

Review

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Chemical constituents of plants from the genus *Neolitsea*

Abstract: The genus *Neolitsea* (Lauraceae) contains over 85 species distributed around the world. These plants have been found to be rich in sesquiterpenes, triterpenes, steroids, and alkaloids. This review summarizes the phytochemical progress and list of all the constituents isolated from the genus *Neolitsea* over the past few decades. Some biological activities of compounds isolated from this genus are also included.

Keywords: biological activity; chemical composition; *Neolitsea*; plant.

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Introduction

The genus *Neolitsea* (Lauraceae) comprises nearly 85 species that are distributed throughout tropical and subtropical Asia and America. In particular, there are 45 species widespread in South China, East China, and Southwest China. The plants of genus *Neolitsea* have been found to be rich in sesquiterpenes, triterpenes, alkaloids, and steroids [1, 2]. The occurrence of a small number of flavonoids, benzenoids, monoterpenes, and benzoquinone

has also been reported [3]. Constituents of the *Neolitsea* genus (Lauraceae) have been reported to possess diverse bioactivities, such as antioxidant, antibacterial, anti-inflammatory activities, and cytotoxicity [3].

This review summarizes the phytochemical progress involving all constituents isolated from the genus *Neolitsea* over the past few decades. Some biological activities of compounds isolated from this genus are also included.

Chemical constituents

The reported chemical constituents from this genus include sesquiterpenes, triterpenes, alkaloids, steroids, flavonoids, essential oils, and some other compounds. Their structures are shown in the following sections, and their names and the corresponding plant sources are collected in Tables 1–5.

Sesquiterpenes (Table 1 and Figure 1)

Sesquiterpenes are the characteristic constituents within the genus *Neolitsea*. From 1966 to 2013, 67 compounds have been isolated. The researched plants include *Neolitsea zeylanica*, *Neolitsea parvigemma*, *Neolitsea aciculata*, *Neolitsea acutotrineria*, *Neolitsea hiiranensis*, and *Neolitsea sericea*, among others. In 1966, six sesquiterpenes **1–6** were isolated from *N. zeylanica* [1]. In the course of further investigation on the chemical constituents of this plant, four novel sesquiterpenes of the furanogermacrane type **7–10** have been isolated from the stems of *N. parvigemma* [2]. In 2011, investigation of *N. hiiranensis* revealed seven new sesquiterpenoids **12–18** and 12 known sesquiterpenoids **19–30** from the leaves of this plant [3]. In 1983, Nozaki et al. isolated a new sesquiterpene dilactone **31**, named neoliacine, from the leaves of *N. aciculata*, and they further examined chemical components of the same plant and isolated the sesquiterpene acid **32** [14, 15]. Four known furanosesquiterpene

Table 1 Sesquiterpenes.

No.	Name	Source	Part	References
1	Linderalactone	<i>N. zeylanica</i> / <i>N. villosa</i>	Root	[1, 4]
		<i>N. parvigemma</i>	Stem/root	[2, 5–7]
		<i>N. dealbata</i>	Bark	[8]
		<i>N. aciculata</i>	Root/trunk	[9]
2	Linderane	<i>N. zeylanica</i>	Root	[1, 4]
		<i>N. villosa</i>	Stem	[5, 6]
		<i>N. parvigemma</i>	Root/trunk	[9]
		<i>N. aciculata</i>	Root	[10]
		<i>N. acutotrinervia</i>	Root	[11]
		<i>N. buisanensis</i>		
3	Neolinderane	<i>N. zeylanica</i>	Root	[1]
		<i>N. aciculata</i>	Root/trunk	[9]
4	Zeylanine	<i>N. zeylanica</i>	Root	[1]
		<i>N. aciculata</i>	Root/trunk	[9]
		<i>N. acutotrinervia</i>	Root	[10]
5	Zeylanicine	<i>N. zeylanica</i>	Root	[1]
		<i>N. parvigemma</i>	Stem/root	[2, 5, 6, 12]
6	Zeylanidine	<i>N. zeylanica</i>	Root	[1, 6]
		<i>N. parvigemma</i>	Stem/root	[2, 5, 7]
		<i>N. dealbata</i>	Bark	[8]
7	Deacetylzeylanine	<i>N. parvigemma</i>	Stem	[2, 7]
8	Parvigemonol	<i>N. parvigemma</i>	Stem	[2]
9	Parvigemon	<i>N. parvigemma</i>	Stem	[2, 6]
10	Neolitrane	<i>N. parvigemma</i>	Stem	[2, 6, 7]
11	Pseudoneolinderane	<i>N. parvigemma</i>	Stem	[2, 6, 7]
		<i>N. dealbata</i>	Bark	[8]
		<i>N. aciculata</i>	Root/trunk	[9]
		<i>N. villosa</i>	Root	[4]
12	Hiiranlactone A	<i>N. hiiranensis</i>	Leaf	[3]
13	Hiiranlactone B	<i>N. hiiranensis</i>	Leaf	[3]
14	Hiiranlactone C	<i>N. hiiranensis</i>	Leaf	[3]
15	Hiiranlactone D	<i>N. hiiranensis</i>	Leaf	[3]
16	(+)- <i>ent</i> -6 α -Methoxyeudesm-4(15)-en-1 β -ol	<i>N. hiiranensis</i>	Leaf	[3]
17	(+) -Villosine	<i>N. hiiranensis</i>	Leaf	[3]
		<i>N. villosa</i>	Root	[4]
18	Hiiranepoxide	<i>N. hiiranensis</i>	Leaf	[3]
19	(6 α ,7 α)-4 β -Hydroxy-10 α -methoxyaromadendrane	<i>N. hiiranensis</i>	Leaf	[3]
20	Spathulenol	<i>N. hiiranensis</i>	Leaf	[3]
21	(-)- <i>ent</i> -4 β -Hydroxy-10 α -methoxyaromadendrane	<i>N. hiiranensis</i>	Leaf	[3]
22	4 β ,10 α -Dihydroxyaromadendrane	<i>N. hiiranensis</i>	Leaf	[3]
23	Pipelol A	<i>N. hiiranensis</i>	Leaf	[3]
24	Deoxysericealactone	<i>N. hiiranensis</i>	Leaf	[3]
		<i>N. sericea</i>		[3]
25	Neoliacinolide A	<i>N. hiiranensis</i>	Leaf	[3]
		<i>N. aciculata</i>		[13]
26	Pseudoneoliacine	<i>N. hiiranensis</i>	Leaf	[3]
		<i>N. acutotrinervia</i>	Root	[10]
		<i>N. villosa</i>		[4]
27	β -Caryophyllene oxide	<i>N. hiiranensis</i>	Leaf	[3]
28	Kobusone	<i>N. hiiranensis</i>	Leaf	[3]
29	Caryolane-1,9-diol	<i>N. hiiranensis</i>	Leaf	[3]
30	<i>trans</i> -Phytol	<i>N. hiiranensis</i>	Leaf	[3]
31	Neoliacine	<i>N. acciculata</i>	Leaf	[14]
32	Neoliacinic acid	<i>N. acciculata</i>	Leaf	[15]
33	Deacetylzeylanidine	<i>N. parvigemma</i>	Leaf/stem	[5, 6]
34	Isolinderalactone	<i>N. aciculata</i>	Root/trunk	[9]
		<i>N. villosa</i>	Root	[4]

(Table 1 Continued)

No.	Name	Source	Part	References
35	Litsealactone	<i>N. aciculata</i>	Root/trunk	[9]
36	Litseaculane	<i>N. aciculata</i>	Root/trunk	[9]
37	Zeylanane	<i>N. aciculata</i>	Root/trunk	[9]
		<i>N. acutotrinervia</i>	Root	[10]
38	Linderadine	<i>N. aciculata</i>	Root/trunk	[9]
		<i>N. acutotrinervia</i>		[4, 10]
		<i>N. villosa</i>	Root	
39	Sericenine	<i>N. sericea</i>	Leaf	[16]
40	Sericeic acid	<i>N. sericea</i>	Leaf	[17]
41	Isosericenine	<i>N. sericea</i>	Leaf	[17]
42	Neosericenine	<i>N. sericea</i>	Leaf	[17]
43	Neolitacumone A	<i>N. acuminatissima</i>	Stem bark	[18]
44	Neolitacumone B	<i>N. acuminatissima</i>	Stem bark	[18]
45	Neolitacumone C	<i>N. acuminatissima</i>	Stem bark	[18]
46	1 β -Acetoxyeudesma-4(15),7(11),8-trien-8,12-olide	<i>N. acuminatissima</i>	Stem bark	[18]
47	Acutotrine	<i>N. acutotrinervia</i>	Root	[10]
48	Acutotrinone	<i>N. acutotrinervia</i>	Root	[10]
49	Zeylaninone	<i>N. acutotrinervia</i>	Root	[10]
50	Acutotrinol	<i>N. acutotrinervia</i>	Root	[10]
51	Linderanine A	<i>N. buisanensis</i>	Root	[11]
52	Linderanine C	<i>N. buisanensis</i>	Root	[11]
53	Linderanine B	<i>N. buisanensis</i>	Root	[11]
54	Linderanine D	<i>N. buisanensis</i>	Root	[11]
55	Daibulactone A	<i>N. daibuensis</i>	Root	[19]
56	Daibulactone B	<i>N. daibuensis</i>	Root	[19]
57	Daibuoxide	<i>N. daibuensis</i>	Root	[19]
58	Sericealactone	<i>N. sericea</i>	Leaf	[8]
59	Neoliacinolide B	<i>N. aciculata</i>	Leaf	[13]
60	Neoliacinolide C	<i>N. aciculata</i>	Leaf	[13]
61	Sericealactonecarboxylic acid	<i>N. aciculata</i>	Leaf	[13]
62	Aciculatalactone	<i>N. aciculata</i>	Leaf	[13]
63	Furanogermenone	<i>N. pallens</i>	Leaf/bark	[20]
64	Germacrene D	<i>N. pallens</i>	Leaf	[20]
65	β -Caryophyllene	<i>N. pallens</i>	Leaf	[20]
66	10-epi- γ -Eudesmol	<i>N. pallens</i>	Bark	[20]
67	Curcumenol	<i>N. pallens</i>	Bark	[20]

lactones **1**, **2**, **5**, **6**, along with a new derivative, deacetylzeylanidine **33**, were isolated from *N. parvigemma* [5]. From *N. sericea*, three new elemene-type sesquiterpenoids **24**, **41**, **58** and two new germacrene-type sesquiterpenoids **39**, **40** were isolated by column chromatography and thin layer chromatography [8]. In 1970, components of *N. aciculata* were investigated, and ten furan sesquiterpenes **1–4**, **11**, **34–38** were isolated from the root and trunk [9]. At the same time, neosericenine **42**, an isomer of sericenine **39**, along with compounds **40** and **41** were isolated from the leaf of *N. sericea* [16, 17]. Phytochemical investigation of *Neolitsea acuminatissima* resulted in the isolation of three new eudesmanolide sesquiterpenes **43–45** and a known eudesmanolide sesquiterpene **41** [18]. Investigation of *N. acutotrinervia* revealed numerous sesquiterpene lactones, including four known furanogermacranolides **2**,

4, **37**, **38**, one known germacranediolide **35**, and four new germacranediolides **47–50** [10]. Chen et al. have isolated two novel sesquiterpenes of the furanogermacrene type, namely parvigemone **9** and neolitrane **10**, along with six known compounds **1–2**, **5–6**, **11**, **33** from the stems of *N. parvigemma* [6]. Compounds **51–54** are not produced naturally in plant, but formed by oxidation of **2** [11]. Seven sesquiterpene lactones **1**, **2**, **11**, **17**, **26**, **34**, **38** were isolated from the roots of *Neolitsea villosa*, in which three compounds **17**, **26**, **38** are new [4]. Three new compounds **55–57** were isolated from the roots of *Neolitsea daibuensis* [19]. In the continuing studies on Lauraceae plants, which are widely distributed in Japan, three germacranes **25**, **59**, **60** and two elemenes **61**, **62** have been isolated from the fresh leaves of *N. aciculata* Koidz [13]. The major constituents of the leaf and bark oil of *Neolitsea pallens* are compounds **63–67** [20].

Table 2 Triterpenes.

No.	Name	Source	Part	References
68	Taraxerone	<i>N. dealbata</i>	Bark	[8]
69	Taraxerol	<i>N. dealbata</i>	Bark	[8]
70	Hiiranterpenone	<i>N. hiiranensis</i>	Leaf	[3]
71	3 β -Methoxy-24,24-dimethyllanosta-9(11),25-diene	<i>N. pulchella</i>	Stem	[13, 20]
72	24,24-Dimethyllanosta-9(11),25-dien-3-one	<i>N. pulchella</i>	Stem	[13, 20]
73	24,24-Dimethyllanosta-9(11),25-dien-3 β -ol	<i>N. pulchella</i>	Stem	[20]
74	24 ξ -Hydroxy-3 β -methoxy-24,25-dimethyl-lanost-9(11)-ene	<i>N. pulchella</i>	Stem	[13, 20]
75	24 ξ -Methoxy-24,25-dirnethyllanost-9(11)-en-3-one	<i>N. pulchella</i>	Stem	[20]
76	3 β ,24 ξ -Dimethoxy-24,25-dimethyllanost-9(11)-ene	<i>N. pulchella</i>	Stem	[20]
77	Sericeol	<i>N. sericea</i>	Heartwood	[21]
78	24Z-Ethylidenelanost-8-en-3-one	<i>N. sericea</i>	Bark	[22]
79	24-Methylenelanost-8-en-3-one	<i>N. sericea</i>	Bark	[22]
80	24Z-Ethylidenelanost-8-en-3 β -ol	<i>N. sericea</i>	Bark	[22]
81	24-Methylenelanost-8-en-3 β -ol	<i>N. sericea</i>	Bark/stem	[22, 23]
82	Cycloartenol	<i>N. sericea</i>	Stem	[23]
83	24-Methylenecycloartanol	<i>N. sericea</i>	Stem	[23, 24]
		<i>N. aciculata</i>		
84	24E-Ethylidenecycloartanol	<i>N. sericea</i>	Stem	[23]
85	24Z-Ethylidenecycloartanol	<i>N. sericea</i>	Stem	[23]
86	24-Methylene-25-methylcycloartanol	<i>N. sericea</i>	Stem	[23, 24]
		<i>N. aciculata</i>		
87	24 β -Ethyl-25-dehydrocycloartanol	<i>N. aciculata</i>	Stem	[24]
88	24,24-Dimethyl-25-dehydrocycloartanol	<i>N. aciculata</i>	Stem	[24]
89	24E-Ethylidenelanost-8-enol	<i>N. sericea</i>	Stem	[23]
90	24Z-Ethylidenelanost-8-enol	<i>N. sericea</i>	Stem	[23]
91	24-Methylene24(25)-dihydroparkeol (IXe)	<i>N. sericea</i>	Stem	[23, 24]
		<i>N. aciculata</i>		
92	Parkeol	<i>N. aciculata</i>	Stem	[24]
93	24 β -Methyllanosta-9(11),25-dien-3-ol	<i>N. aciculata</i>	Stem	[24]
94	24 β -Ethyllanosta-9(11),25-dien-3-ol	<i>N. aciculata</i>	Stem	[24]
95	24,24-Dimethyllanosta-9(11),25-dien-3-ol	<i>N. aciculata</i>	Stem	[24]
96	24-Methylenelanosta-7,9(11)-dienol (Xe)	<i>N. sericea</i>	Stem	[23]
97	24-Methylenedammarenol	<i>N. sericea</i>	Stem	[23]
98	Lupeol	<i>N. sericea</i>	Stem	[23, 24]
		<i>N. aciculata</i>		
99	Lupenone	<i>N. fuscata</i>	Bark	[25]
100	β -Amyrin	<i>N. sericea</i>	Stem	[23]

Triterpenes (Table 2 and Figure 2)

Most of the triterpenes reported in the genus *Neolitsea* are tetracyclic, and a few of them are pentacyclic. These triterpenes are dammaranes, lanostanes, cycloartanes, oleananes, and lupanes. A phytochemical investigation of the crude chloroform extract of the *Neolitsea dealbata* bark revealed two common triterpenes **68**, **69**, which were reported for the first time from this plant [21]. Investigation of the ethyl acetate-soluble extract of the leaves of *N. hiiranensis* led to the isolation of hiiranterpenone **70** [3]. Chan and Hui isolated three C₃₂ triterpenes **71–73** by column chromatography of the light petroleum extract [23]. In addition, analysis of a larger quantity of a similar extract led to the discovery

of three related minor triterpenes **74–76** [22, 23]. Compound **77**, a new cycloartane, was reported from *N. sericea* in 1993, and further investigation of this plant revealed three new lanostanes **78–80**, along with a known compound **81** [24, 43]. In 1992, several triterpenes **81–99** were isolated from the alcohol extract of *N. sericea*, among which **86**, **93**, and **94** are new compounds [39, 40]. Lupenone **100** was isolated from the stem bark of *Neolitsea fuscata* [25].

Alkaloids (Table 3 and Figure 3)

In 2001, 15 alkaloids **101–103**, **106**, **107**, **124–129**, **133–135**, **137** were isolated from the stem bark of *N. acuminatissima*.

Table 3 Alkaloids.

No.	Name	Source	Part	References
101	Lauroitsine/(+)-Norboldine	<i>N. villosa</i> / <i>N. sericea</i>	Stem/leaf	[12, 26]
		<i>N. acuminatissima</i>	Stem bark	[18, 27]
		<i>N. konishii</i> / <i>N. aurata</i>	Bark	[28, 29]
		<i>N. paraciculata</i>		[30]
		<i>N. buisanensis</i>		
102	Boldine	<i>N. acuminatissima</i>	Stem/leaf	[18, 31]
		<i>N. villosa</i> / <i>N. parvigemma</i>		[26, 27]
		<i>N. konishii</i> / <i>N. sericea</i>		[12, 29]
103	Isoboldine	<i>N. acuminatissima</i>	Stem/leaf	[18, 29]
		<i>N. konishii</i> / <i>N. fuscata</i>		[12, 25]
104	Isocorydine	<i>N. sericea</i> / <i>N. aurata</i>	Stem/leaf	[12]
105	Laurotetanine	<i>N. aciculata</i> / <i>N. villosa</i>	Stem/leaf	[26, 32]
		<i>N. konishii</i> / <i>N. sericea</i>		[29, 30]
				[12]
106	<i>N</i> -Methylaurotetanine	<i>N. acuminatissima</i>	Stem/leaf	[18, 26]
		<i>N. villosa</i> / <i>N. konishii</i>		[12, 29]
107	(-)-Thalicsimidine	<i>N. acuminatissima</i>	Stem bark	[18]
108	(+)-11-Methoxynorboldine	<i>N. aurata paraciculata</i>	Bark	[28]
109	Hernovine	<i>N. aurata paraciculata</i>	Bark	[28, 33]
		<i>N. variabilima.</i>		
110	10- <i>O</i> -Methylhernovine	<i>N. aurata paraciculata</i>	Bark	[28]
111	Lindcarpine	<i>N. aurata paraciculata</i>	Bark	[28]
112	<i>N,O</i> -Dimethylhernovine	<i>N. aurata paraciculata</i>	Bark	[28]
113	Glaucine	<i>N. parvigemma</i>	–	[31]
		<i>N. konishii</i>		
114	Corydine	<i>N. parvigemma</i>	–	[31]
		<i>N. konishii</i>		
115	Neolitsinine	<i>N. pulchella</i>	Leaf	[34]
116	Isomeric pulchelline	<i>N. pulchella</i>	Leaf	[34]
117	Corytuberine	<i>N. konishii</i>	–	[29]
118	Nnornuciferine	<i>N. konishii</i>	–	[29]
119	<i>N</i> -Methylhernovine	<i>N. variabilima</i>	Bark	[33]
120	Nuciferine	<i>N. sericea</i>	Bark	[30]
121	Glaziovine	<i>N. konishii</i>	Stem/leaf	[29]
		<i>N. sericea</i> / <i>N. aurata</i>	Stem	[12]
122	Stepharine	<i>N. konishii</i>	–	[29]
123	Isodomesticine	<i>N. villosa</i>	Stem/leaf	[12, 26]
124	Neolitacumonine	<i>N. acuminatissima</i>	Stem bark	[18]
125	Liriodenine	<i>N. acuminatissima</i>	Stem bark	[18]
126	(-)-Norushisunine	<i>N. acuminatissima</i>	Stem bark	[18]
127	(+)-Cassythine	<i>N. acuminatissima</i>	Stem bark	[18]
128	(-)-Anonaine	<i>N. acuminatissima</i>	Stem bark	[18, 35]
		<i>N. aurata</i> / <i>N. sericea</i>		[30]
129	Actinodaphnine	<i>N. acuminatissima</i>	Stem bark	[18, 31]
		<i>N. konishii</i> / <i>N. sericea</i> / <i>N. parvigemma</i> / <i>N. villosa</i>	Stem	[26, 29]
			wood	[30]
130	(+)-11-Methoxynorcassythine	<i>N. aurata paraciculata</i>	Bark	[28]
131	Nandigerine	<i>N. aurata paraciculat</i>	Bark	[28, 33]
		<i>N. variabilima.</i>		
132	Roemerine	<i>N. parvigemma</i>	Leaf	[18, 31]
		<i>N. konishii</i> / <i>N. sericea</i>		[35]
		<i>N. aurata</i>		[30]
133	<i>N</i> -Methylactinodaphnine	<i>N. parvigemma</i>	Stem bark	[18, 31]
		<i>N. konishii</i>		
		<i>N. acuminatissima</i>		
134	(+)- <i>O</i> -Methylflavinantine	<i>N. acuminatissima</i>	Stem bark	[18]
135	(+)-Reticuline	<i>N. acuminatissima</i>	Stem bark	[18, 32]

(Table 3 Continued)

No.	Name	Source	Part	References
		<i>N. aciculata/N. villosa</i>		[29]
136	(+)-Norjuziphine	<i>N. villosa</i>	Stem	[26]
137	Oxoglaucine	<i>N. acuminatissima</i>	Stem bark	[18, 31]
		<i>N. parvigemma/N. konishii</i>		
138	(+)-11-Methoxynorneolitsine	<i>N. aurata paraciculata</i>	Bark	[28]
139	Neolitsine	<i>N. pulchella</i>	Leaf	[34]
140	Ovigerine	<i>N. aurata paraciculata</i>	Bark	[28]
141	<i>N</i> -Methylovigerine	<i>N. aurata paraciculata</i>	Bark	[28]
142	Methoxyannomontine	<i>N. parvigemma</i>	–	[31]
		<i>N. konishii</i>		
143	(+)-Cocclaurine	<i>N. villosa</i>	Stem	[26]
144	(+)-Juziphine	<i>N. villosa</i>	Stem	[26]
145	Pallidine	<i>N. villosa/N. konishii</i>	Stem	[26, 29]
146	Litsericine	<i>N. sericea/N. aurata</i>	Leaf	[27, 35]
		<i>N. buisanensis</i>		[30]
147	<i>N</i> -Methylitsericine	<i>N. aurata</i>	–	[35]
148	Daibucarboline A	<i>N. daibuensis</i>	Root	[19]
149	Daibucarboline C	<i>N. daibuensis</i>	Root	[19]
150	Daibucarboline B	<i>N. daibuensis</i>	Root	[19]
151	(6a <i>R</i>)-Normecambroline	<i>N. dealbata</i>	Bark	[36]

Table 4 Steroids.

No.	Name	Source	Part	References
152	24 α -Ethylcholestan-3 α -ol	<i>N. sericea</i>	Stem	[23]
153	24 α -Ethylcholest-4-en-3-one	<i>N. sericea</i>	Stem	[23]
154	24 α -Ethylcholesta-4,22-dien-3-one	<i>N. sericea</i>	Stem	[23]
155	β -Sitosterol	<i>N. hiiranensis</i>	Leaf	[3]
		<i>N. parvigemma</i>	Root	[4, 5, 11]
		<i>N. buisanensis</i>	Stem bark	[18]
		<i>N. villosa</i>	Wood	[37]
		<i>N. acuminatissima</i>		
156	Stigmasterol	<i>N. sericea</i>	Stem bark	[18]
		<i>N. acuminatissima</i>	Wood	[37]
157	β -Sitosteryl-D-glucoside	<i>N. acuminatissima</i>	Stem bark	[18]
158	Stigmasteryl- β -D-glucoside	<i>N. acuminatissima</i>	Stem bark	[18]
159	Campesterol	<i>N. sericea</i>	Wood	[37]
160	14 α ,24 α -Dimethyl-5 α -cholest-9(11)-en-3 α -ol	<i>N. aciculata</i>	Stem	[38]
161	14 α ,24 β -Dimethyl-5 α -cholest-9(11)-en-3 α -ol	<i>N. aciculata</i>	Stem	[38]
162	14 α -Methyl-24 α -ethyl-5 α -cholest-9(11)-en-3 α -ol	<i>N. aciculata</i>	Stem	[38]
163	24-Methylcholesterol	<i>N. sericea</i>	Stem	[39]
164	24 β -Methyl-22-dehydrolathosterol	<i>N. sericea</i>	Stem	[39]
165	24 α -Ethylcholestan-3 β -ol	<i>N. sericea</i>	Stem	[39]
166	Citrostadienol	<i>N. aciculata</i>	Stem and branch	[40]
167	24-Methylene-31-norlanost-9(11)-enol	<i>N. aciculata</i>	Stem and branch	[40]
168	24 α -Ethyl-31-norlanost-9(11)-enol	<i>N. sericea</i>	Stem and branch	[40]
169	24 β -Ethyl-31-norlanosta-9(11)-25-dienol	<i>N. sericea</i>	Stem and branch	[40]
170	(24 <i>S</i>)-24-Ethylcholest-4-ene-1-ol-3-one	<i>N. sericea</i>	Heartwood	[41]
171	(24 <i>S</i>)-24-Ethylcholest-4-ene-6-ol-3-one	<i>N. sericea</i>	Heartwood	[41]

Table 5 Other compounds.

No.	Name	Source	Part	References
172	13 ² -Hydroxy-(13 ² S)-pheophytin	<i>N. hiiranensis</i>	Leaf	[3]
173	α -Tocopheryl quinine	<i>N. hiiranensis</i>	Leaf	[3]
174	α -Tocopherol	<i>N. hiiranensis</i>	Leaf	[3]
175	Ficaprenol-11	<i>N. hiiranensis</i>	Leaf	[3]
176	Linolenic acid	<i>N. hiiranensis</i>	Leaf	[3]
177	Syringaldehyde	<i>N. hiiranensis</i>	Leaf	[3]
178	Syringic acid	<i>N. hiiranensis</i>	Leaf	[3]
179	(+)-Lyoniresinol	<i>N. acuminatissima</i>	Stem bark	[18]
180	(+)-Syringaresinol	<i>N. acuminatissima</i>	Stem bark	[18]
181	($\pm$)-Glaberide I	<i>N. acuminatissima</i>	Stem bark	[18]
182	Vanillin	<i>N. hiiranensis</i>	Leaf	[3]
		<i>N. acuminatissima</i>	Stem bark	[18]
183	Isovanillin	<i>N. acuminatissima</i>	Stem bark	[18]
184	<i>p</i> -Methoxybenzoic acid	<i>N. acuminatissima</i>	Stem bark	[18]
		<i>N. hiiranensis</i>	Leaf	[3]
185	Methylparaben	<i>N. acuminatissima</i>	Stem bark	[18]
186	2,6-Dimethoxy- <i>p</i> -benzoquinone	<i>N. acuminatissima</i>	Stem bark	[18]
187	Kaempferol 3- <i>O</i> -rhamnoside	<i>N. pavigemma</i>	–	[31]
		<i>N. konishii</i>		
188	Quercetin 3- <i>O</i> -rhamnoside	<i>N. pavigemma</i>	–	[31]
		<i>N. konishii</i>	Leaf	[42]
		<i>N. sericea</i>		
189	Taxifolin 3- <i>O</i> -rhamnoside	<i>N. pavigemma</i>	–	[31]
		<i>N. konishii</i>		
190	Quercetin 3- <i>O</i> - β -D-glucoside	<i>N. sericea</i>	Leaf	[42]
191	Neoastilbin	<i>N. sericea</i>	Leaf	[42]
192	Isoastilbin	<i>N. sericea</i>	Leaf	[42]
193	Neoisostilbin	<i>N. sericea</i>	Leaf	[42]
194	Docosanyl ferulate	<i>N. pavigemma</i>	–	[31]
		<i>N. konishii</i>		
195	Tetracosanyl ferulate	<i>N. pavigemma</i>	–	[31]
		<i>N. konishii</i>		
196	Hexacosanyl ferulate	<i>N. pavigemma</i>	–	[31]
		<i>N. konishii</i>		
197	Blumenol A	<i>N. pavigemma</i>	–	[31]
		<i>N. konishii</i>		
198	Roseoside	<i>N. pavigemma</i>	–	[31]
		<i>N. konishii</i>		
199	<i>N</i> -trans-Feruloylmethoxytyramine	<i>N. pavigemma</i>	–	[31]
		<i>N. konishii</i>		
200	<i>trans</i> - β -Ocimene	<i>N. pallens</i>	Fruit	[20]
201	Sabinene	<i>N. pallens</i>	Fruit	[20]

Among them, compound **124** was a new benzyloisoquinoline alkaloid. Their structures were established on the basis of analysis of NMR and mass spectral data [18]. The first chemical investigation of *N. villosa* (Bl.) Merr. led to the isolation of ten known isoquinoline alkaloids **101**, **104–106**, **121**, **128**, **133**, **136**, **143**, **144** from the stem of this plant [26]. In 1965, three new alkaloids **115**, **139**, **145** were found in the ethanolic extract of the dried leaves of *Neolitsea pulchella* [34]. Kozuka et al. reported the isolation and identification of two alkaloids **104**, **134** from

Neolitsea ariculata in 1984 [32]. Three new oxygenated noraporphine alkaloids **130**, **137**, **138** along with eight known aporphine alkaloids **121**, **108–112**, **140**, **141** were isolated from the bark of the Chinese tree, *Neolitsea aurata* var. *paraciculata*, which was the first report of chemical constituents of this plant [28]. In 1998, Chen et al. reported eight alkaloids **101**, **113**, **114**, **128**, **129**, **131**, **132**, **142** from *N. parvigemma* and *Neolitsea konishii*, and compounds **129**, **113**, **114**, **131**, **132** were isolated for the first time from this genus [31]. In 2001, 15 alkaloids were isolated from the

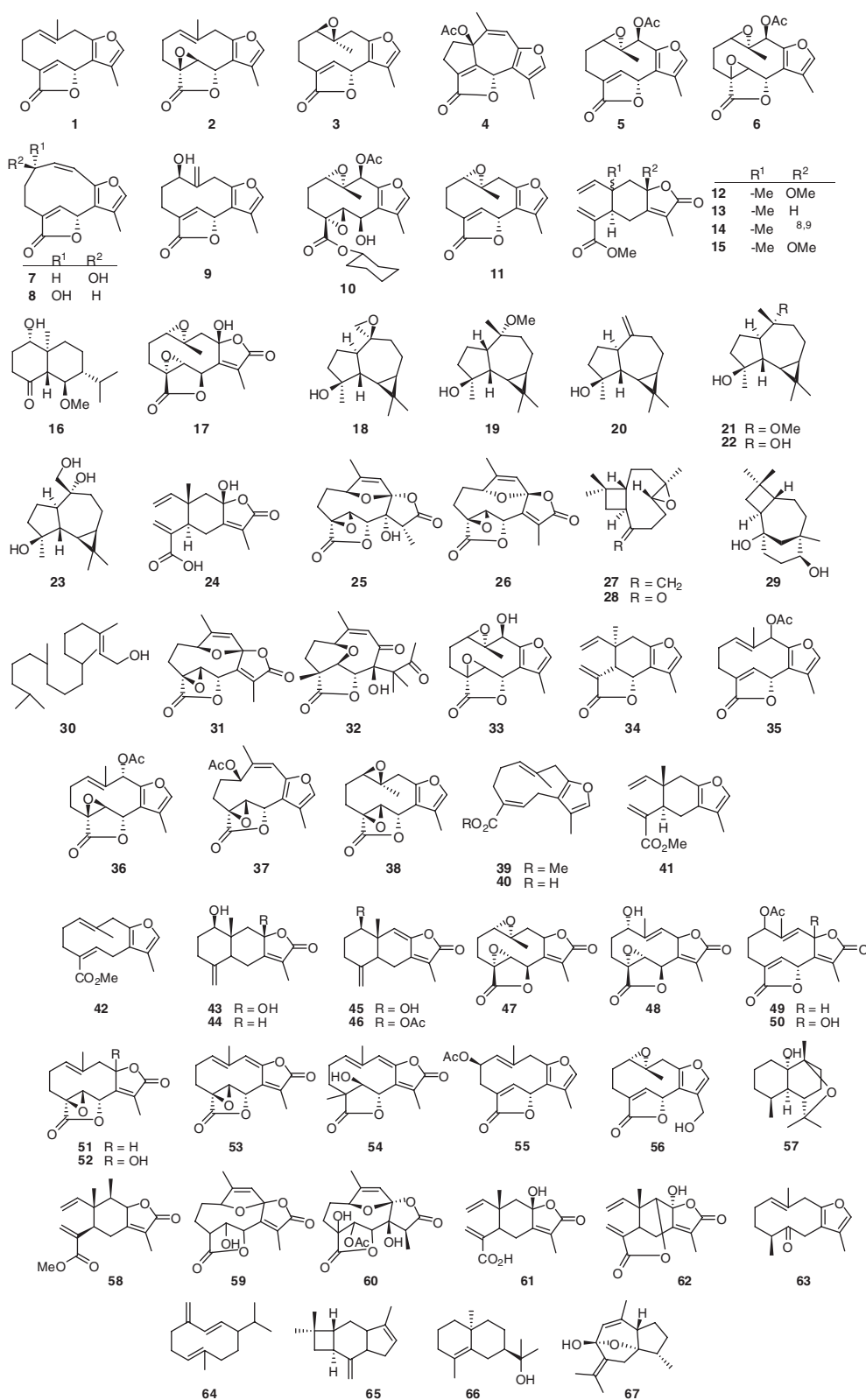


Figure 1 Sesquiterpenoid structures.

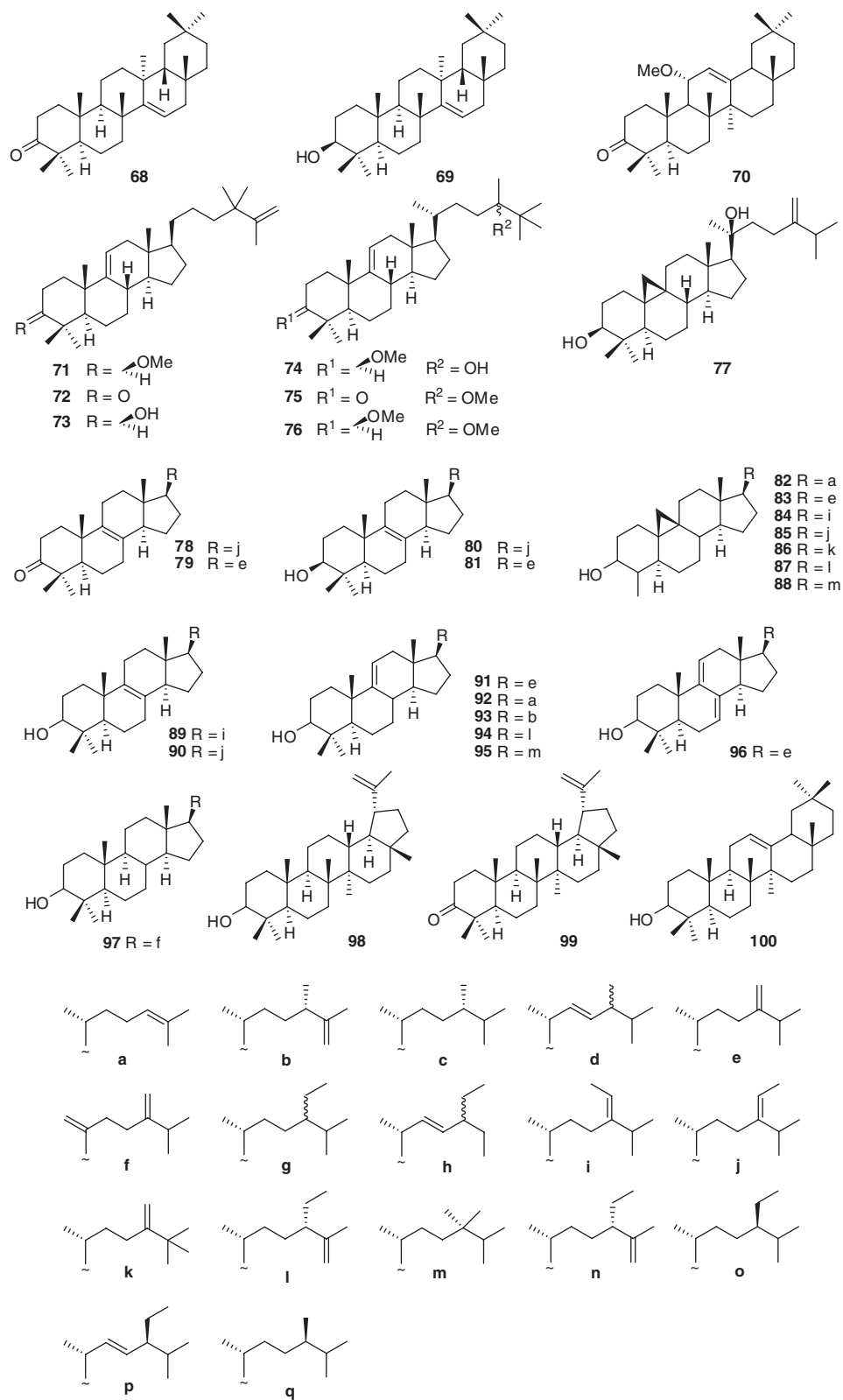


Figure 2 Triterpenoid structures.

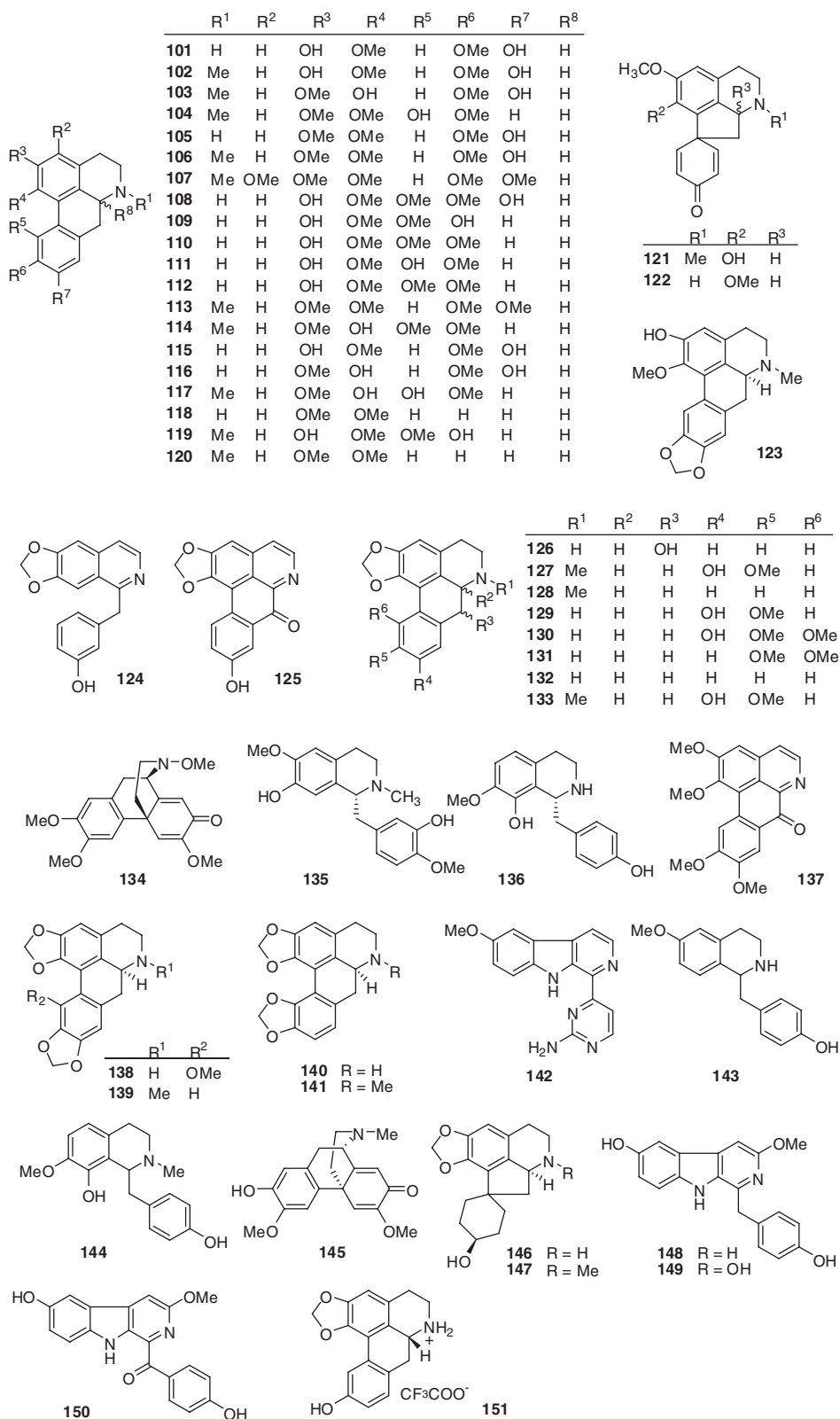


Figure 3 Alkaloid structures.

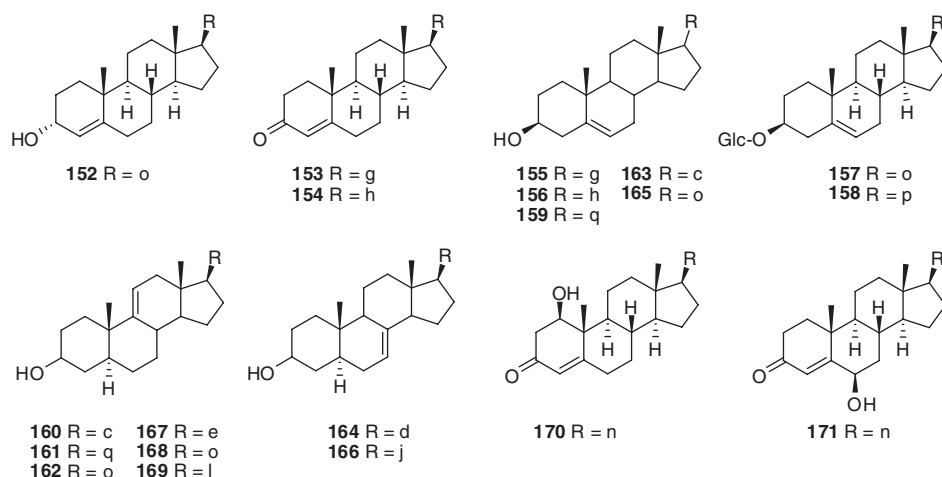


Figure 4 Steroids (see Figure 2 for definition of the R groups).

stem bark of *N. acuminatissima*. Among them, compound **123** is a new benzyloisoquinoline alkaloid, whose structure was established on the basis of analysis of NMR and mass spectral data [18]. By combination of centrifugal partition chromatography and common separation methods, 12 known alkaloids were isolated from *N. konishii* and characterized [29]. Compounds **121** and **117** were isolated from *Neolitsea buisanensis*, *N. sericea*, and *N. aurata* [27, 30]. In addition, compounds **118**, **131**, **135** were isolated from *N. aurata* [35]. Lu and Su isolated three alkaloids **108**, **112**, **147** from *Neolitsea variabilissima* [33]. In 2010, a new aporphine alkaloid **149** was reported from the bark of *N. dealbata* [36]. In 2011, Wong et al. reported three new β -carboline alkaloids **120**, **148**, **150** from the root of *N. dai-buensis* [19]. A total 14 new alkaloids and 37 known alkaloids were reported from this genus.

Steroids (Table 4 and Figure 4)

Four steroids, a mixture of **155** and **156**, and a mixture of **157** and **158**, were isolated from *N. acuminatissima* [18]. Komae and Hayashi detected phytosterols (**155**, **156**, **159**) in the wood of *N. sericea* by using gas chromatography [37]. *Neolitsea sericea* and *Daemia extensa* (Asclepiadaceae) seem to be the only plants containing 3α -hydroxy sterols in a higher plant. Yano et al. investigated the constituents of the stem of this plant and isolated two new 4α -methylsterols and three new 3α -hydroxy- 14α -methyl- $\Delta^{9(11)}$ sterols; they are compounds **168** and **169**, 24α - and 24β -epimers of 14α , 24 -dimethyl- 5α -cholest-9(11)-en- 3α -ol, compounds **160** and **161**, and 14α -methyl- 24α -ethyl- 5α -cholest-9(11)-en- 3α -ol

162 [38, 40]. The ethyl acetate extract from the wood of *N. sericea* contained two new steroidal compounds **170** and **171** [41]. Further study on the sterols from *N. sericea* extract led to the isolation of compounds **163**–**167** [39, 40].

Others (Table 5 and Figure 5)

From the fruit oil of *N. pallens*, Padalia et al. isolated *trans*- β -ocimene **200** and sabinene **201** [20]. Investigation of *N. sericea* var. *aurata* revealed occurrence of six flavone rhamnosides **187**–**193** [42]. In 1998, three flavonoids, kaempferol-3-*O*-rhamnoside **187**, quercetin-3-*O*-rhamnoside **188**, and taxifolin-3-*O*-rhamnoside **189**, three ferulates, docosanyl ferulate **194**, tetracosanyl ferulate **195**, and hexacosanyl ferulate **196**, two cyclohex-2-en-1-ones, blumenol A **197**, and roseoside **198**, and one amide, *N-trans*-feruloylmethoxytyramine **199** were isolated from *Neolitsea pavigemma* and *N. konishii* [31]. From the leaves of *Neolitsea cassia*, de Silva et al. isolated a water-soluble arabinoxylan [44]. Chang et al. isolated three lignans, (+)-lyoniresinol **179**, (+)-syringaresinol **180**, and ($\pm$)-glaberide I **181**, four benzenoids, vanillin **182**, isovanillin **183**, *p*-methoxybenzoic acid **184**, and methylparaben **185**, together with one paraquinone, 2,6-dimethoxy-*p*-benzoquinone (**186**), from the stem bark of *N. acuminatissima* [18]. The following compounds were also isolated from the leaves of *N. hiiranensis*: 13^2 -hydroxy-(13^2S)-pheophytin (**172**), α -tocopheryl quinone (**173**), α -tocopherol (**174**), ficaprenol-11 (**175**), linolenic acid (**176**), syringaldehyde (**177**), syringic acid (**178**), vanillin (**182**) and *p*-anisic acid (**184**) [3].

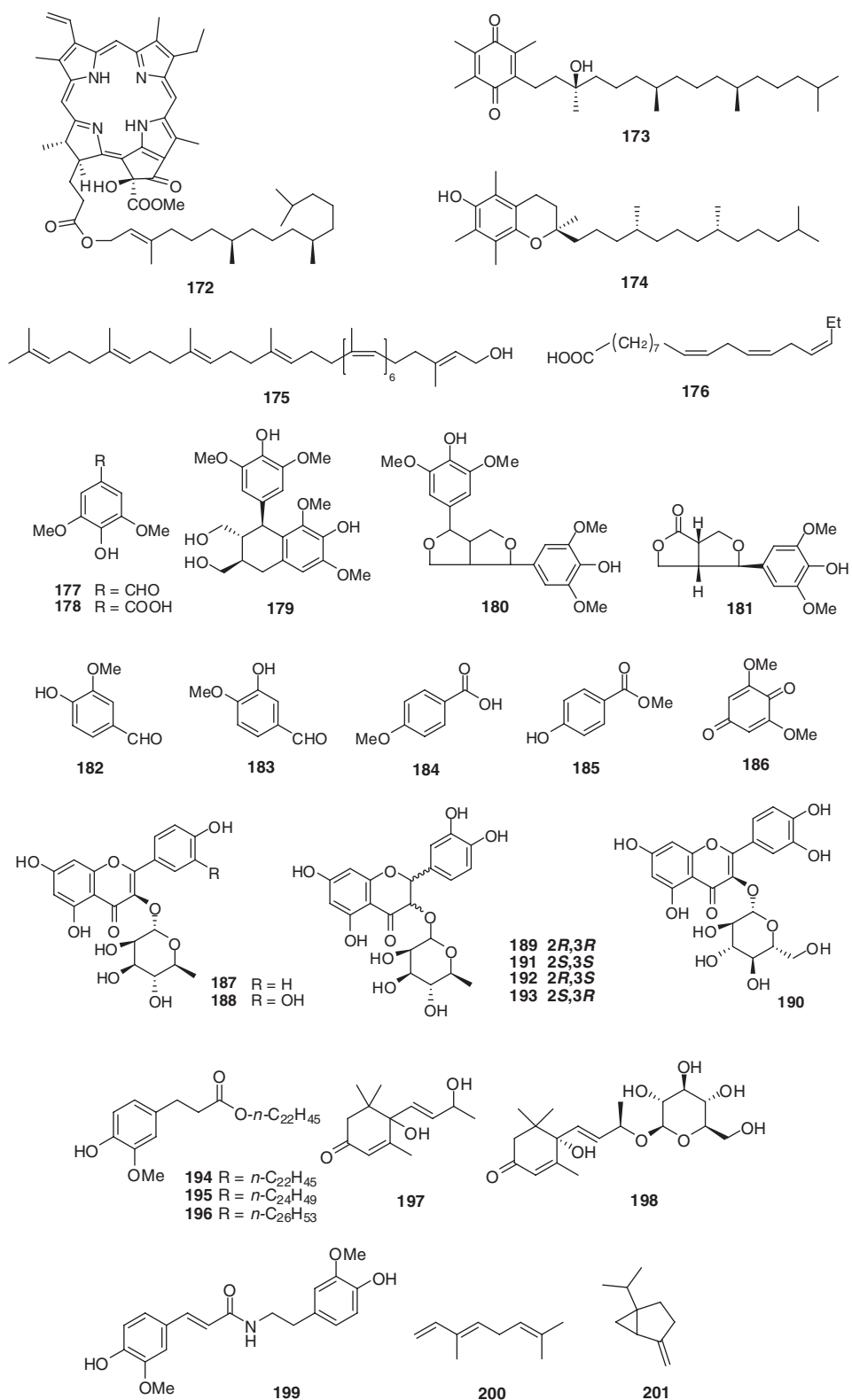


Figure 5 Structures of other compounds.

Biological activities

Anti-inflammatory activity

The anti-inflammatory effects of compounds **13** and **15** were evaluated by their suppression of the N-formyl-methionyl-leucyl-phenylalanine (fMLP)-induced generation of the superoxide anion, an inflammatory mediator produced by neutrophils. And the inhibitory activity against fMLP-induced superoxide production with IC_{50} values of 21.86 ± 3.97 and 25.78 ± 4.77 μ M, respectively [3]. Six furanogermacranes **1**, **5–7**, **10**, **11** were tested for anti-inflammatory activities. Among them, compounds **1** and **11** show significant inhibitory effects on superoxide anion generation by human neutrophils in response to fMLP/CB: the IC_{50} of compounds **1** and **11** were found to be 3.21 and 8.48 mg/mL, respectively [7]. Compounds **34** and **163**, 7-O-methylnaringenin and prunetin, which were isolated from *N. dai-buensis*, exhibit moderate inducible nitric oxide synthase inhibitory activity, with IC_{50} values of 18.41, 0.30, 19.55, and 10.50 μ M, respectively [19]. The essential oil of *N. aciculata* exhibit moderate to strong antibacterial activity against drug-susceptible and -resistant *Propionibacterium acnes* and *Staphylococcus epidermidis*, which are known as acne-causing bacteria. In addition, the essential oil reduces the *P. acnes*-induced secretion of tumor necrosis factor- α (TNF- α) and interleukin-8 (IL-8) in THP-1 cells, highlighting its anti-inflammatory effects [45].

Antitumor activity

Neoliacine **31**, a sesquiterpene lactone isolated from the leaves of *N. aciculata*, exhibits moderate cytotoxicity in HeLa cell culture *in vitro* [14]. Compounds **44**, **45**, and **184** selectively inhibit Hep 2,2,15 cells with IC_{50} values in the range of 0.24–0.04 μ g/mL. 2,6-Dimethoxy-*p*-benzoquinone is marginally cytotoxic to Hep G2 cells [18]. A known elemene-type sesquiterpene, isolinderalactone **34**, shows promising antitumor activity *in vitro* against all tumor cells tested: KB (ED_{50} =2.990 ppm), P-388 (0.816 ppm), A-549 (1.420 ppm), and HI-29 (1.528 ppm) [4]. Recently, Su et al. reported the chemical components and *in vitro* anticancer activities of the essential oil isolated from the leaf of *N. variabilissima*. The anticancer activities of oil were evaluated and the results showed that the oil exhibits cytotoxic activity against human oral, liver, lung, colon, melanoma, and leukemic cancer cells [46]. The presence of β -caryophyllene, τ -cadinol, and α -cadinol significantly contributes to the anticancer activity of *N. variabilissima* leaf

oil [46]. Compound **164** selectively inhibits the growth of cervical cancer cells (HeLa) with an IC_{50} of 4.0 μ M [40].

Vasoconstricting activity

Thaliporphine, isolated from *N. konishii*, has been found to possess vasoconstricting action and selectively inhibits expression of inducible, but not constitutive, nitric oxide synthase [29].

Antifungal and antibacterial activities

The hydro-distilled leaf essential oil of *N. parvigemma* exhibits antifungal activity against seven fungi, including *Aspergillus clavatus*, *Aspergillus niger*, *Chaetomium globosum*, *Cladosporium cladosporioides*, *Myrothecium verrucaria*, *Penicillium citrinum*, and *Trichoderma viride*. Besides, the oil also possesses anti-wood-decay activity induced by fungi *Trametes versicolor*, *Phaneochaete chrysosporium*, *Phaeolus schweintzii*, and *Lenzites sulphureu* [47]. The essential oil isolated from *N. aciculata* and *N. sericea* possesses antimicrobial activities [45, 48].

Others

The bark and leaves of *N. cassia* can be used for the treatment of fractures [44]. Several antiplatelet aggregation sesquiterpenes and alkaloids were also isolated from *N. konishii*, *N. villosa*, *N. parvigemma*, *N. variabilissima*, and *N. aurata* and characterized [2]. Aporphine alkaloids, commonly present in this genus, have been shown to possess various pharmacological activities, such as choleric and smooth muscle relaxing properties for boldine and hypotensive and hyperlipidemia-reducing properties in tested animals for dicentrine [12].

Conclusions

The genus *Neolitsea* includes 85 species, and some of them have been used as traditional herbal medicines. The chemical investigation of the *Neolitsea* genus has revealed that this genus contains numerous and complicated constituents, and many components with significant bioactivities have been isolated. This review reveals that only a few species have been investigated, with many species receiving little or no attention. Further phytochemical and biological studies should be carried out on these plants.

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