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Triterpenoids and Pharmacological Activities from *Kadsura* (Schisandraceae) were gathered from 1987 to 2022

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Abstract: The genus *Kadsura* is a commonly used herb in Chinese folklore, with sedative, hypnotic and beneficial effects, mainly for the treatment of rheumatoid arthritis, insomnia and other conditions. Modern pharmacological studies have shown that triterpenoids are one of the main components to possess these medicinal effects. In addition, triterpenoids in genus *Kadsura* also exhibited anti-tumor, cholesterol synthesis inhibition, anti-HIV, antioxidant and hepatoprotective activities. At present, there are few literatures reported on the triterpenoids in this genus. Therefore, the purpose of this paper is to review the triterpenoids in the genus *Kadsura* and their pharmacological activities, introduce the research progress on their germplasm resources, clinical applications and developmental applications, and provide references for further research and development of the plant resources of this genus.

Keywords: *Kadsura*; Triterpenoids; Pharmacological activities; Clinical applications; Developing applications.

1. Introduction

The genus *Kadsura* belongs to the family Schisandracea [1], with about 28 species, mainly distributed in eastern and southeastern Asia. There are 8 species in China, namely *K. ananosma, K. coccinea, K. heteroclita, K. induta, K. japonica, K. longipedunculata, K. oblongifolia* and *K. renchangiana*. In addition, *K. heteroclita* also includes two varieties of *K. polysperma* and *K. interior*. The genus *Kadsura* has the effect of activating blood circulation, resolving blood stasis,

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benefiting qi, promoting the production of body fluid, dispelling wind and removing dampness [2], which were recorded in ancient prescriptions. The chemical composition of this genus mainly containing triterpenoids, lignans, volatile oils and polysaccharides, the main active ingredients are triterpenoids and lignans. Among them, lanostane and cycloartane-type triterpenoids are the most abundant active constituents in the genus *Kadsura*, with the most prominent activities in anti-tumor, anti-HIV and antioxidant effects. Researchers found that the cycloartane-type triterpenoids obtained from *K. heteroclita* had significant anti-HIV effects, which is important for the research and development of novel anti-HIV drugs.

The roots, stems, fruits of *Kadsura* plants are usually used for medicinal purposes. It has made great strides in the clinical treatment of diseases. For example, Shenqi Schisandra Tablets are used to treat insomnia, spontaneous sweating and tuberculosis, etc. In addition, extracts of *K. longipedunculata* can reduce the rejection reaction during liver transplantation. In recent years, the genus *kadsura* has also been used mostly for the development of the food industry. Such as the production of wine, fruit drinks and health products. At present, it is still a popular topic of discussion among domestic and foreign scholars, triterpenoids are the most promising group of components, which have outstanding performance in preventing liver damage by drugs. Nowadays, there is a lack of systematic summary of the triterpenoid composition of genus *Kadsura*, and the relevant review articles are incomplete in their description [3-4]. Therefore, in this paper, we systematize the structural types of triterpenoids in the genus *Kadsura*, and review the current status of pharmacological research and the progress of plant resources, clinical applications and exploitation of this genus, aiming to provide a scientific basis for subsequent research and development.

2. Resource Distribution

Genus *Kadsura* belongs to the family Schisandraceae and grows mostly in mountainous areas in mixed woods, bushes or forest margins, or entwined with other forest trees [1]. By observing the macro-morphological characteristics and seed coat micromorphology of a large number of samples of the genus *Kadsura*, researchers found that most of the seeds of this genus are kidney-shaped, oval, heart-shaped or kidney-shaped oblate [5]. By reviewing the historical development of S*chisandra chinensis* and observing a large number of samples, the family Schisandraceae containing the genus *Schisandra* and genus *Kadsura*. The genus *Kadsura* is subdivided into two subgenera: Subg. *Cosbaea* and Subg. *Kadsura*. Their main characteristics and distribution are shown in Table 1.

Table 1. species comparison morphological characteristics of genus *Kadsura*

NO.	Species	Characteristic	Origin
1	*K. ananosma*	Leaves papery, elliptic; receptacle of male flowers elongated apically, with branched appendages	SW Yunnan.
2	*K. coccinea*	Leaves leathery, leaves generally oblong; receptacle of male flowers with branched subulate appendages apically; tepals red	Jiangxi, Hunan, etc.
3	*K. heteroclita*	Evergreen woody vine, glabrous; branchlets brown, black when dry, base rounded and obtuse, entire margin with sparse small serrations.	Fujian, Guangdong, etc.
4	*K. induta*	Woody vine, annual branches tomentose, basal margin serrulate, apex shortly acuminate. Staminal cluster nearly ovate, staminal group containing 70-80 stamens. Leaf blade ovate, blade pointed at the front and rounded at the base.	W Guangxi, SE Yunnan.
5	*K. interior*	Evergreen woody vine, glabrous, new branches dark green, base persisting with several triangular bud scales.	SW Yunnan.
6	*K. japonica*	Lianas, glabrous throughout. Leaf blade sub oblong, entire margin denticulate. Flowers solitary, base in leaf axils; stamens 34-55, coherent into trapezoids. Small berries sub globose; seeds 1-3 per carpel, mostly reniform.	Taiwan
7	*K. longipedunculata*	Lianas, all parts glabrous. Leaf blade mostly ovate-lanceolate, margin denticulate. Flowers solitary, base in leaf axils, with 30-70 stamens, filaments very short. Small berries with thin pericarp.	Anhui, Fujian, Guangdong, etc.
8	*K. oblongifolia*	Lianas. Leaves oblong. Flowers solitary, dioecious, with ca. 25 stamens, almost without filaments, similar in appearance to the tepals. Aggregate fruit sub globose, berry ellipsoidal, exocarp thinly leathery.	Guangdong, Guangxi, Hainan.
9	*K. polysperma*	Vines, glabrous throughout. Leaves papery, ovate, ovate-elliptic, narrowly elliptic, or oblong-elliptic; whole or upper part with sparse callose denticles.	Sichuan
10	*K. renchangiana*	Whole plant glabrous. Leaf blade papery, margin subentire or serrulate, secondary veins 7-9. fr. Sep-Nov, obovate berries.	Guangxi, Guizhou.

3. Chemical composition

In recent years, Chinese and foreign scholars isolate various chemical components from the genus *kadsura*, including triterpenoids, lignans, polysaccharides and volatile oils, of which triterpenoids are the main characteristic components. So far, 264 species of triterpenoids have been isolated from this genus. According to the type of structure, they are divided into lanostanes, cycloartanes, nortriterpenoids, schinortriterpenoids and pentacyclic triterpenoids. The main structures of the genus are lanostane and cycloatenane-type, and mostly in the form of triterpene acids or triterpene lactones. The specific names and structural classification are shown in Table 2 and Figures 1-13.

Table 2. triterpenoids isolated from genus *Kadsura*

NO	Name	Plant	Part	Ref.
	Intact lanostanes			
1	epianwuweizic acid	*K. induta*	stems	[6]
2	anwuweizonic acid	*K. induta*	roots	[6]
3	kadpolysperin N	*K. polysperma*	stems	[7]
4	kadpolysperin D	*K. polysperma*	stems	[7]
5	kadnanosic acid B	*K. ananosma*	stems	[8]
6	(24*Z*)-3-oxo-12*α*-acetoxyanosta-8,24-dien-26-oic acid	*K. longipedunculata*	roots and stems	[9]
7	(24*Z*)-3-oxo-12*α*- hydroxyanosta-8,24-dien-26-oic acid	*K. longipedunculata*	roots	[9]
8	3-hydroxy-12-acetoxycoccinic acid	*K. coccinea*	roots	[10]
9	3-hydroxy-12-hydroxylcoccinic acid	*K. coccinea*	roots	[11]
10	coccinone D	*K. coccinea*	roots	[12]
11	coccinic acid	*K. coccinea*	roots	[13]
12	schisanhenric acid	*K. heteroclita*	stems	[14]
13	12*α*-acetoxycoccinic acid	*K. heteroclita*	stems	[15]
14	12*α*-hydroxycoccinic acid	*K. heteroclita*	stems	[15]
15	12*β*-acetoxycoccinic acid	*K. heteroclita*	stems	[15]
16	12*β*-hydroxycoccinic acid	*K. heteroclita*	stems	[15]
17	*iso*-anwuweiziic acid	*K. heteroclita*	stems	[15]
18	3-hydroxy-neo-kadsuranicacid	*K. coccinea*	roots	[11]
19	coccinone A	*K. coccinea*	roots	[12]
20	coccinilactone B	*K. coccinea*	roots	[16]
21	kadnanolactone C	*K. ananosma*	stems	[8]
22	20(*R*), 24(*E*)-3-oxo-9*β*-lanosta-7,24-dien-26-oic acid	*K. coccinea*	roots and stems	[18]
23	coccinone B	*K. coccinea*	roots	[12]
24	kadcoccinone G	*K. coccinea*	roots	[14]
25	kadcoccinone H	*K. coccinea*	roots	[14]

26	kadcoccinone I	*K. coccinea*	roots	[14]
27	kadcoccinone J	*K. coccinea*	roots	[14]
28	kadcoccinone K	*K. coccinea*	roots	[14]
29	kadcoccinone L	*K. coccinea*	roots	[14]
30	kadcoccinone M	*K. coccinea*	roots	[14]
31	kadcoccinone N	*K. coccinea*	roots	[14]
32	kadcoccinone O	*K. coccinea*	roots	[14]
33	kadcoccinone P	*K. coccinea*	roots	[14]
34	kadcoccinone Q	*K. coccinea*	roots	[14]
35	kadcoccinone F	*K. coccinea*	stems	[18]
36	coccinone C	*K. coccinea*	roots	[12]
37	kadcoccinone D	*K. coccinea*	stems	[18]
38	kadcoccinone E	*K. coccinea*	stems	[18]
39	kadindutic acid	*K. induta*	stems	[6]
40	coccinilactone A	*K. coccinea*	roots	[19],[20]
	3,4-Secolanostanes			
41	kadnanosic acid A	*K. ananosma*	stems	[8]
42	kadsuracoccin acid A	*K. coccinea*	roots	[16]
43	kadpolysperin B	*K. polysperma*	roots	[21]
44	kadpolysperin H	*K. polysperma*	roots	[21]
45	manwuweizic acid	*K. ananosma*	roots and stems	[8]
46	kadpolysperin J	*K. polysperma*	roots	[21]
47	kadpolysperin K	*K. polysperma*	roots	[21]
48	seco-coccinic acid K	*K. coccinea*	roots	[16]
49	seco-neokadsuranic acid A	*K. coccinea*	stems	[15]
50	kadcoccinic acid J	*K. coccinea*	stems	[22]
51	kadpolysperin I	*K. polysperma*	stems	[21]
52	schisanlactone E	*K. polysperma*	roots	[23]
53	schisphenthin A	*K. longipedunculata*	fruits	[24]
54	seco-coccinic acid I	*K. coccinea*	roots	[16]
55	3-ethylmanwuweizate	*K. heteroclita*	stems	[25]
56	26-methylmanwuweizate	*K. heteroclita*	stems	[25]
57	schisanlactone F	*K. ananosma*	roots	[8]
58	kadsuracoccinic acid A	*K. coccinea*	roots	[16],[26],[27]
59	kadsuracoccinic acid B	*K. coccinea*	roots	[16],[26],[27]
60	kadsuracoccinic acid C	*K. coccinea*	roots	[16],[26],[27]
61	kadsuric acid	*K. coccinea*	roots	[16],[26],[27]
62	micranoic acid A	*K. coccinea*	roots	[16],[26],[27]
63	kadcoccitone C	*K. coccinea*	stems	[28]
64	3,4-seco-(24*Z*)-lanosta-4(30),8,24-triene-3,26-dioic acid	*K. heteroclita*	roots	[15]
65	schisphenthin B	*K. longipedunculata*	fruits	[24]
66	seco-coccinic acid L	*K. coccinea*	roots	[16]

67	kadcoccilactone R	*K. coccinea*	roots	[16],[26],[27]
68	kadnanolactone D	*K. ananosma*	stems	[8]
69	kadcotrione C	*K. coccinea*	stems	[28]
70	kadcoccinic acid B	*K. coccinea*	stems	[22]
71	kadcoccinic acid A	*K. coccinea*	stems	[22]
72	kadcoccinic acid G	*K. coccinea*	stems	[22]
73	kadcoccinic acid H	*K. coccinea*	stems	[22]
74	acetyl aleuritolic acid	*K. heteroclita*	stems	[29]
75	seco-coccinic acid G	*K. coccinea*	Roots	[16]
76	seco-coccinic acid H	*K. coccinea*	roots	[16]
77	seco-coccinic acid J	*K. coccinea*	roots	[16]
78	sphendilactone	*K. longipedunculata*	roots and stems	[30]
79	kadcoccinic acid I	*K. coccinea*	stems	[22]
80	seco-coccinic acid A	*K. coccinea*	roots	[19]
81	seco-coccinic acid B	*K. coccinea*	roots	[19]
82	seco-coccinic acid C	*K. coccinea*	roots	[19]
83	seco-coccinic acid D	*K. coccinea*	roots	[19]
84	seco-coccinic acid E	*K. coccinea*	roots	[19]
85	seco-coccinic acid F	*K. coccinea*	roots	[19]
	18(13→12)-Abeolanostanes			
86	kadindutic acid	*K. induta*	stems	[31]
87	ananosic acid B	*K. polysperma*	stems	[7]
88	kadpolysperin F	*K. polysperma*	stems	[21]
89	ananosic acid A	*K. polysperma*	stems	[7]
90	kadpolysperin G	*K. polysperma*	stems	[21]
91	kadpolysperin E	*K. polysperma*	stems	[21]
92	ananosic acid C	*K. polysperma*	stems	[7]
93	ananosic acid D	*K. polysperma*	stems	[7]
94	kadpolysperin C	*K. polysperma*	stems	[21]
95	kadpolysperin L	*K. polysperma*	stems	[21]
96	kadpolysperin M	*K. polysperma*	stems	[21]
97	20(*R*),24(*E*)-3-oxo-9*β*-lanosta-7,24-dien-26-oic acid	*K. heteroclita*	stems	[32]
	14(13→12)-Abeolanostanes			
98	kadcoccine acid A	*K. coccinea*	stems	[20]
99	kadcoccine acid B	*K. coccinea*	stems	[20]
100	kadcoccine acid E	*K. coccinea*	stems	[20]
101	kadcoccine acid C	*K. coccinea*	stems	[20]
102	kadcoccine acid D	*K. coccinea*	stems	[20]
103	kadcoccine acid F	*K. coccinea*	stems	[20]
104	kadcoccine acid G	*K. coccinea*	stems	[20]
105	kadcoccine acid H	*K. coccinea*	stems	[20]
106	kadcoccine acid I	*K. coccinea*	stems	[20]

107	kadcoccine acid J	*K. coccinea*	stems	[20]
108	kadcoccine acid K	*K. coccinea*	stems	[20]
109	kadcoccine acid L	*K. coccinea*	stems	[20]
110	kadcoccine acid M	*K. coccinea*	stems	[20]
111	kadcoccine acid N	*K. coccinea*	stems	[20]
112	kadcoccinic acid D	*K. coccinea*	stems	[22]
113	kadcoccinic acid E	*K. coccinea*	stems	[22]
114	kadcoccinic acid F	*K. coccinea*	stems	[22]
115	neokadsuranic acid B	*K. longipedunculata*	stems	[9]
116	neokadsuranic acid C	*K. longipedunculata*	stems	[9]
117	kadcoccitane A	*K. coccinea*	roots	[33]
118	kadcoccitane D	*K. coccinea*	roots	[33]
119	kadcoccitane C	*K. coccinea*	roots	[33]
120	kadcoccitane B	*K. coccinea*	roots	[33]
121	kadpolysperin A	*K. polysperma*	stems	[21]
122	neokadsuranic acid A	*K. longipedunculata*	stems	[35]
123	kadcoccinone A	*K. coccinea*	stems	[18]
124	kadcoccinone B	*K. coccinea*	stems	[18]
	Norlanostanes			
125	kadnanolactone E	*K. ananosma*	stems	[8]
	14(13→12):16(17→13)-Diabeolanostanes			
126	kadcoccitone A	*K. coccinea*	roots	[28]
127	kadcoccitone B	*K. coccinea*	roots	[28]
	18(13→12)-Abeo-13,17-seco-14β-lanostanes			
128	kadcotrione A	*K. coccinea*	stems	[28]
	14(13→12)-Abeo-12,13-secolanostanes			
129	kadcotrione C	*K. coccinea*	stems	[28]
	14(13→12)-Abeo-13,18-dinorlanostanes			
130	kadcotrione B	*K. coccinea*	stems	[34]
	Schiglautane			
131	kadcoccinone C	*K. coccinea*	stems	[18]
	Intact cycloartanes			
132	cycloatenone acid	*K. coccinea*	stems	[23]
133	schisandronic acid	*K. coccinea*	stems	[36]
134	heteroclic acid	*K. coccinea*	stems	[27]
135	kadsulactone	*K. coccinea*	stems	[27]
136	24-methylenecycloartenone	*K. coccinea*	roots and stems	[27]
137	ananosin C	*K. ananosma*	stems	[37]
138	ananosin D	*K. ananosma*	stems	[37]
139	schizandronic acid	*K. japonica*	roots and stems	[38]
	3,4-Secocycloartanes			
140	coccinetane A	*K. coccinea*	stems	[16]

141	coccinetane B	*K. coccinea*	stems	[16]
142	coccinetane E	*K. coccinea*	stems	[16]
143	coccinetane C	*K. coccinea*	stems	[16]
144	coccinetane F	*K. coccinea*	stems	[16]
145	coccinetane D	*K. coccinea*	stems	[16]
146	coccinetane G	*K. coccinea*	stems	[16]
147	coccinetane H	*K. heteroclita*	stems	[16]
148	heteroclitalactone A	*K. heteroclita*	stems	[36]
149	heteroclitalactone B	*K. heteroclita*	stems	[36]
150	heteroclitalactone C	*K. heteroclita*	stems	[36]
151	nigranoic acid	*K. heteroclita*	stems	[36]
152	kadsuranic acid A	*K. heteroclita*	stems	[23]
153	ananosin B	*K. ananosma*	stems	[37]
154	ananosin E	*K. ananosma*	stems	[37]
155	polysperlactone B	*K. polysperma*	stems	[39]
156	polysperlactone C	*K. polysperma*	stems	[39]
157	kadsuranic acid B	*K. heteroclita*	stems	[40]
158	heteroclitalactone F	*K. heteroclita*	stems	[36]
159	xuetongsu E	*K. heteroclita*	stems	[40]
160	changnanic acid	*K. heteroclita*	stems	[36]
161	xuetongsu F	*K. heteroclita*	stems	[40]
162	Xuetonin A	*K. heteroclita*	leaves	[41]
163	Xuetonin B	*K. heteroclita*	leaves	[41]
	14(13→12)-Abeocycloartanes			
164	longipedlactone K	*K. ananosma*	stems	[42]
165	longipedlactone L	*K. ananosma*	stems	[42]
166	longipedlactone M	*K. ananosma*	stems	[42]
167	longipedlactone H	*K. ananosma*	stems	[42]
168	longipedlactone N	*K. ananosma*	stems	[42]
169	longipedlactone D	*K. ananosma*	stems	[42]
170	longipedlactone G	*K. ananosma*	stems	[42]
171	longipedlactone O	*K. ananosma*	stems	[42]
172	longipedlactone P	*K. ananosma*	stems	[42]
173	longipedlactone I	*K. ananosma*	stems	[42]
174	longipedlactone A	*K. ananosma*	stems	[42]
175	longipedlactone F	*K. ananosma*	stems	[42]
176	longipedlactone J	*K. ananosma*	stems	[42]
177	kadheterilactone A	*K. heteroclita*	stems	[43]
178	kadheterilactone B	*K. heteroclita*	stems	[43]
179	xuetonglactone A	*K. heteroclita*	stems	[44]
180	xuetonglactone C	*K. heteroclita*	stems	[44]
181	heteroclitalactone D	*K. heteroclita*	stems	[36]
182	schisphenthin C	*K. longipedunculata*	fruits	[24]
183	xuetonglactone D	*K. heteroclita*	stems	[44]

184	xuetongsu C	*K. heteroclita*	stems	[40]
185	xuetongsu D	*K. heteroclita*	stems	[40]
186	schisanlactone B	*K. induta*	roots and stems	[6]
187	kadcoccilactone Q	*K. coccinea*	stems	[27]
188	heteroclitalactone M	*K. heteroclita*	stems	[45]
189	renchanglactone A	*K. renchangiana*	stems	[40],[64]
190	heteroclitalactone G	*K. heteroclita*	stems	[45]
191	heteroclitalactone H	*K. heteroclita*	stems	[45]
192	heteroclitalactone I	*K. heteroclita*	stems	[45]
193	heteroclitalactone J	*K. heteroclita*	stems	[45]
194	heteroclitalactone K	*K. heteroclita*	stems	[45]
195	heteroclitalactone L	*K. heteroclita*	stems	[45]
196	schisanlactone A	*K. longipedunculata*	roots and stems	[46]
197	ananosin A	*K. ananosma*	stems	[37]
198	polysperlactone A	*K. polysperma*	stems	[39]
199	kadsudilactone	*K. heteroclita*	stems	[29]
200	heteroclitalactone P	*K. heteroclita*	stems	[40]
201	xuetonglactone E	*K. heteroclita*	stems	[44]
202	xuetonglactone F	*K. heteroclita*	stems	[44]
203	heteroclitalactone E	*K. heteroclita*	stems	[36]
204	xuetonglactone B	*K. heteroclita*	stems	[44]
205	xuetongsu A	*K. heteroclita*	stems	[40]
206	xuetongsu B	*K. heteroclita*	stems	[40]
207	kadcoccilactone P	*K. coccinea*	stems	[27]
208	longipedlactone B	*K. longipedunculata*	stems	[47],[48]
209	longipedlactone E	*K. longipedunculata*	stems	[47],[48]
210	longipedlactone C	*K. longipedunculata*	stems	[47],[48]
	Kadlongilactones			[47],[48]
211	kadlongilactone C	*K. longipedunculata*	stems	[47],[48]
212	kadlongilactone D	*K. longipedunculata*	stems	[47],[48]
213	kadlongilactone E	*K. longipedunculata*	stems	[47],[48]
214	kadlongilactone B	*K. longipedunculata*	stems	[49]
215	kadlongilactone A	*K. longipedunculata*	stems	[49]
216	kadlongilactone F	*K. longipedunculata*	stems	[47],[48]
217	kadcoccilactone K	*K. coccinea*	stems	[27]
218	kadcoccilactone L	*K. coccinea*	stems	[27]
219	kadcoccilactone M	*K. coccinea*	stems	[27]
220	kadcoccilactone N	*K. coccinea*	stems	[27]
221	kadcoccilactone O	*K. coccinea*	stems	[27]
	3,4:9,10-Disecocycloartanes			
222	kadlongilactone A	*K. longipedunculata*	leaves and stems	[47],[48]

223	kadlongilactone B	*K. longipedunculata*	leaves and stems	[47],[48]
224	kadlongilactone C	*K. longipedunculata*	leaves and stems	[47],[48]
225	kadnanolactone A	*K. ananosma*	stems	[8]
226	kadcoccilactone A	*K. coccinea*	leaves and stems	[50]
227	kadcoccilactone C	*K. coccinea*	leaves and stems	[50]
228	kadcoccilactone G	*K. coccinea*	stems	[50]
229	xuetongdilactone A	*K. longipedunculata*	stems	[51]
230	xuetongdilactone B	*K. longipedunculata*	stems	[51]
231	xuetongdilactone C	*K. longipedunculata*	stems	[51]
232	heteroclitalactone N	*K. heteroclita*	stems	[52]
233	kadcoccilactone V	*K. coccinea*	stems	[53]
	Nortriterpenoids			
234	schintrilactone A	*K. longipedunculata*	stems	[54]
235	schintrilactone B	*K. longipedunculata*	stems	[54]
236	schintrilactone C	*K. longipedunculata*	stems	[31],[54],[55]
237	schintrilactone D	*K. longipedunculata*	stems	[31],[54],[55]
	Schinortriterpenoids			
238	kadcoccilactone S	*K. coccinea*	stems	[56]
239	xuetongdilactone E	*K. heteroclita*	stems	[51]
240	xuetongdilactone F	*K. heteroclita*	stems	[51]
241	micrandiactone H	*K. coccinea*	stems	[55]
242	kadnanolactone B	*K. ananosma*	stems	[8]
243	micrandilactone I	*K. longipedunculata*	stems	[48]
244	kadcoccilactone B	*K. coccinea*	leaves and stems	[50]
245	kadcoccilactone D	*K. coccinea*	leaves and stems	[50]
246	kadcoccilactone E	*K. coccinea*	leaves and stems	[50]
247	kadcoccilactone F	*K. coccinea*	leaves and stems	[50]
248	kadcoccilactone H	*K. coccinea*	stems	[50]
249	kadcoccilactone I	*K. coccinea*	stems	[50]
250	kadcoccilactone J	*K. coccinea*	stems	[50]
251	kadnanolactone G	*K. ananosma*	stems	[8]
52	kadnanolactone H	*K. ananosma*	stems	[8]
253	kadnanolactone I	*K. ananosma*	stems	[8]
254	micrandilactone C	*K. ananosma*	stems	[8]
255	micrandilactone B	*K. ananosma*	stems	[8]
256	wuweizidilactone H	*K. ananosma*	stems	[8]

257	xuetongdilactone D	*K. heteroclita*	stems	[51]
	Oleanane			
258	*β*-amyrin	*K. interior*	stems	[57]
259	germanicol C	*K. interior*	stems	[57]
	Ursane			[57]
260	*α*-amyrin	*K. interior*	stems	[57]
261	ursolic acid	*K. interior*	stems	[57]
	Lupane			[57]
262	lupenol	*K. interior*	stems	[57]
263	lupenone	*K. interior*	stems	[57]
	lsofernane			
264	sorghumol	*K. heteroclita*	stems	[58]

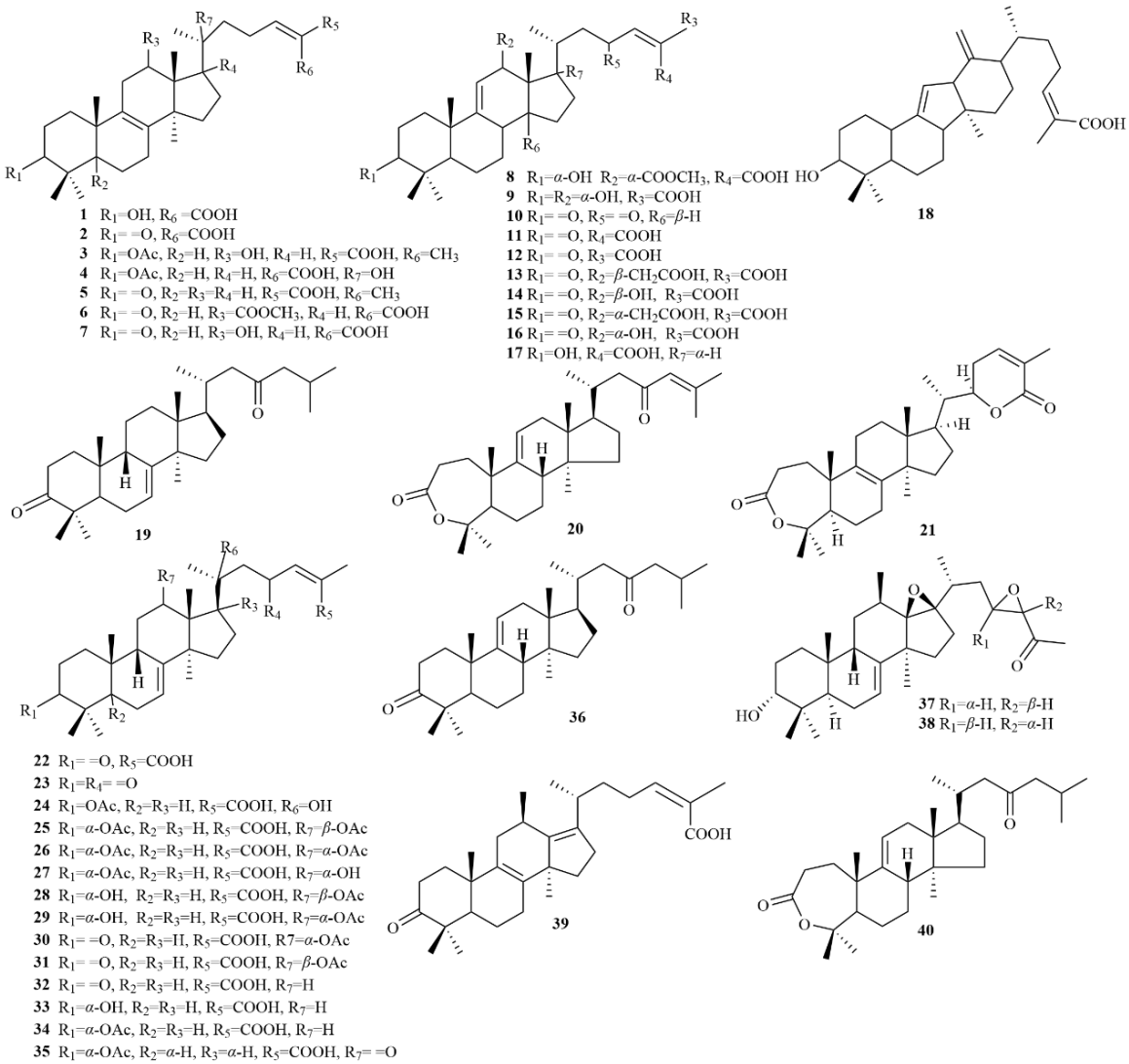

Figure 1. The structures of intact lanostane triterpenoids

3.1. Lanostanes

3.1.1. Intact Lanostanes

Lanostane-type triterpenoids belong to tetracyclic triterpenes which are regarded as the most abundant chemical components in the genus *Kadsura*. This group of compounds (**1**-**40**) comprises the original tetracyclic core structure. Its structure is characterized by A/B, B/C and C/D rings in trans, an oxygen-containing substitution at C-3, a double bond at C-7/C-8, C-8/C-9 or C-9/C-11, and C-20 is *R*-. The specific structure is shown in Figure 1.

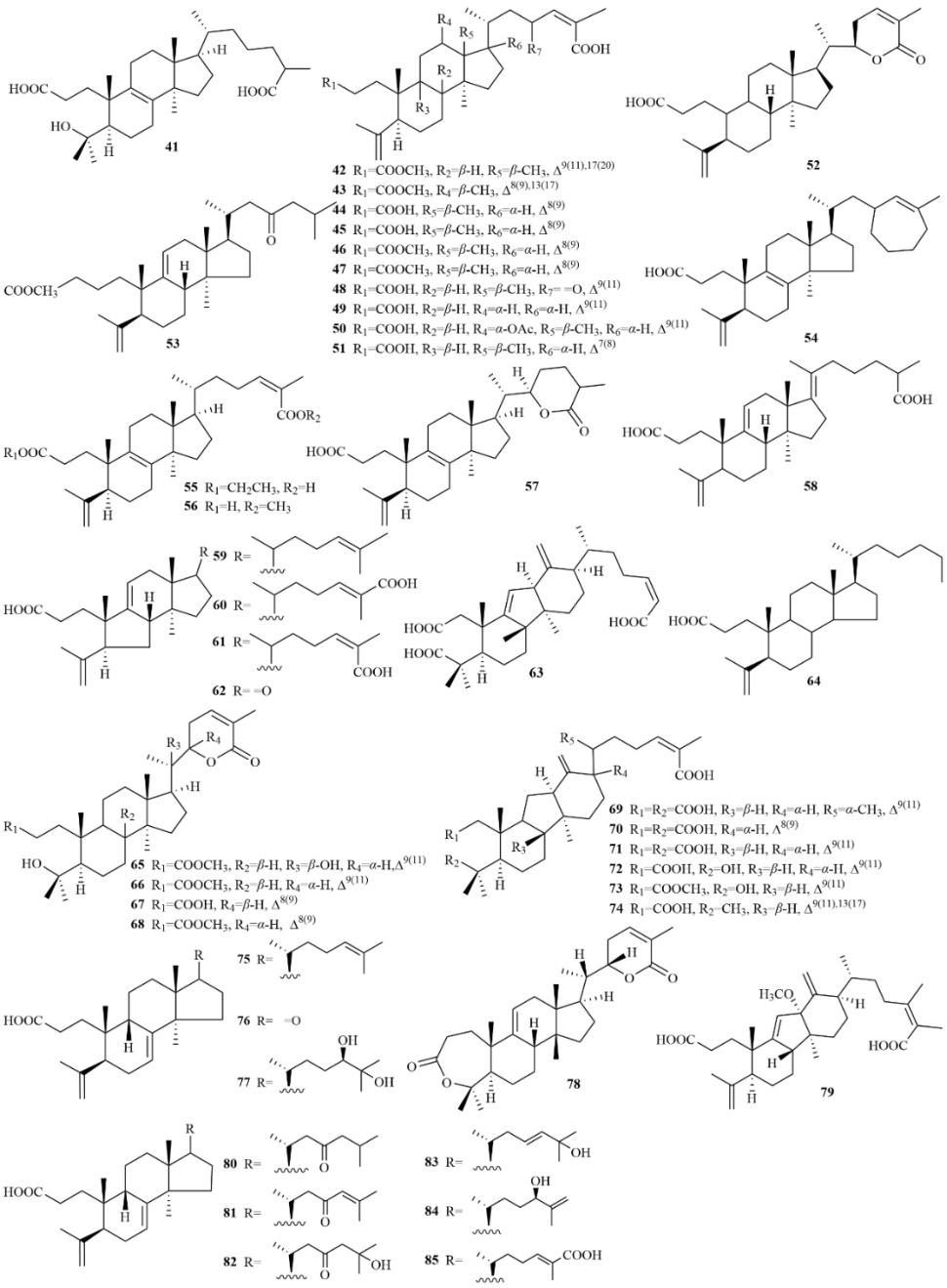

Figure 2. The structures of 3,4-seco-lanostanes triterpenoids

3.1.2. 3,4-Secolanostanes

The structures of 3,4-secolanostanes (**41**-**85**) are characterized by the oxidative cracking of C-3 and C-4 by Baeyer-Villiger followed by the formation of 3,4-lactone group, the formation of a double bond between C-4 and C-28, the formation of a double bond between C-24 and C-31 of the side chain, and the formation of C-21 is a carboxyl group. The specific structure is shown in Figure 2.

3.1.3. 18(13→12)-Abeolanostanes

The conformation of this group of compounds (**86**~**97**) is feature by a borated methyl group or an exocyclic double bond at C-12, which are currently isolated only from plants such as *K. induta, K. coccinea* and *K. polysperma*, the specific structures of which are shown in Figure 3.

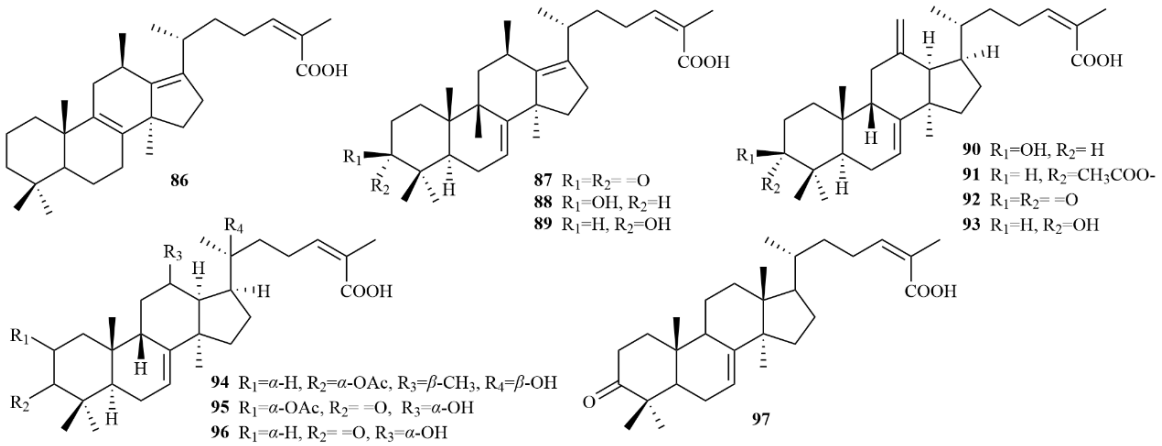

Figure 3. The structures of 18(13→12)-abeo-lanostanes triterpenoids

3.1.4. 14(13→12)-Abeolanostanes

The compounds in this group (**98**~**124**) are formed by breaking C-13 and C-14 in the structure of lanostane-type triterpenoids and forming a new ring between C-12 and C-14, generated *via* Wagner-Milwyn rearrangement, as shown in Figure 4.

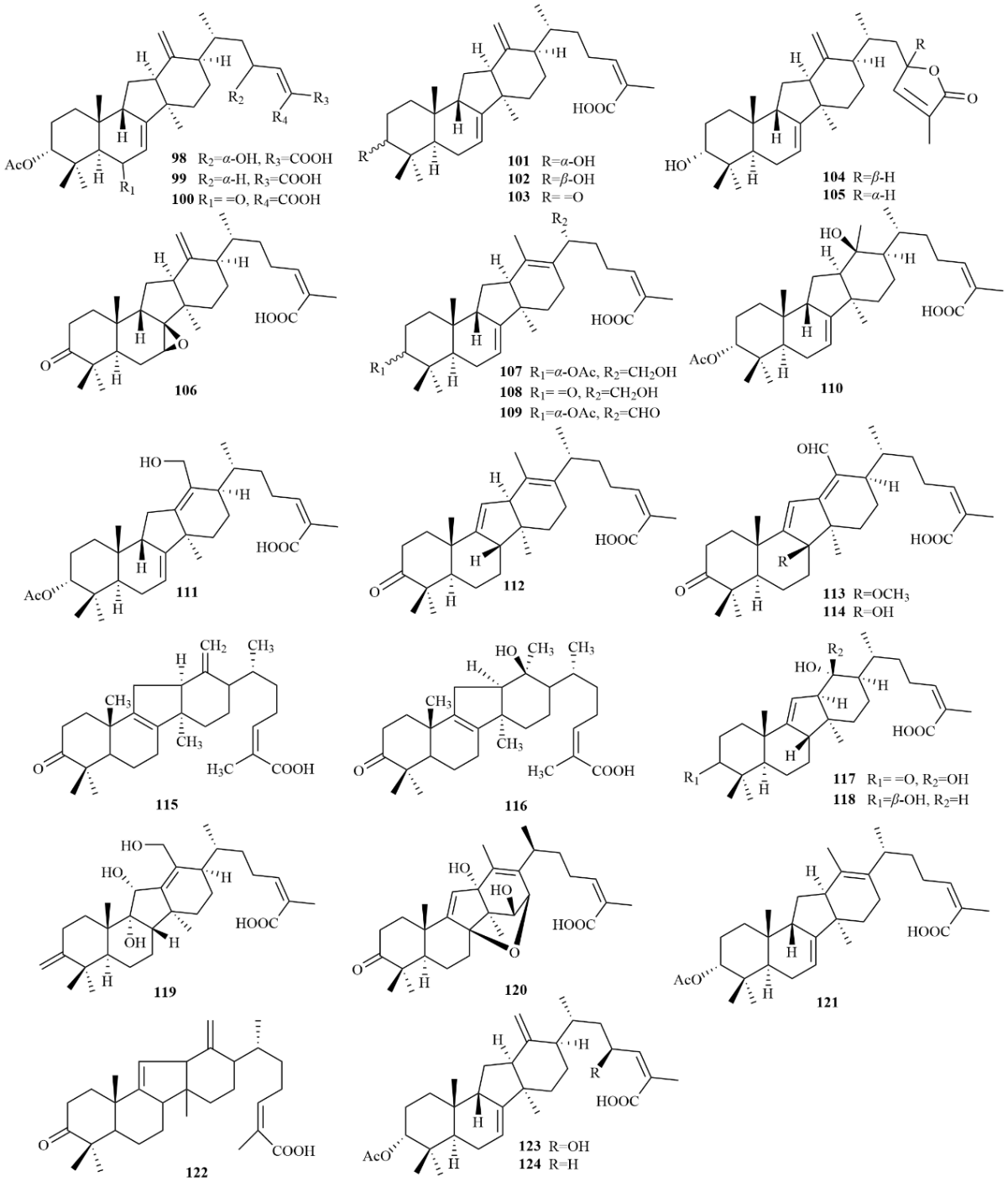

Figure 4. The structures of 14(13→12)-abeo-lanostanes triterpenoids

3.2. Other Lanostanes

3.2.1. Norlanostanes

This type of triterpene is subjected to a series of oxidative cleavages, where its carbon molecules are lost from the periphery, the C_8 side chain disappears, and C-17 becomes an oxy group. Kadnanolactone E (**125**) isolated from *K. coccinea* belongs to this conformation (Figure 5).

3.2.2. 14(13→12):16(17→13)-Diabeolanostanes

Compounds **126** and **127** have a 6/6/5/5 tetracyclic core and a C_9 side chain. Oxidative cleavage is carried out intermediate to C-13 and C-17 and reconstruction of cyclo-pentane rings by hydroxyl aldehyde adduction. This method is a main way of forming a 6-fused ring system. Both compounds of this type were found from the *K. coccinea* (Figure 5).

3.2.3. 18(13→12)-Abeo-13,17-seco-14b-lanostane

Kadcotrione A (**128**) is found in the roots of *K. coccinea*. This compound has a uniquely 6/6/6 triplet ring with a meth group on C-12 and the meth group on C-14 is *β*-. See Figure 5 for the structure.

3.2.4. 14(13→12)-Abeo-12,13-secolanostane

Kadcotrione C (**129**) has a 6/6/5 ternary ring system with a structural backbone similar to that of iso-malabaricane type triterpenoids. Possessing due to the distinctive C_{13} side chain and Me-28, this composition may be produced from 14(13→12)-Abeolanostane-type triterpenes by oxidative cleavage. The specific structure is shown in Figure 5.

3.2.5. 14(13→12)-Abeo-13,18-dinorlanostane

Kadcotrione B (**130**), which found in stems of *K coccinea*, and the researchers speculated that it was likely derived from compound **129** by cleaving C-13 and C-17. The oxygen atom that subsequently forms C-17 (figure 5).

3.2.6. Schiglautane

This compound (**131**) has a special 6/6/9 ternary ring system contains a scarce oxacyclic [4.3.1] decyl system with C-12 and C-14 forming an epoxy bridge bond. The meth groups at the C-10, C-14 and C-20 are *β*-, *α*- and *α*-, in agreement with the lanostane-type triterpenoids, the specific structure of which is shown in Figure 5.

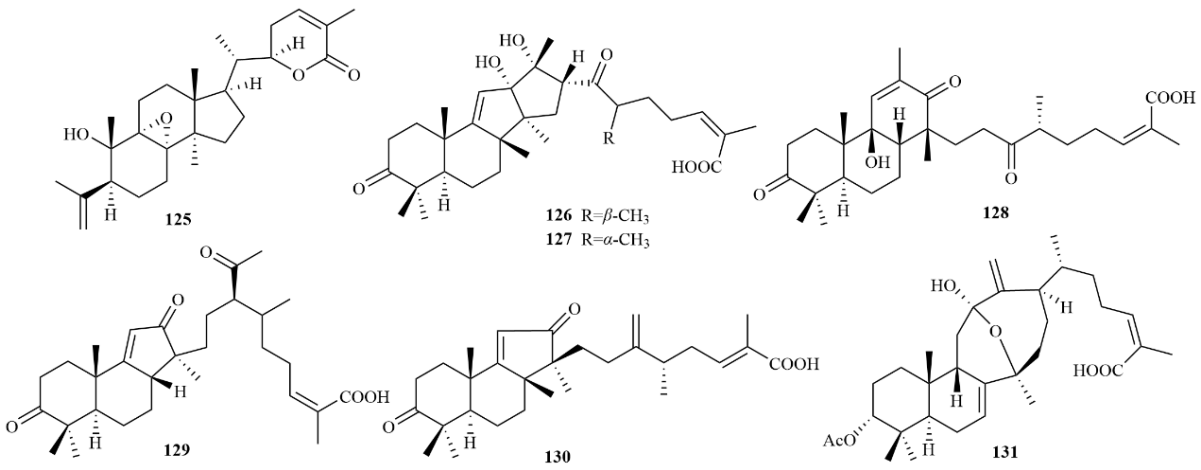

Figure 5. The structures of other lanostane triterpenoids

3.3. Cycloartanes

3.3.1. Intact Cycloartanes

The C-3 of compounds **132**~**139** is mainly substituted by carbonyl or hydroxyl, and the side chain is predominantly 24(*Z*)-ene-26-acid or 22,26 lactone rings. Eight cyclolartane-type triterpenoids have been isolated from the genus *Kadsura*. The structures are shown in Figure 6.

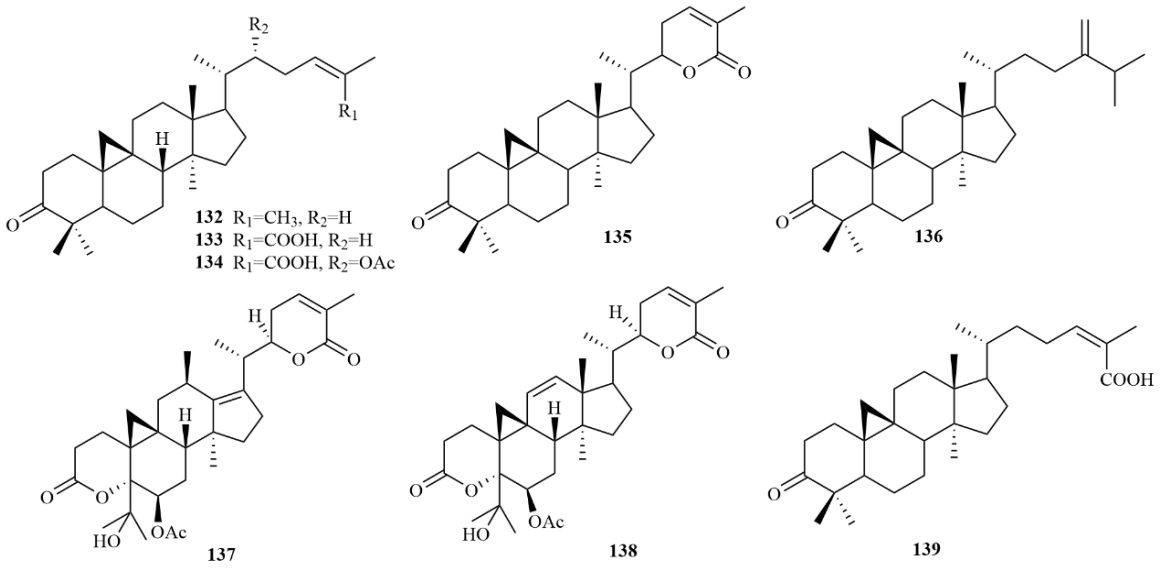

Figure 6. The structures of intact cycloartanes triterpenoids

2.3.2. 3,4-Secocycloartanes

Compounds **140-163** are characterized by broken C-3 and C-4 bonds, C-3 is typically a carboxylic acid or a carboxylic acid derivative, and the side chain is generally 24(*Z*)-ene-26-acid or 22, 26 lactone rings. The specific structures are shown in Figure 7.

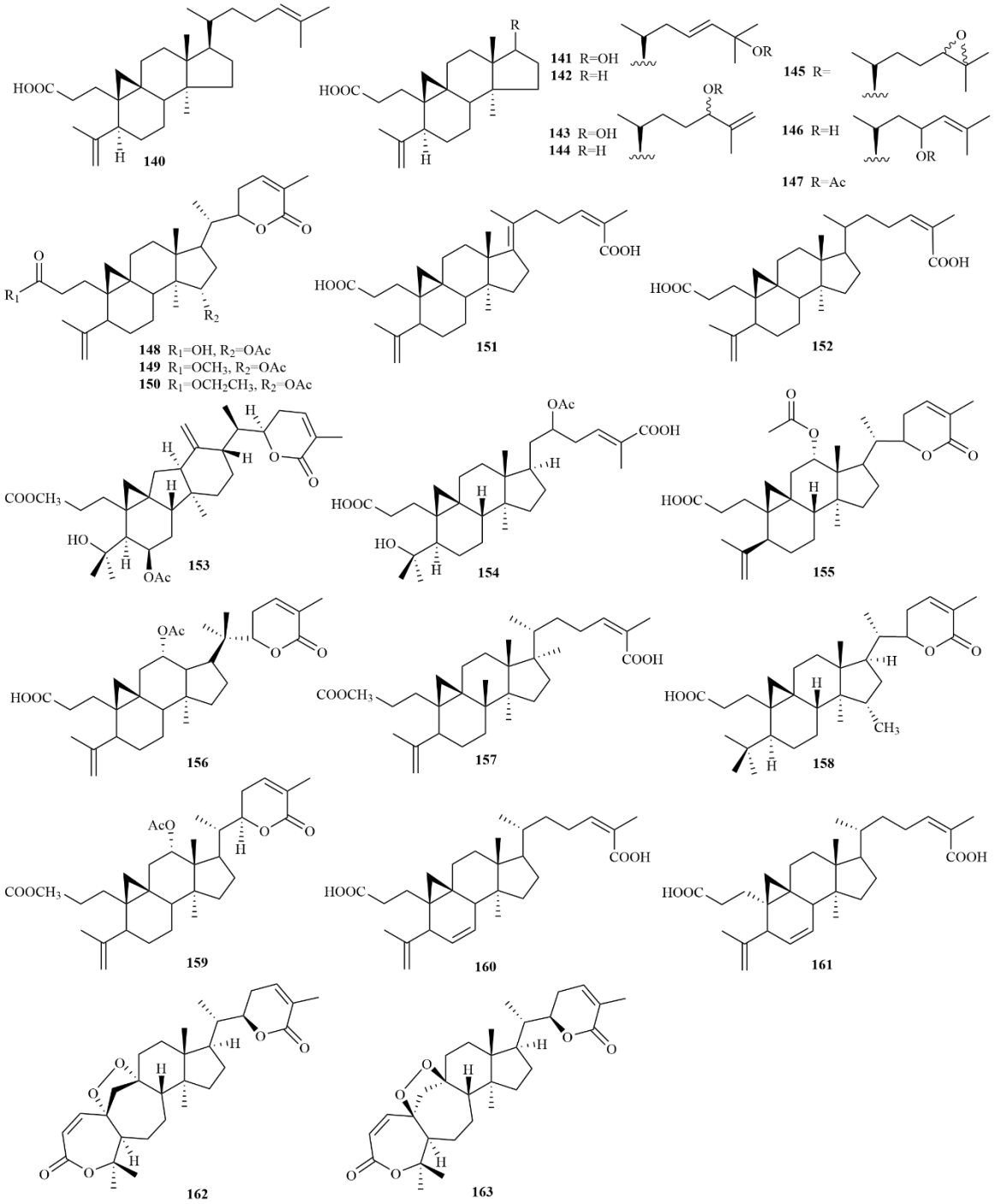

Figure 7. The structures of 3,4-Seco-cycloartanes triterpenoids

3.3.3. 14(13→12)-Abeocycloartanes

This group of compounds (**164**~**210**) is due to C-13 and C-14 bond breakage, forming a new ring by joining C-12 with C-14, whose C-9 is broken with C-10 to form a heptad ring, while a heptad ester ring is formed by Baeyer-Villiger oxidation after ring opening by breakage at C-3 and C-4. The C-19 methyl group of some compounds dehydrogenates with C-9 to form a ternary ring (Figure 8).

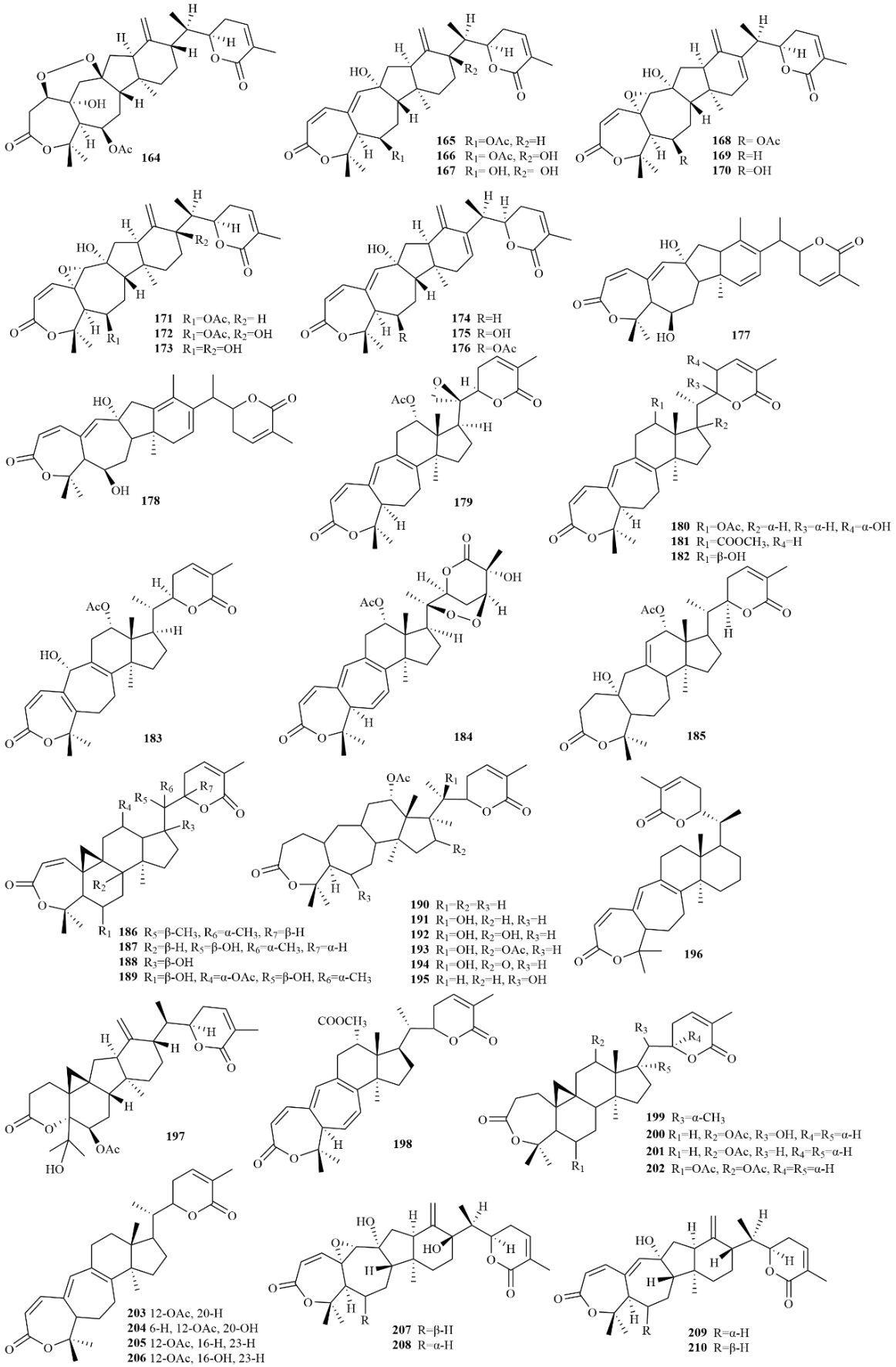

Figure 8. The structures of 14(13→12)-abeocycloartanes triterpenoids

3.3.4. Kadlongilactones

The compounds in this group consist of 14(13→12)-abeocyclolanostane-type compounds that undergo a series of oxidation, dehydrogenation, and cyclization reaction to create the A to F rings 7/7/5/6/6/6 (Figure 9). At present, such compounds (**211**-**221**) are only found in *K. longipedunculata* and *K. coccinea.*

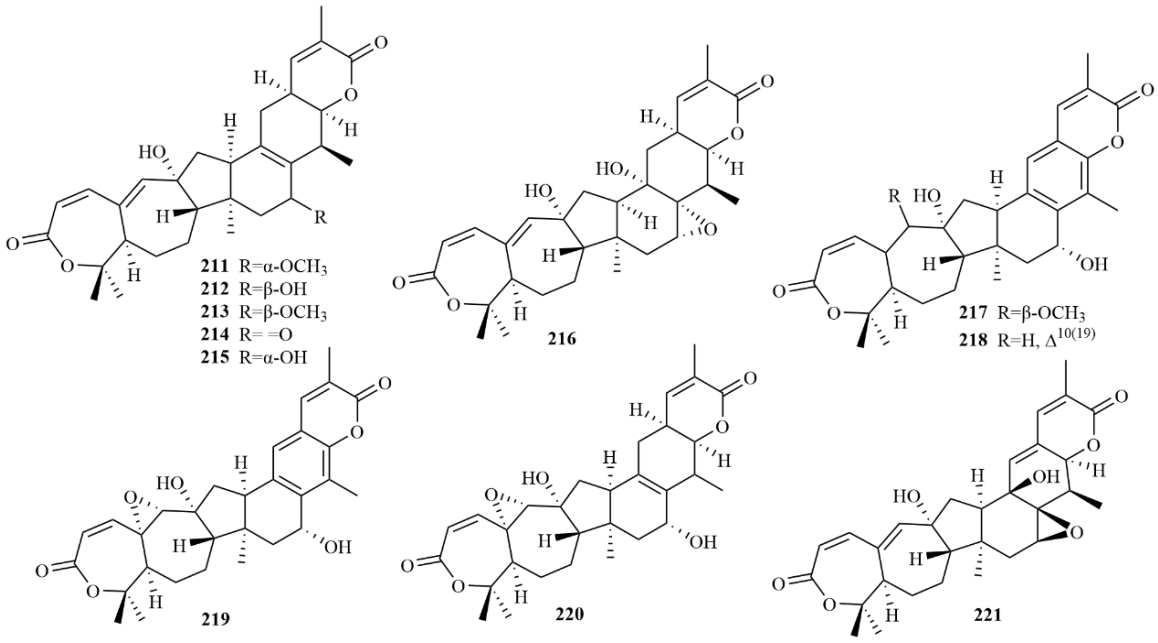

Figure 9. The structures of kadlongilactone triterpenoids

3.3.5. 3,4:9,10-Disecocycloartanes

The compounds in this group (**222**-**233**) are formed by the oxidative cracking between C-9 and C-10 in 3,4-secocycloartane. Therefore, most of the compounds in this group usually have oxygen-containing substituents or double bonds at the C-9 and C-10. The compounds in this group are mainly derived from *K. longipedunculata*, *K. ananosma* and *K. coccinea* (Figure 10).

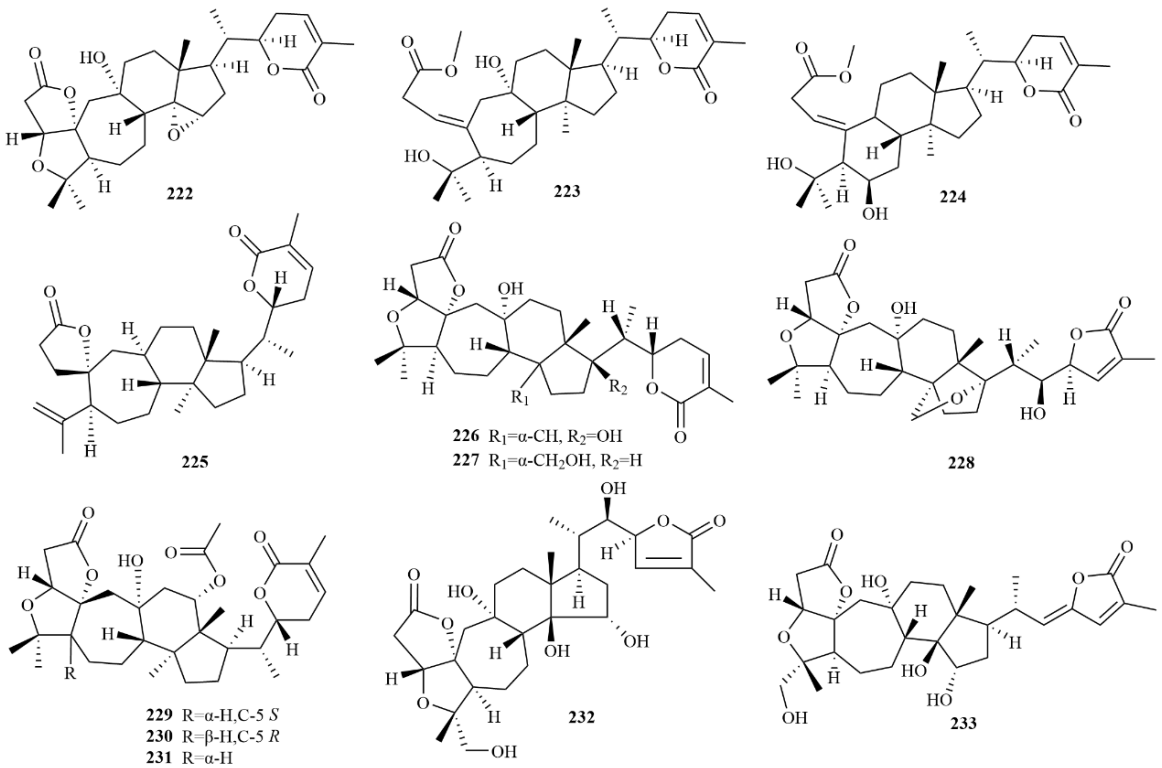

Figure 10. The structures of 3,4:9,10-disecocycloartane triterpenoids

3.4. Nortriterpenoids

Four highly oxygenated desmethyl triterpenoids (**234**-**237**) with a pentacosanol skeleton were obtained from the stems of *K. longipedunculata*, a group of compounds with a unique 7/5/6 fusion ring (Figure 11).

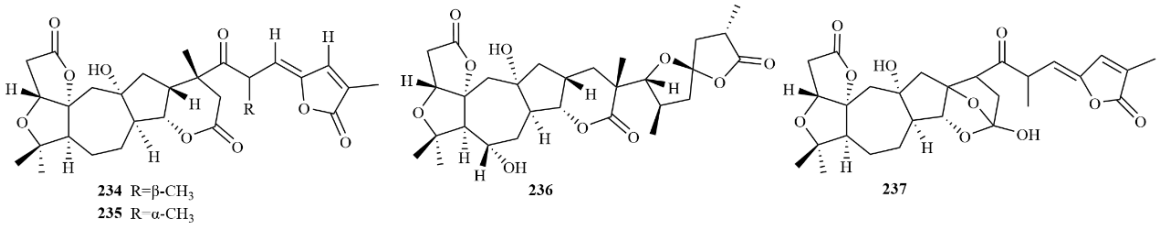

Figure 11. The structures of nortriterpenoids

3.5. Schinortriterpenoids

This group of compounds (**238-257**) is presumably formed by C-28 decarboxylation of 3,4:9,10-disecocycloartane. Then, a series of oxidations and backbone rearrangements formed various triterpenoids. Their parent nucleus is a 7/6/5 fusion ring (Figure 12).

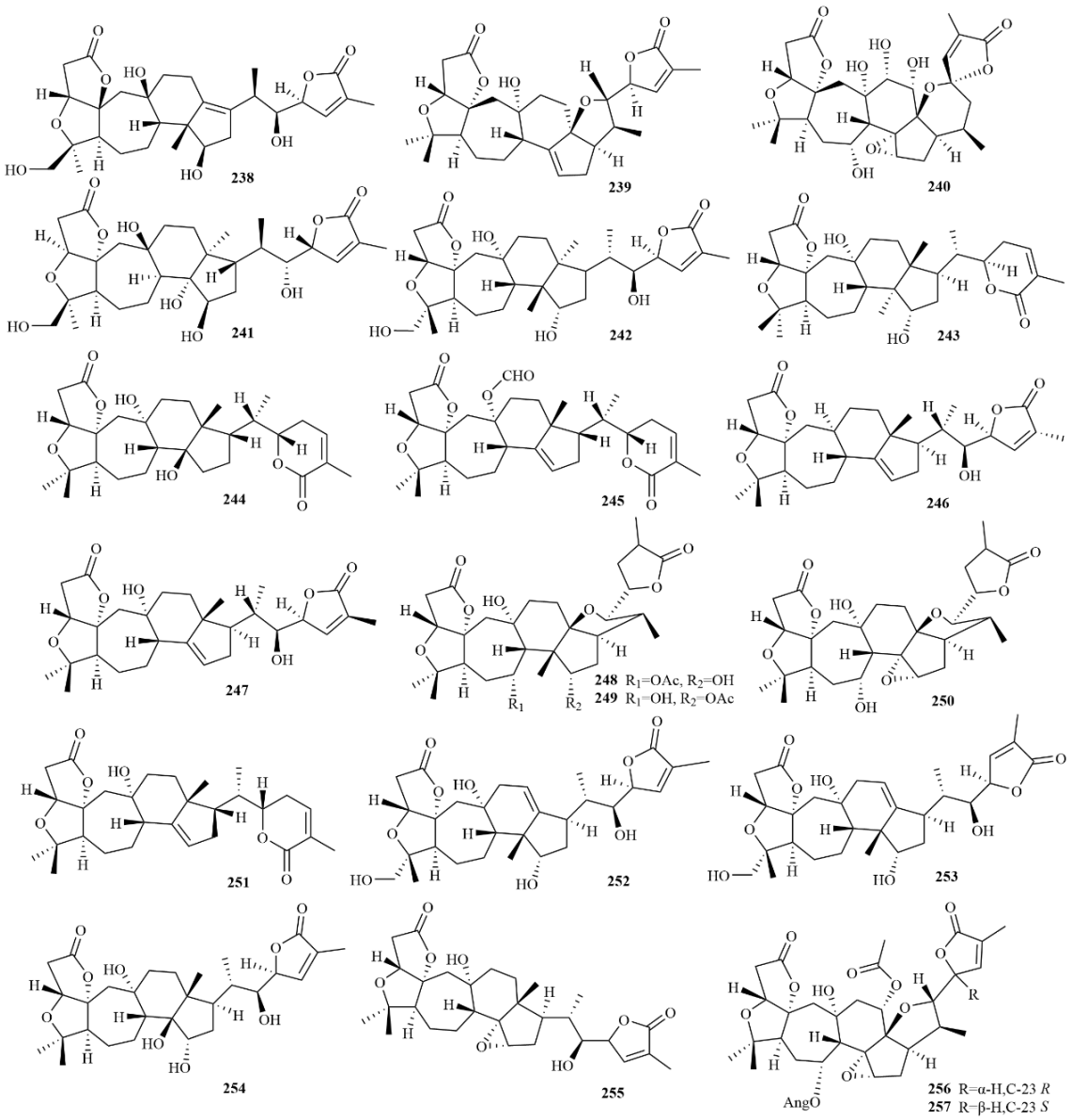

Figure 12. The structures of schinortriterpenoids

3.6. Pentacyclic Triterpene

3.6.1. Oleanane-Type Triterpenoid

The compounds in this group (**258**~**259**) are also known as *β*-amyrane, the carbon frame is mostly a five-ring parent nucleus, the ring configuration A/B、B/C、C/D are trans, while D/E is *cis*, the methyl group at C-8, C-10 and C-17 on the parent nucleus are *β*-oriented, and the methyl group at C-14 is *α*-oriented, the specific structure is shown in Figure 13.

3.6.2. Ursane-Type Triterpenoid

Compounds **260**~**261** is also known as *α*-amyrane. The molecular structure differs from that of the oleanolane-type triterpenoids in that the two methyl substitution positions on the E ring are different, i.e., one methyl group at each of the C-19 and C-20. The specific structure is shown in Figure 13.

3.6.3. lupane-Type Triterpenoid

This group of compounds (**262**~**263**) differs from the oleanolane type triterpenoids in that the C-21 and C-19 are connected into a five-membered ring E ring, and the isopropyl at C-19 is *α*-oriented. Both D and E rings are trans, i.e. A/B, B/C, C/D, and D/E are trans; the specific structures are shown in Figure 13.

3.6.4. lsofernane-Type Triterpenoid

The isofernane type can be considered as an isomer of the lupane type, which differs from the lupane type in that the *α*-isopropyl at the C-22. Sorghumol (**264**), which was isolated from the *k. heteroclita*, belongs to this configuration (Figure 13).

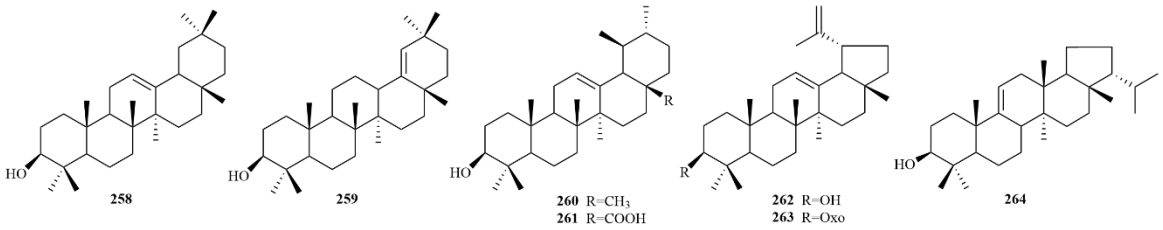

Figure 13. The structures of pentacyclic triterpenoids

4. Bioactivities

4.1. Antitumor Activity

The researchers tested seco-coccinic acids A-F by leukemia cells HL-60 with 5-fluorouracil as a positive control. These compounds were found to significantly inhibit the proliferation of leukemic HL-60 cells at different concentrations, with seco-coccinic acid A having the strongest activity and seco-coccinic acids B~F having slightly weaker activity. A series of activity screening of the chemical components obtained from *k. coccinea* is important for the subsequent search of new efficient and low toxic antitumor components. Zhang et al. [34] examined the six triterpenes isolated kadcoccinones A-F were screened for antitumor toxicity and found that the activity of kadcoccinone B was greater than that of kadcoccinone C, probably due to the cleavage and condensation reactions between C-12 and C-14, which reduced the cytotoxic activity. In addition, kadcoccinone E was more cytotoxic than its isoform kadcoccinone D, suggesting that the 23*S*, 24*R* conformation may potentiate the potency of cytotoxic activity compared to the 23*R*, 24*S* conformation of the epoxide moiety.

Yang et al. evaluated the in vitro cytotoxicity of compounds longipedlactone A-M against cancer cell lines using 10-hydroxycamptothecin as a positive control. The results showed that longipedlactones A, F, J, and M had significant cytotoxic activity in vitro against three human tumor cells, A549, HT-29, and K562. Researchers suggested that this might be related to the presence of double bonds of C-10 and C-19 forming a co-choke system with *α*, *β* unsaturated lactones, and verified the above speculation by further pharmacological experiments [42]. Pu et al. isolated the compounds Kadlongilactones A-D from *K. longipedunculata* and found that all the compounds had a significant cytotoxic effect on A549, HT-29 and K562, but Kadlongilactone C had the strongest effect [47]. In addition, kadcoccine acids A-H were screened for tumor cell toxicity in vitro and only

kadcoccine acid H was found to have weak cytotoxicity; kadlongilactones A-B showed significant inhibition activity against K562, A549, and Bel7402 cell lines [20].

4.2. Anticoagulant Activity

Xu et al. evaluated the anti-platelet aggregation effect of Kadcoccitanes A, C and D. It was illustrated that the inhibition rates of Kadcoccitanes C-D were 12.4 ± 12.5% and 19.4 ± 14.4% ($p<0.05$). Furthermore, Kadcoccitanes A and D also showed inhibition of coagulation factors [33]. It has been shown that the extract of *K. longipedunculata* can significantly inhibit thrombosis and platelet aggregation in the body through a damaged intravenous route of administration, as well as reduce the phosphorylation of downstream signaling molecules mitogen-activated protein kinase, which is a potential drug for the development of prevention and treatment of cardiovascular diseases [81].

4.3. Anti-HIV Activity

Researchers tested the anti-HIV activity of kadcoccnic acids A-H and found that kadcoccinics acid D and H were able to significantly inhibit HIV viral activity [28]. The kadcoccitones A and C isolated from the roots of *K. coccinea* showed moderate activity in the anti-HIV-1 activity test [62]. Xu et al. [59] screened the isolated triterpenes for cytotoxicity in tumor cell lines. The results showed that longipedlactones A and F had significant cytotoxicity against HepG2 and Bel7402 tumor cell lines.

Additionally, screening of active ingredients for HIV-1 protease and reverse transcriptase inhibition was also done. The assay results showed that compounds nigranoic acid and kadsuranic acid A exhibited strong inhibition of HIV-1 PR, while schisandronic acid showed medium activity and the other compounds showed only weak activity. Li et al. found that micrandilactone C had a strong inhibiting effect on HIV-1 cells and significantly inhibited HIV-1 infection of C8166 cells and reduced cytopathic lesions [63].

4.4. Hepatoprotective Activity

K. longipedunculata was first published in '*Shennong Ben Cao Jing*'. Its effect is good at nourishing the liver and kidneys and has high medicinal value. In conjunction with recent reports, it has made great progress in the repair of liver injury. Research shows that vinegared *K. longipedunculata* soaked in vinegar significantly reduced the elevation of alanine aminotransferase (ALT) and aspartate aminotransferase (AST) and increased the activity of glutathione (GSH-Px) and superoxide dismutase (SOD) in serum of rats with liver injury, inhibit the expression of hepatocytes hypoxia-inducible factor-1α (HIF-1α), and effectively reduce the effect of acute liver injury on rat organism [78]. Shao et al. [48] found in the cytotoxic activity test of the isolated obtained compounds that micrandilactone I had moderate hepatoprotective activity against *N*-acetyl-*p*-aminophenol (APAP)-induced cytotoxicity in HepG2. Cell survival was 53.04%.

The triterpenoid component of *K. longipedunculata* has a protective effect against liver injury, based on this, some related proprietary Chinese medicines have achieved good therapeutic results. Among them, the extract of *K. longipedunculata* was used to treat fatty liver in rats by affecting the expression of peroxidase receptor and adenosine-activated protein kinase [81]. The alcoholic extract of *K. longipedunculata* showed a significant inhibitory effect on APAP-induced hepatocyte apoptosis and was able to significantly ameliorate drug-induced pathological damage [79].

Moreover, it was reported that the alcoholic extract of *K. longipedunculata* could also alleviate atherosclerosis in rats by enhancing antioxidant capacity.

4.5. Antioxidant Activity

Yan et al. used the DPPH method to test the in vitro antioxidant activity of *K. coccinea* and found that its ethanolic extract had good activity, suggesting that *K. coccinea* has some prospect in the development of natural antioxidants [77]. In addition to this, the protective effect and mechanism of the extract of *K. longipedunculata* on oxidative stress in diabetic mice were investigated [80], it was found that the extract can reduced the blood glucose level and malondialdehyde level in diabetic mice, improve renal tissue damage caused by oxidative stress. It is speculated that the mechanism of action may be related to the upregulation of antioxidant factors and downstream genes.

Scholars investigated the antioxidant capacity of *K. longipedunculata* through 1,1-diphenyl-2-trinitrophenylhydrazine and thyroid cancer cell experiments. The results reveal that *K. longipedunculata* has a certain antioxidant capacity, which can alleviate the damage caused by oxidative stress to the organism [81].

4.6. Cholesterol Biosynthesis Inhibitory Activity

Kangouri et al. found that the ethanol extract of *K. heteroclita* was effective in inhibiting cholesterol biosynthesis, where Compound **122** was identified as responsible for this biological activity [35]. Besides, the compounds **49** and **64** have also been reported to have cholesterol synthesis inhibitory effects [15].

5. Clinical Applications

The genus *Kadsura* has a long history of use in China, it is commonly used in the treatment of insomnia and liver and kidney damage due to its traditional effects of strengthening the spleen, benefiting the qi and calming the mind. Achieved good treatment results. Clinical observations have shown that Shenqi Schisandra Tablets can significantly shorten the time to sleep and improve the sleep quality of patients with insomnia [67]. Adjunctive treatment of nephrotic syndrome with *K. longipedunculata* on basis of conventional treatment resulted in a reduction in edema and a gradual decrease in albumin and lipids [68]. Fu et al. used Wuzhi tablets to treat and prevent liver damage, and the results showed that the drug could effectively reduce the occurrence of liver damage during anti-tuberculosis treatment with high safety [69]. Zhang et al. conducted a phase II_b clinical trial research on the effectiveness and safety of Nanwuweizi softcapsule in the treatment of insomnia. According to research findings, high doses of Nanwuweizi softcaspule have outstanding efficacy and better safety for insomnia [70].

6. Developing Applications

6.1. New Drug Discovery

Cycloartane-type of triterpenoids from *K. heteroclita* can significantly restrains HIV integrase and reverse transcriptase activities. Its high antiviral activity and low toxic side effects are significance for the research and development of anti-HIV drugs [65]. To investigate the anti-inflammatory effects and targets of action of total triterpene alcoholic extracts of *K. heteroclita* on rheumatoid arthritis by pharmacological experiments, the results showed that inflammatory cells

were significantly reduced, and inflammation was alleviated in the treatment group, which laid the foundation for the development of new anti-rheumatic drugs. Furthermore, extracts of *K. longipedunculata* can increase the concentration of tacrolimus in the blood of liver transplant patients, reduce the rejection reactions triggered after transplantation. It can also improve the patient's liver function and reduce the impact of postoperative adverse reactions [66].

6.2. Food Development

Genus *Kadsura* is often used in the food industry for its good antioxidant, hepatoprotective and vasodilating effects. A health drink made from *K. longipedunculata* was able to relieve fatigue and enhance the quality of sleep of patients [70-72]. The fruit of *K. coccinea* contains 14 kinds of hydrolyzed amino acids, with a high content of essential amino acids, as well as many essential minerals [73-74]. Zhao et al. used the ethanolic extract of *K. longipedunculata* compounded with Vc and other components, discovery of a compound preservative that efficiently inhibits egg spoilage bacteria [75-76].

7. Conclusions

China is rich in the genus *Kadsura*, which has a long history of medicinal use and a large number of precedents of clinical application. With the continuous research on this genus, its modern pharmacological effects have been greatly developed. In particular, its main pharmacological component-triterpene [82], has been reported to have rich pharmacological activity [83-84]. It is effective in anti-HIV, antioxidant, anticoagulant, cholesterol biosynthesis inhibition and liver protection. A review of the literature in recent years revealed a lack of relevant reports on this genus. Additionally, there is still no complete quality standard system for the genus *Kadsura*, and the mechanism of action of its active ingredients still needs to be studied.

Currently, the research and development of monomeric compounds of the genus *Kadsura* is most prominent in the study of kadsuric acid, which not only inhibits the ubiquitination modification of autophagy receptor p62 and prevents the activation of receptor function, but also significantly inhibits tumor cell growth. It has great significance for the development of autophagy inhibitors and novel anti-tumor drugs. Today, it is found that *K. longipedunculata* extract stimulates the fuselage to produce TNF-α and activate mitogen-activated protein kinase to elicit different immune responses. At the same time, the extract can also significantly relive the rejection reaction caused by transplantation and reduce the postoperative adverse effects. The mechanism of action can be explored in the future in terms of regulation of the immune system. In clinical applications, the root bark of *K. longipedunculata* can be used to treat joint and muscle pain, prostate enlargement, etc. Which deserves further exploration. Moreover, Because of its good antioxidant and hepatoprotective effects, the genus *Kadsura* is used as a health food and natural preservative in many countries and regions.

In recent years, researchers have continued to isolate new chemical components from genus *Kadsura*, which play an increasingly important role in modern medicine. Therefore, more comprehensive pharmacological activity exploration and mechanism of action studies should be conducted subsequently to provide more possibilities for the development of new drugs and new products, and to further exploit the medicinal and economic value of the genus *Kadsura*.

Acknowledgments

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Competing Interests

Authors have declared that no competing interests exist.

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