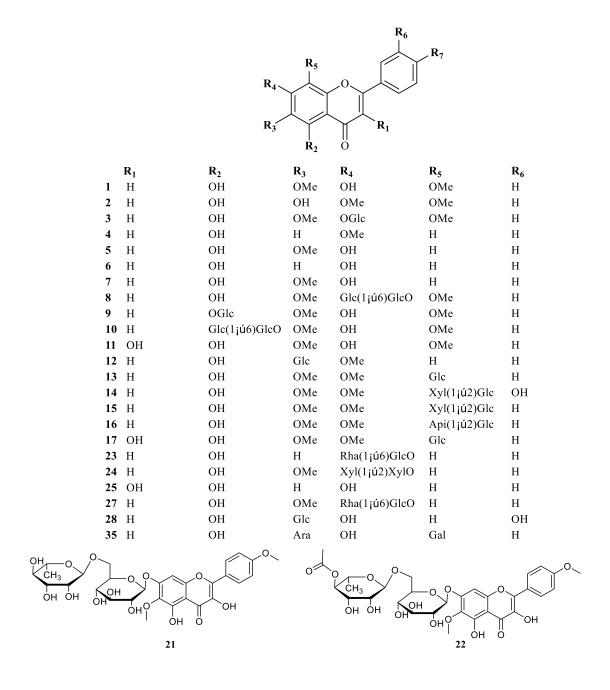


Figure 1. Flavonoids and their glycosides isolated from the genus

Figure 1. Flavonoids and their glycosides isolated from the genus (continued..)

Table 2. Chemical constituents of flavonoids and their glycosides

No	Compound Name	Source	Ref.
1	5,7-dihydroxy-6,8,4'-trimethoxy flavone		
2	5,6,4'-trihydroxy-7,8-dimethoxy flavone	L. pauciflorus	[1, 19-21]
3	5-hydroxy-6,8,4'-trimethoxy-flavone-7-O-β-D-glucoside	1 0	
4	5-hydroxy-7,4'-dimethoxy flavone	C. kingianus	[1]
5	5,7-dihydroxy-6,4'-dimethoxy flavone	C. Kingianus	[1]
6	Apigenin	A. superbus	[17]
7	5,7,4'-trihydroxy-6-methoxy flavone	Chirita fimbrisepala HandMazz (C. fimbrisepala)	[17, 22] [23]
8	5-hydroxy-6,8,4' -trimethoxy-7-O-[β -D-glucose-($1\rightarrow 6$)]- β -D-glucoseflavonoid glycoside	L. pauciflorus	[19]
9	7-hydroxy-6,8,4'-trimethoxy-5-O-β-D-glucoflavone glycoside	L. pauciflorus	
10	7-hydroxy-6,8,4'-trimethoxy-5-O-[β -D-glucose-($1\rightarrow$ 6)]- β -D-glucose flavonoid glycoside		[3, 19, 20]

11	5,7-dihydroxy-6,8,4'-trimethoxy flavonol		
12	4',5-dihydroxy-7-methoxy-6-C-β-D-glucoflavone glycoside	L. pauciflorus	[20]
13	4',5-dihydroxy-6,7-dimethoxy-8-C-β-D-glucoflavone glycoside		
14	5,3',4'-trihydroxy-6,7-dimethoxy-8-C-[β -D-xylose-($1\rightarrow 2$)]- β -D-glucoflavonecarboglycoside		
15	5,4'-dihydroxyl-6,7-dimethoxy-8-C-[β -D-xylose-($1\rightarrow 2$)]- β -D-glucoflavonecarboglycoside	C. flabellatus	[24]
16	5,4'-dihydroxyl-6,7-dimethoxyl-8-C-[β -D-apiofuranosyl (1 \rightarrow 2)]- β -D-glucopyranosyl flavone		
17	5,4'-dihydroxy-6,7-dimethoxy-8-C-β-D-glucose flavonol	B. hygrometrica	[25]
18	2 (R)-Eriodictyol-8-C-B-D-glucopyranoside	C. longgangensis var.	[26]
19	2 (S)-Eriodictyol-8-C-B-D-glucopyranoside	hongyao	[=0]
20	5,7,3'4'-tetrahydroxy-6-C-β-D-glucodihydroflavone carbon glycoside	C. linearifolia	[18]
21	Pectolinarin		
22	4"'-acetyl-Pectolinarin	C. flabellatus	[27]
23	linarin		
24	mahuangchiside	C. fimbrisepala	[23]
25	kaempferol		
26	5,7-dihydroxy-8-C-β-D-glucochroone carbon glycoside		
27	5-hydroxy-6,4'-dimethoxy-7-[α -L-rhamnose-(1 \rightarrow 6)]-O- β -D-glucochromone glucoside	Aeschynanthus	
28	5,7,3',4'-tetrahydroxy-6-C-β-D-glucoflavonol carbon glycoside	moningeriae (A. moningeriae)	[28]
29	5,7-dihydroxy-6-C-β-D-gluco dihydro flavone carbon glycoside		
30	5,7,3',4'-tetrahydroxy-6-C-β-D-gluco dihydro flavonol carbon glycoside		
31	naringenin		
32	evofolin B		
33	hemiphloin	Aeschynanthus	_
34	prunin	bracteatus Wall. ex A.	[29]
35	corymboside	DC. (A. bracteatus)	
36	pyrroside B		
37	ormocarpin		

3.2. Phenylethanol Glycosides

The number of glycogroups in most phenylethanol glycosides in Gesneriaceae ranges from one to three, and the types of glycogroups are rich and varied. In addition, aromatic acyl substituents are often associated, and coffee acyl substituents are the most common. The phenylethanol glycosides described in this review were derived from eight genera of Gesneriaceae. Figure 2 shows the structures of phenylethanol glycosides. Table 3 summarizes the names, sources, and references of phenylethanol glycosides.

Figure 2. Phenylethanol glycosides isolated from the genus

Table 3. Chemical constituents of phenylethanol glycosides

No	Compound Name	Source	Ref.
38	(7S)-methoxyl-3,4-dihydroxyphenylethanol-8-O-β-D-apiofuranosyl (1→6)-β-D-glucopyranoside		
39	(7R)-methoxyl-3,4-dihydroxyphenylethanol-8-O- β -D-apiofuranosyl (1 \rightarrow 6)- β -D-glucopyranoside		
40	(7S)-methoxyl-3,4-dihydroxyphenylethanol-8-0-β-D-glucopyranoside		
41	(7R)-methoxyl-3,4-dihydroxyphenylethanol-8-0-β-D-glucopyranoside		
42	(7ξ) -methoxyl-3,4-dihydroxyphenylethanol-8-O-β-D-apiofuranosyl $(1\rightarrow 3)$ -[β-D-glucopyranosyl $(1\rightarrow 6)$]-4-O-trans-caffeoyl-β-D-glucopyranoside	C. flabellatus	[27]
43	3,4-dihydroxyphenylethanol-8-O- β -D-apiofuranosyl (1 \rightarrow 6)- β -D-glucopyranoside		
44	3,4-dihydroxyphenylethanol-8-O- β -D-apiofuranosyl (1 \rightarrow 2)- β -D-glucopyranoside		
45	4-hydroxyphenylethanol-8-O-β-D-glucopyranoside		
46	3,4-dihydroxyphenylethanol-8-O-β-D-glucopyranoside		
47	isonuomioside A		
48	sanangoside		
49	aeschynanthoside A	A. bracteatus	[20]
50	aeschynanthoside B	A. bracieatus	[29]
51	aeschynanthoside C		
52	aeschynanthoside D		
53	3,4-dihydroxyphenyl alcohol-6-O-caffeoyl-β-D-glucopyranoside (calceolarioside B)	C. longgangensis var. hongyao	[30] [26, 31]
54	3,4-dihydroxyphenyl alcohol-β-D-glucopyranosyl (1→3)-6-O-caffeoyl-β-D-glucopyranoside (plantainoside D)	C. longgangensis var. hongyao	[31]
55	3, 4-dihydroxyphenyl alcohol-3-O-cafeoyl-β-D-glucopyranoside (plantainoside A)		
56	3, 4-dihydroxyphenyl alcohol-6-O-glucopyranosylcafeoyl-β-D-glucopyranoside (chiritoside C)	C. eburnea	[32]
57	3, 4-dihydroxyphenyl alcohol-2-O-cafeoyl-β-D-glucopyranoside (plantaninoside B)		
58	3, 4-dihydroxy-phenyl alcohol- β -D-glucopyranosyl $(1\rightarrow 3)$ -4-O-cafeoyl- β -D-glucopyranoside (plantamajoside)	C. longgangensis var. hongyao	[30] [26] [32]
59	3, 4-dihydroxyphenyl alcohol-4-O-cafeoyl-β-D-glucopyranoside	C. eburnea	[32]

60	β-D-Glucopyranoside,2-(3,4-dihydroxyphenylethyl,4-[(2E)-3-(4-hydroxy-3-methoxyphenyl)-2-propenoate]	C. linearifolia	[33]
61	1'-O-β-D-(3,4-dihydroxyphenyl)-ethyl-β-D- apiofuranosyl (1 \rightarrow 3')-glucopyranoside		F2.41
62	1'-O-β-D-(3,4-dihydroxyphenyl)-ethyl-β-D-apiofuranosyl (1 \rightarrow 3')-β-D-glucopyranosyl (1 \rightarrow 6')-glucopyranoside	C. flabellatus	[34]
63	lugrandoside	Selaginella tarmariscina	[34]
64	isolugrandoside	(Beauv.) Spring	[54]
65	paraboside A	Paraboea glutinosa (P.	[35]
66	paraboside B	glutinosa)	[55]

3.3. Quinones

There are also many quinones in the plants of Gesneriaceae family, most of which are 9,10 anthraquinones. The substituents are mostly hydroxyl and methyl groups. The quinones in this review were derived from seven members of Gesneriaceae. Figure 3 shows the structures of quinone compounds. Table 4 summarizes the names, sources, and references of quinones.

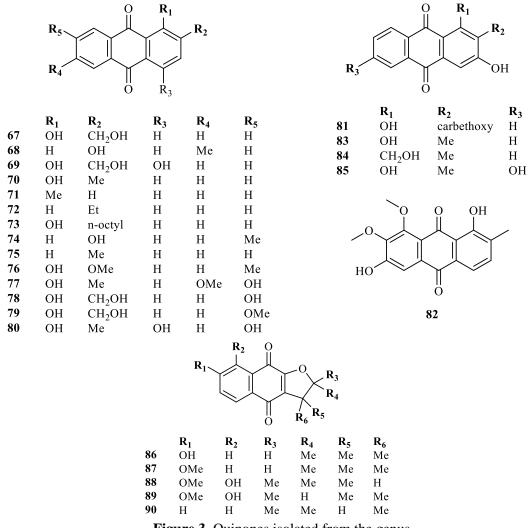


Figure 3. Quinones isolated from the genus

Table 4. Chemical constituents of quinones

No.	Compound Name	Source	Ref.
67	1-hydroxy-2-hydroxymethyl anthraquinone		
68	2-hydroxy-6-methyl anthraquinone	C. linearifolia	[18]
69	1,4-dihydroxy-2-hydroxymethyl anthraquinone		
70	1-hydroxy-2-methyl anthraquinone		
71	1-methyl anthraquinone	C. linearifolia	[33]
72	2-ethyl anthraquinone		
73	2-octyl-1-hydroxy-9,10-anthraquinone		
74	2-hydroxy-7-methyl-9,10-anthraquinone	C. longgangensis var. hongyao	[9]
75	2-methyl-9,10-anthraquinone		
76	1-hydroxy-2-methoxy-7-methy lanthraquinone		
77	1,7-dihydroxy-6-methoxy-2-methy lanthraquinone	C. eburnea	[36]
78	1,7-dihydroxy-2-hydroxymethyl-9,10-anthraquinone		
79	1-hydroxy-7-methoxy-2-hydroxymethyl-9,10-anthraquinone	H. subcapitata	[37]
80	1,4,7-trihydroxy-2-methyl-9,10-anthraquinone		
81	1,3-dihydroxy-2-ethoxycarbonyl-9,10-anthraquinone		
82	rhynchotechol	Rhynchotechum	
83	rubiadin	vestitum (R. vestitum)	[38]
84	Rubiadin-1-methylether		
85	6-hydroxy-rubiadin		
86	7-hydroxy-2,3-dihydro-2,3,3-trimethylnaphtho [2,3-b] furan-4,9-dione	C. longgangensis var. hongyao	[9, 26]
87	(3R)-7-methoxy-R-dunnione	C. linearifolia	[18]
88	tenuiflorone	Paliavana tenuiflora	[39]
89	7-metoxy-8-hydroxy-α-dunnione	Mansf (P. tenuiflora)	[37]
90	α -isodunnione	Sinningia allagophylla (S. allagophylla)	[40]

3.4. Phenolic Acids

Phenolic acids are the most important organic acid, and there are a variety of phenolic acids in Gesneriaceae. This review describes phenolic acids from 11 species of Gesneriaceae plants. Some polyesters are also found in these compounds. For example, compounds **101**, **103** [20], and **115** [41] were separated from *L. pauciflorus*. Figure 4 shows the structures of phenolic acids. Table 5 summarizes the names, sources, and references of phenolic acids.

Figure 4. Phenolic acids isolated from the genus

Figure 4. Phenolic acids isolated from the genus (continued..)

Table 5. Chemical constituents of phenolic acids

No.	Compound name	Source	Ref.
91	1'-O-β-D-(4-hydroxyphenylethyl)-β-D- apiofuranosyl (1 \rightarrow 2')-glucopyranoside	B. hygrometrica	[25]
92	paraboside I		_
93	paraboside II	P. glutinosa	[35]
94	paraboside III		
95	4-ethenyl-2-methoxyphenol	O. acericula	[42]
96	isovanillic acid	A I	Г1
97	vanillic acid	Aeschynanthus longicaulis (A. longicaulis)	[1, 43]
98	3,4-dimethoxy cinnamic acid	Puraboeo rutescens (P. rutescens)	[1]
99	2,6-dimethyl-4-methoxy-5-hydroxybenzoic acid	A. superbus	[17]
100	ferulic acid	L. pauciflorus A. bracteatus	[20] [29]
101	diisobutyl phthalate		
102	syringic acid	L. pauciflorus	[20]
103	Phthalic acid-bis-(2-ethylhexyl) ester		
104	3,4-dihydroxy-phenylacetic acid glycol ester	C. flabellatus	[24]
105	2,4-dihydroxy-3,6-dimethylbenzoate	B. hygrometrica	[25]
106	caffeic acid	C. longgangensis var.	[26]
107	gallic acid	hongyao	[26]

108	veratric acid		
109	ethylparaben	A. bracteatus	[29]
110	cinnamic acid	A. Dracteatus	[29]
111	4-hydroxybenzoic acid		
112	phenyl ethyl 2-acetate	O. acericula	[42]
113	2-(p-hydroxyphenyl) ethyl hexacosanoate	P. tenuiflora	[20]
114	2-(3,4-dihydroxyphenyl) ethyl hexacosanoate	r. tenugiora	[39]
115	bis (2-butylhexyl) phthalate	L. pauciflorus	[41]
116	P-hydroxyphenyl ethanol	B. hygrometrica	[25]
117	1,4-Dihydroxy-2-naphthalenecarboxylic acid methyl ester-4-O-β-L-Rhamnopyranosyl (1→6)-β-D-Glucopyranoside	C. longgangensis var. hongyao	[9, 26]
118 119	hydroxytyrosol Apocynin	C. flabellatus	[24]
120	4-hydroxyphenylethanol	C. flabellatus	[27]
121	koaburaside	J	
122	coniferyl alcohol		
123	(R)-2-hydroxy-1 (4-hydroxy-3-methoxyphenyl)		
	propan-1-one		
124	vanillin		
125	syringaldehyde		
126	coniferaldehyde		
127	1-(3,4-dimethoxyphenyl)-1,3-propanediol		
128	3,4-dihydroxypropiophenone		
129	1-(2-hydroxy-5-methoxyphenyl)-1,2-propanediol	A. bracteatus	[29]
130	C-veratroylglycol		
131	2,4-dihydroxyacetophenone		
132	piceol		
133	2-methoxy-4-(3-methoxy-1-propenyl)-phenol		
134	syringenin		
135	1,3-dihydroxy-1-(4-hydroxy-3,5-dimethoxyphenyl) propan-2-one		
136	x-hydroxypropioguaiacone		
137	alaschanioside C		
138	Benzene acetaldehyde	O. acericula	[42]
139	Benzene ethanol	O. acericaia	[42]
140	3,5-dimethoxy-4-hydroxy-trans-stilbene	L. pauciflorus	[41]
141	platyphylloside	C 1	
142	hirsutanonol	C. longgangensis var.	[44]
143	hirsutanonol-5-O-β-D-glucopyranoside hongyao		
144	trans-3,5-dimethoxy-4-hydroxycinnamaldehyde	A. bracteatus	[45]

3.5. Terpenoids

Terpenoids are derived from meglutaric acid, and most of the molecular formula follows the $(C_5H_8)_n$ general formula. Terpenoids are abundant in Gesneriaceae, which include monoterpenes,

sesquiterpenes, diterpenes, triterpenes, and terpenes. Figure 5 shows the structures of terpenoids. Table 6 summarizes the names, sources, and references of terpenoids.

Figuer 5. Terpenoids isolated from the genus

Figuer 5. Terpenoids isolated from the genus (*continued.*.)

Table 6. Chemical constituents of terpenoids

No.	Compound name	Source	Ref.
145	cryptomeridiol		
146	4 (15)-eudesmene- 1β , 6α -diol	A. longicaulis	[1, 43]
147	2,5-bornanediol		
148	grasshopper ketone		
149	9-hydroxylinalool	A. bracteatus	[29]
150	epidihydrophaseic acid		
151	AM-2	A L	
152	AM-6	Aeschynanthus mengxinensis (A. mengxinensis)	[46]
153	AM-8	mengxinensis)	
154	linalool		
155	A-terpilenol	Q. acericula	[42]
156	germacrone	O. acericaia	
157	citronellol		
158	succinic acid		
159	N-hexadecanoic acid	C. longgangensis var. hongyao	[26]
160	N-tetradecanoic acid		
161	eleven carbonate	C linearifolia	Γ101
162	palmitic acid	C. linearifolia	[18]
163	twenty-seven alkanoic acid		
164	glycerol monoleate	C. linearifolia	[33]
165	triglyceride dodicarboxylate		

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166	palmitic acid	C. kingianus	[47,
167	stearic acid	Rhynchotechum ellipticum (R. ellipticum)	48] [49]
168	9,12-octadecadienoic acid	Rhyhenoteenum empiteum (R. empiteum)	[۲۷]
169	(Z, Z, Z)-9,12,15- octadecanotrienoic acid	C. kingianus	[47, 48]
170	tetracanoic acid	R. vestitum	[38]
171	hexanoic acid	O. acericula A. moningeriae	[42] [50]
172	2-ethyl-hexanoic acid		
173	octylic acid		
174	n-nonanoic acid		
175	decylic acid		
176	dodecanoic acid	O. acericula	[42]
177	myristic acid		
178	11,14-eicosadienoate ethyl ester		
179	oleic acid		
180	triacontane	C. longgangensis var. hongyao	[9, 26]
181	mannitol	C. tonggungensis var. nongyao	[>, 20]
182	7-octene-1,6-diol	A. bracteatus	[29]
183	octatriacontane	C. linearifolia	[18]
184	2-ethyl-4-butanol		
185	3-ene-1-hexanol		
186	hexanal		
187	1-octene-3-ketone		
188	1-ene-3-octanol	O. acericula	[42]
189	3-octanol		[]
190	trans-2-enononone		
191	nonyl alcohol		
192	1,6-diene-3-octanol		
193	decanol		
194	presilphiperfolan-9-ol	P. tenuiflora	[39]
195	3,10-dihydroxyacoronene	L. pauciflorus	[41]
196	dodecyl alcohol	L. pauciflorus	[51]
197	N-triethanol	T A	r- 1
198	cleroindicin B	S. allagophylla	[40]
199	cleroindicin C	S. amagopriyuu	
200	AM-15	A. mengxinensis	[46]

3.6. Triterpenoids

Triterpenes are composed of several isoprenoids joined end-to-end with a hydroxyl molecule removed. Triterpenoids in Gesneriaceae are pentacyclic triterpenoids, and their skeletons are of the ursane and oleanane type. Most of the 28 substituents are carboxyl or glycoside with glucose. Figure 6 shows the structures of triterpenes. Table 7 summarizes the names, sources, and references of triterpenes.

Figure 6. Triterpenoid isolated from the genus

 Table 7. Chemical constituents of triterpenoid

No	Compound name	Source	Ref.
201	barbinervic acid	A. moningeriae	[1] [28]
202	3β,19α-dihydroxy-12-ene-28-ursolic acid		
203	28-O-β-D-glucopyranosyl pomolic acid	P. rutescens	[1]
204	lupeol	A. superbus Aeschynanthu maculatus (A. maculatus)	[17, 22] [17]
205	3-hydroxy-20 (29)-lupen-28-oic acid	A. superbus A. maculatus C. longgangensis var. hongyao C. linearifolia	[17, 22] [17] [26] [33]
206	3-hydroxy-5,12-oleanadien-28-oic acid		[17,
207	3,24-dihdroxy-12-oleanen-28-oic acid	A. superbus	22]
208	3,24-dihdroxy-12-ursen-28-oic acid		
209	12-ursolic acid-3-O-β-D-glucoside		
210	12-oleanolic acid-28-O-β-D-glucoside		
211	12-oleanolic acid-3-O-β-D-glucoside		
212	4-epipinfaensin	A 7 .	[17]
213	paradrymonoside	A. maculatus	[17]
214 215	trachelosperogenin A1 nigaichigoside F1		
216	nigaichigoside F2		
217	suavissimoside F1		
218	3β-hydroxy-9,12-oleanadien-28-oic acid	C. kingianus	[46,
		21 1111/3111111111	47]
219	2α,3β,19β-trihydroxy-olean-12-ene-23,28-dioic acid	A. mengxinensis	[52]
220	2α,3β,21β-trihydroxyolean-12-ene-28-oic acid	11. mengwatensis	[32]
221	$2\alpha,3\beta,23$ -trihydroxyurs-12-ene-28-oic acid	A. mengxinensis	[46, 52]
222	CK01	C. kingianus	[46]
223	AM-1		
224	AM-7		
225	AM-3	A. mengxinensis	[46]
226	AM-9		
227	AM-11		
228	oleanolane-3-O-β-D-glucoside	R. ellipticum	[49]
229	24-hydroxytormentic acid		
230	24-hydroxytormentic acid ester glucoside	D. alutinasa	[52]
231	28-O-β-D-glucopyranosyl (1 \rightarrow 6)-β-D-glucopyranosyl-24-hydroxytormenticacid	P. glutinosa	[53]
232	2,3,19,24-tetrahydroxy-12-ene-28-ursolate-28- O-β-D-glucoside	A. moningeriae	[28]

3.7. Steroids

Steroids are a class of thickened tetracyclic aliphatic compounds with a cyclopentane polyhydrophenanthrene nucleus. Steroidal compounds in Gesneriaceae plants contain 3-position hydroxyl groups or glycosides with glucose, and 20-position substituents are chained hydrocarbon groups. β -carotenoside (235) was isolated from the aboveground portion of *A. superbus* and *A. maculatus* [17, 22], and the compound was found in five species of Gesneriaceae. In addition, the methanol extract of *A. superbus* contained β -sitosterol (236) [17, 22], and β -sitosterol was found in up to 11 species of Gesneriaceae. Figure 7 shows the structures of steroids. Table 8 summarizes the names, sources, and references of steroids.

Figure 7. Steroids isolated from the genus

Table 8. Chemical constituents of steroids

No	Compound Name	Source	Ref.
233	stigmasterol	R. ellipticum C. linearifolia A. moningeriae A. maculatus P. tenuiflora	[17, 22] [18] [28] [49] [39]
234	Steroidal-5,22 (E)-diene-3-β-alcohol	A. maculatus A. longicaulis A. mengxinensis	[17, 22] [43] [52]
235	β-daucosterol	C. linearifolia R. ellipticum P. glutinosa A. moningeriae C. longgangensis var. hongyao	[18, 33] [49] [53] [28] [9]
236	β-sitosterol	P. rutescens A. longicaulis	[1] [1]

		C. longgangensis var.	[26]
		hongyao A. moningeriae	[28]
		C. linearifolia	[33]
		R. ellipticum	[49]
		P. glutinosa	[53]
		C. eburnea	[36]
		P. tenuiflora	[39]
		L. pauciflorus	[54]
		B. hygrometrica	[12]
237	β-sitosteryl-D-glucoside-6'-palmitate	C. longgangensis var. hongyao	[9, 26]
238	3-O-β-D-glucostigmasterol glycoside	A. moningeriae	[28]

3.8. Volatiles and Fatty Oils

The lipid soluble components of *C. flabellatus* were extracted by the Soxhlet extraction method. The lipid soluble components were methyl esterified, and their chemical constituents were analyzed by GC-MS [55]. A total of 47 compounds were identified, including fatty acids, terpenes, alkanes, alcohols, ketones, and methyl ester, accounting for 84.34% of the liposoluble components.

The chemical constituents of volatile oil in *A. moningeriae* were analyzed and extracted by SPME [50]. The components of the volatile oil were separated and identified by GC-MS, and the relative content of each component was determined by the area normalization method. Sixty-three types of components were separated. Among these, 58 components were identified, accounting for approximately 98.06% of the total chemical constituents. The ingredient with the highest content in this study was [2R-(2à,4aà,8aá)]-4a,8-dimethyl-2-(1-methylethenyl)-1,2,3,4,4a,5,6,8a-octahydronaphthalene (12.80%).

3.9. Other Components

In addition to the eight chemical compounds mentioned above, there are many other compounds in the plants of Gesneriaceae family, such as lignans and sugars.

Two naphthol dimer compounds allagophylldimer D (250) and allagophylldimer E (251) were isolated and identified in *S. allagophylla* [50]. Figure 8 shows the structures of other compounds. Table 9 summarizes the names, sources, and references of other compounds.

Ultra-high-performance liquid chromatography quadrupole time-of-flight mass spectrometry (UPLC-Q-TOF-MS) was used to analyze the chemical components in *L. wilsonii* [30]. The results showed that 57 components were identified, which included 42 phenylethanoid glycosides, five benzyl alcohol glycosides, six flavonoids, and four other components. Forty-three of these compounds were first identified in Gesneriaceae, and one benzyl alcohol glycoside may be a new compound.

Table 9. Chemical constituents of other compounds

No	Compound Name	Source	Ref.
239	2-O-α-D-furan fructosyl-α-D-glucose	B. hygrometrica	[25]
240	3',4',9,9-Tetrahydroxy-4,5-dimethoxy-2,7'-cyclolignan	C. longgangensis var. hongyao	[9, 26]
241	D-(+)-raffinose	L. pauciflorus	[54]
242	icariol A2		
243	balanophonin		
244	guaiacylglycerol-b-ferulic acid ether		
245	(7S, 8R) dehydrodiconiferyl alcohol 9'-glucopyranoside	A. bracteatus	[29]
246	dianthoside		
247	6'-O-β-D-apiofuranosyl-dianthoside		
248	caprolactam	C. linearifolia	[18]
249	α-D-furanfructose	B. hygrometrica	[12]
250	allagophylldimer D		
251	allagophylldimer E		
252	6,8-dimethoxybenzocoumarin	S. allagophylla	[40]
253	warmingiin A		
254	warmingiin B		

Figure 8. Other components isolated from the genus

Figure 8. Other components isolated from the genus (*continued..*)

4. Pharmacological Activities

4.1. Antioxidant Activity

Tian [17] used DPPH, ABTS, and FRAP to comprehensively evaluate the antioxidant activities of different solvent extracts of A. superbus, A. maculatus, and R. ellipticum and the isolated compounds $in\ vitro$. The results showed that ethyl acetate and methanol fractions of A. superbus and ethyl acetate and methanol fractions of A. maculatus had better antioxidant activities than other fractions. The scavenging ability of the three plant extracts on DPPH free radicals and ABTS free radicals and the reducing ability on Fe³⁺ are all dose-dependent.

Qiao et al. [55] used a 96-well plate method to determine the antioxidant capacity of fat-soluble ingredients. The test results showed that the fat-soluble component of *C. flabellatus* had a certain scavenging effect on DPPH. Kang et al. [56] used DPPH, ABTS, and FRAP for the first time to study the *in vitro* antioxidant activity of *C. kingianus* and *A. mengxinensis*. It was found that among the four extracts, the methanol extract of *C. kingianus* had a stronger DPPH free radical scavenging ability (IC₅₀=4.92 μ g/mL) than the positive control BHT (IC₅₀=18.79 μ g/mL). The scavenging ability of the methanol extract of *C. kingianus* to ABTS free radicals (IC₅₀=11.10 μ g/mL) was slightly lower than that of BHT (IC₅₀=6.04 μ g/mL). In addition, the ability of extract of *C. kingianus* to reduce Fe³⁺ (FRAP=2,403.77±38.05 μ molTE/g) was higher than BHT (FRAP=1,748.49±3.46 μ molTE/g). Among the four extracts, the methanol extract of *C. kingianus* showed the highest antioxidant capacity.

Liu [57] used two analytical methods, namely, DPPH and FRAP, to determine the antioxidant activity of each fraction of *A. moningeriae in vitro*. The results showed that the order of the antioxidant activity of DPPH and FRAP *in vitro* was water fraction > ethyl acetate extraction fraction > 70% crude extract > petroleum ether fraction; 30% methanol enrichment fraction > 50% methanol enrichment fraction > 10% methanol enrichment fraction > 70% methanol enriched fraction. Chen [1] used the DPPH microplate method to determine the antioxidant activity of the compounds isolated from *A. longicaulis* and *L. pauciflorus*. Among these, 5,7-dihydroxy-6,8,4'-trimethoxyflavone (1) (IC₅₀=17.01 μ g/mL) and vanillic acid (97) (IC₅₀=13.63 μ g/mL) both exhibited significant antioxidant activity. However, the antioxidant activity of 5,6,4'-trihydroxy-7,8-dimethoxyflavone (2) (IC₅₀=51.7 μ g/mL) was slightly lower than the positive control BHT.

4.2. Antibacterial Activity

For the first time, Chen [1] studied the antibacterial activities of extracts from three Gesneriaceae plants and their compounds. Analysis of the extracts of *A. longicaulis* and *L. pauciflorus* on SA, MRSA, and ESBLs-SA revealed that the antibacterial effect of *A. longicaulis* was better than that of *L. pauciflorus*, which mainly existed in the parts of petroleum ether and ethyl acetate. Tian [17] studied the *in vitro* antibacterial activity of *A. superbus*, *A. maculatus*, and *R. ellipticum* total methanol extracts. The total methanol fraction of *A. superbus* had an inhibitory effect on SA and MRSA. When the concentration was 250 µg·disc⁻¹, the inhibition zone for SA was 9 mm, and the inhibition zone for MRSA was 8 mm. The total methanol part of *A. maculatus* had an inhibitory effect on SA, and the

inhibition zone was 9 mm; the total methanol part of *R. ellipticum* had an inhibitory effect on SA, and the inhibition zone was 8 mm.

Wei et al. [21] used the paper diffusion method to track the activity of the extracts from P. rutescens and L. pauciflorus and found that the ethyl acetate fractions of the two plants had the best antibacterial activity against SA, MRSA, and ESBLs-SA. Barbinervic acid isolated from P. rutescens had the best inhibition of SA activity (IC₅₀=0.098 g/L, **201**) and ESBLs-SA activity (IC₅₀=0.270 mg/L). Meanwhile, 3β , 19α -dihydroxy-12-ene-28-ursolic acid (IC₅₀=0.130 g/L, **202**) had the best inhibitory activity against MRSA.

Xu et al. [5] found that lysionotin (1) 200 μg/mL *in vitro* test has a significant anti-TB effect. Zhang et al. [58] studied the clinical observation test of *L. pauciflorus* tablets in adjuvant treatment of retreatment of pulmonary tuberculosis. The experiment found that the negative conversion rate of sputum bacteria in the treatment group (95.7%) was significantly higher than that in the control group (79.6%) (P<0.05), and there were also significant differences between the two groups in drug-resistant cases (P<0.01). This may be due to the fact that the phytoplankton enhances the bactericidal activity of sensitive drugs and prevents the sensitive drugs from developing selective resistance.

4.3. Enzyme Activation/Inhibition Activity

For the first time, Chen [1] conducted α -glucosidase inhibitory activity experiments on monomer compounds, extracts, and various parts of *L. pauciflorus* Maxim and *A. longicaulis*, and found that *L. pauciflorus* total acetone water extract (IC₅₀=415.30 µg/mL), ethyl acetate (IC₅₀=312.67 µg/mL), and n-butanol (IC₅₀=884.10 µg/mL) have α -glucosidase inhibitory activity, and the ethyl acetate part has the highest activity. The α -glucosidase inhibitory activity of these three parts is higher than that of all parts of *A. longicaulis*. 5,6,4'-trihydroxy-7,8-dimethoxy flavone (2) (IC₅₀=55.50 µg/mL) and vanillic acid (97) (IC₅₀=13.63 µg/mL) had α -glucosidase inhibitory activity.

Tian [17, 59] used the 96-well plate method to study the *in vitro* α-glucosidase inhibitory activity of *A. superbus*, *A. maculatus*, and *R. ellipticum* solvent extracts. The results showed that the *in vitro* α-glucosidase inhibitory activity of each part of the three plants was in the order of *R. ellipticum* petroleum ether component ($IC_{50}=112.4~\mu g/mL$) > *A. maculatus* petroleum ether component ($IC_{50}=127.3~\mu g/mL$) > *A. superbus* petroleum ether component ($IC_{50}=230.2~\mu g/mL$) > *R. ellipticum* ethyl acetate component ($IC_{50}=351.4~\mu g/mL$) > *A. maculatus* ethyl acetate component ($IC_{50}=750.8~\mu g/mL$) > *A. maculatus* the methanol component ($IC_{50}=1,350.6~\mu g/mL$). The inhibition rate of the first five components was higher than the positive control Acarbose ($IC_{50}=1,103.01~\mu g/mL$), and had a certain concentration dependence. In addition, 5,7,4'-trihydroxy-6-methoxy flavone ($IC_{50}=40.06~\mu g/mL$, 7) and lupeol ($IC_{50}=25.41~\mu g/mL$, 204), and ursolic acid ($IC_{50}=4.42~\mu g/mL$, 205) had good *in vitro* α-glucosidase inhibitory activity.

Yao [27] used the 96-well plate method to study the effects of phenethyl alcohol and glycosides isolated from *C. flabellatus* on mushroom tyrosinase. Using arbutin as positive control, compound 42 showed certain mushroom tyrosinase inhibitory activity, which was concordant to the activity of this type of compound (containing caffeoyl) in the literature. Compounds 43–46 and 120 had no inhibitory activity and showed agonistic activity, which may be related to the caffeoyl compound structure and may be used in the treatment of white disease or vitiligo.

4.4. Anti-Alzheimer's Activity

Wang et al. [60] explored the intervention mechanism of *C. flabellatus* extract for Alzheimer's disease (AD) through UPLC-Q-TOF/MS metabolomics. Statistical analysis showed that the metabolic profiles of the AD model group were significantly separated from the control group, while the CF group was closer to the control and positive groups. A total of 28 potential AD-related biomarkers were detected, and metabolic pathways were established by MetPA. This study elucidated the involvement of metabolic pathways in oxidation, disorders of energy metabolism, and neuromodulator disorders. In addition, this is the first time that a metabolomics study has been used to determine the therapeutic mechanism of CF extract on AD model mice.

Zeng et al. [61] studied the effect and mechanism of action of *C. flabellatus* (SDC) extract and isolated isonuomioside A (isA) on A β_{25-35} -induced brain injury. The experiment was completed by inducing brain injury by infusion of A β_{25-35} (200 μ M, 3 μ l/20 g, i.c.v.) and then dosing with SDC extract (155 mg/kg, i.g.) or isA (20 mg/kg, i.g.) over 4 weeks. In addition, the antagonism of MK-801 (NMDA receptor blocker, 10 μ M) in the presence of isA (10 μ M) or SDC (20 μ g/ml) extracts was studied in A β_{25-35} (20 μ M, 24 h)-induced PC-12 and N9 cells to assess whether the effects induced by isA and SDC extracts were mediated through the NMDAR2B/CamK II/PKG pathway. It was demonstrated that isA and SDC extracts ameliorated A β_{25-35} -induced brain injury by inhibiting apoptosis, oxidative stress, and autophagy, possibly through the NMDAR2B/CamK II/PKG pathway.

Zhang et al. [62] investigated the intervention effect and mechanism of carbenoside B (CB) on Alzheimer's disease (AD) induced by amyloid β -protein fragment 25-35 (A β_{25-35}). A mouse model of AD was established by injecting A β_{25-35} into the brain. Y maze and new object recognition experiments were used to determine the learning and memory ability of mice. Pathological changes in the hippocampus were observed by HE staining, Nissner staining, and electron microscopy. The levels of A $\beta_{1-42}/A\beta_{1-40}$ and p-Tau in the brain were detected by enzyme-linked immunosorbent assay. The content or activity of MDA, SOD, and GSH-Px in serum was detected using biochemical methods. The level of reactive oxygen species in the brain was detected using flow cytometry. Protein western blotting was used to detect the expression levels of LC₃B, Beclin-1, and P62-related autophagy proteins in the brain. In addition, PC-12 cells were cultured *in vitro* and combined with autophagy inhibitor 3-methyladenine (3-MA) to observe whether the effect of CB on A β_{25-35} -induced PC-12 cells is related to autophagy.

The results showed that CB could significantly improve the learning and memory ability of mice with A β_{25-35} -induced mice, brain injury and improve hippocampus injury and neuronal atrophy. In addition, it can also reduce the levels of A β 1-42/A β 1-40, p-Tau, and oxidative stress, and enhance the level of autophagy. *In vitro* results showed that CB could significantly improve the migration and proliferation ability of PC-12 cells. In summary, CB can alleviate AD model damage induced by A β_{25-35} by enhancing autophagy.

4.5. Other Activities

Zheng et al. [63] used guinea pigs to determine that the water decoction of L. pauciflorus had antitussive effect, could increase the secretion of the trachea of mice, and had an expectorant effect. It had a certain protective effect on the asthma-like features caused by histamine inhalation in guinea pigs. The animals were quieter and less active after the medication. The drug had a certain sedative effect on the central nervous system. Wang [31] used preliminary pharmacodynamic experiments to observe the effect of the methanol extract of C. longgangensis var. hongyao on the writhing response induced by acetic acid in mice. The experimental results show that the writhing times of mice using the methanol extract of C. longgangensis var. hongyao and the n-butanol part of the methanol extract of C. longgangensis var. hongyao were (3.4 ± 4.3) and (4.7 ± 9.8) , respectively, which were significantly different from the model group (17.2 ± 14.0) (P<0.05). Studies have shown that the methanol extract of C. longgangensis var. hongyao has a significant inhibitory effect on acetic acid-induced pain in mice.

Han et al. [64] found that the antihypertensive effect of lysionotin increased with the increase in plasma drug concentration during intravenous infusion, and decreased with the decrease in plasma drug concentration after entering the elimination phase. The maximum antihypertensive effect occurs 5–10 minutes after the maximum blood concentration is reached. Sun et al. [65] studied the effect of lysionotin (1) on the hemodynamics of anesthetized thoracotomy cats. Intravenous injection of lysionotin at a dose of 2.5 mg/kg did not result in significant changes in HR, dP/dtmax, t-dP/dtmax, and CO. When the dose was increased to 5 mg/kg, blood pressure and TPVR decreased further, while HR, dP/dtmax, t-dP/dtmax, and CO significantly decreased. The results show that the hypotensive effect of low-dose lysionotin is mainly caused by the relaxation of blood vessels, and the inhibitory effect of larger doses of lysionotin on the heart may also be involved in its antihypertensive effects.

Chen et al. [36] used the MTT method to assess the cytotoxic activity of the compounds obtained from the *C. eburnea* fraction. Compounds **55–59** had varying degrees of inhibitory effects on the human lung cancer SPC-A1 cells. Compounds **58** and **59** had weak cytotoxic effects on SPC-A1 cells.

The half inhibitory concentrations (IC₅₀) were 207.23 μ mol/L and 180.34 μ mol/L. Compounds **55–57** showed no cytotoxicity (IC₅₀> 300 μ mol/L). Compounds **55–59** had no cytotoxicity to liver cancer HepG2 cells, gastric cancer SGC-7901 cells and lung large cell carcinoma NCI-H460 cells, and its IC₅₀ was> 300 μ mol/L.

Cao et al. [66] took the senescence-accelerated mouse prone 8 (SAMP8) as the animal model, and gave the mice different doses of the extract of *C. flabellatus* (CF) via gavage for one month. The degree of renal senescence was observed by β -galactosidase staining, and the degree of renal fibrosis was evaluated by Masson staining and the expression levels of Col-I, α -SMA and FN. The protein expression levels of the NRF2 pathway and the WnT/ β -catenin/RAS pathway in renal tissues were detected. In addition, β -galactosidase (β -GAL)-induced NRK-52E cells were used as an *in vitro* model to screen the effective components. The separation of 3,4-dihydroxyphenyl ethanol (SDC-0-14, 16) and 3, 4-dihydroxyphenylethanol-8-O-(4-O-trans-caffeoyl- β -D-apiofuranosyl-(1 \rightarrow 3)- β -D-glucopyranosyl (1 \rightarrow 6)- β -D-pyran glycosidase (SDC-1-8) can delay the senescence of NRK52E cells. It has been shown that CF ethanol extract may reduce renal fibrosis in SAMP8 mice through the Wnt/ β -catenin/RAS pathway. Hence, SDC-0-14, SDC-0-16 and SDC-1-8 may be the material basis for their anti–renal senescence effects.

5. Conclusions

Gesneriaceae plant resources are abundant, widely distributed, and have broad applications and development potential. In recent years, researchers have extensively studied Gesneriaceae, yet not all pharmacological properties of this family have been investigated, including mechanisms of action and structure-activity relationships of its active components. New techniques for the isolation, purification, and structural identification of chemical components, pharmacological activities, and mechanisms of action of the compounds or/and extracts of the plants from Gesneriaceae family are thus necessary.

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Supporting Information

Supporting information accompanies this paper on $\underline{\text{http://www.acgpubs.org/journal/records-of-natural-products}}$

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