ChemInform Abstract: Chemical and Pharmacological Studies of the Plants from Genus Celastrus

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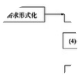
7 AUTHORS, INCLUDING:


Manli Zhang
Hebei Medical University


Shi Qing
Beijing University of Chemical Technology


Yu-Cheng Gu
Syngenta


Hiromasa Kiyota
Okayama University

REVIEW

Chemical and Pharmacological Studies of the Plants from Genus *Celastrus*

by **Xiao-Hui Su**[a]), **Man-Li Zhang**[a]), **Wen-Hong Zhan**[a]), **Chang-Hong Huo**[a]), **Qing-Wen Shi***[a]), **Yu-Cheng Gu**[b]), and **Hiromasa Kiyota**[c])

[a]) School of Pharmaceutical Sciences, Hebei Medical University, 361 Zhongshan East Road, Shijiazhuang 050017, Hebei Province, P. R. China (e-mail: shiqingwen@hebmu.edu.cn)
[b]) Jealott's Hill International Research Centre, Syngenta, Berkshire, RG42 6EY, UK
[c]) Graduate School of Agricultural Sciences, Tohoku University, 1-1 Tsutsumidori-Amamiya, Aoba-ku, Sendai 981-8555, Japan

The plants of genus *Celastrus*, distributed in Asia, have been used as natural insecticides and folk medicines to treat fever, chill, joint pain, edema, rheumatoid arthritis, and bacterial infection in China for a long time. This contribution reviews the chemical constituents, **1**–**144**, isolated from the plants in genus *Celastrus* in the past few decades, and their biological activities. The compounds listed are sesquiterpenes (β-agarofurans), diterpenes, triterpenes, alkaloids, and flavonoids.

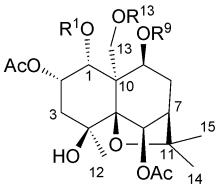
Contents

1. Introduction. – The genus *Celastrus* comprise *ca.* 50 species throughout the world. They are widely distributed in Asia, especially in China [1]. The plants of Celastraceae family have been used as natural insecticides [2], and also as important folk medicines to treat fever, chill, joint pain, edema, rheumatoid arthritis, and bacterial infection in China for a long time [3]. For example, *C. hypoleucus* has been used for the treatment of inflammation and detumescence [4]. *C. orbiculatus* has been used to treat rheumatoid arthritis and bacterial infection in folk medicine [5]. Previous studies on chemical constituents have disclosed the presence of various β-dihydroagarofuran sesquiterpene polyol esters and alkaloids [4]; some of them exhibited insecticidal or insect antifeedant activities, and antitumor activities [6][7]. Recently, the antitumor-promoting activity of β-dihydroagarofuran compounds has also been reported [8].

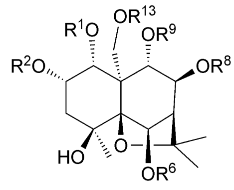
In this review, we summarize the phytochemical progress, and list all of the compounds isolated from the genus *Celastrus* over the past few decades. Also included are the biological activities of compounds isolated in recent years, and a few structure–activity relationships were also discussed.

2. Phytochemical and Biological Studies. – 2.1. *Sesquiterpenes* (*β-Agarofurans* **1**–**97**). The family Celastraceae is well-known to produce various *β*-dihydroagarofuran derivatives. We now list 97 compounds of this type which were obtained since 1980s. The plants investigated include C. *angulatus*, *C. orbiculatus*, *C. paniculatus*, *C. stephanotiifolius*, *C. flagellaris*, *C. gemmatus*, *C. hindsii*, *C. rosthornianus*, *etc*. The most substitution variation was found in positions C(4), C(6), and C(13) of the skeleton. For example, the C(4) of compounds **1**–**27** are all replaced by a OH group in comparison to the others (*Table*). The ^{13}C-NMR spectra of *β*-dihydroagarofuran derivatives have two common characteristics at δ(C) 89.0 and 50.0 ppm, which indicate the presence of C(5) and C(10), respectively.

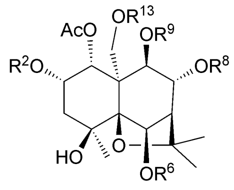
The insecticidal sesquiterpene polyol esters **1**–**22** were all isolated from the root bark of *C. angulatus* except compound **5**, which was obtained from the leaves of the same plant (*Table*). Compounds **16**–**20** exhibited insecticidal activity against the larvae of *Mythimna separata* with the KD_{50} values of 168.8, 58.9, 91.4, 271.5, and 159.8 μg/g, respectively. The presence of a *β*-furancarbonyloxy group in **16** and **17** was considered to be the reason why **18**–**20** were more active than **16** and **17** [16]. Sesquiterpenoids **23**–**36** were isolated from *C. paniculatus* subsp. *paniculatus*, *C. rosthornianus*, *C. hindsii*, *C. paniculatus*, *C. angulatus*, and *C. flagellaris*, respectively. The root of *C. orbiculatus* yielded 14 sesquiterpene esters, **37**–**50** (*Table*). Compounds **48**–**52** were also obtained from the seeds of *C. stephanotiifolius* together with **61**–**63** and **66**–**70**. Sesquiterpenes **39**, **42**–**44**, **46**, and **47**, a diterpene, celaphanol A (**98**), and a triterpene, celastrol (**111**), were tested for their effects on LPS-induced NF-*κ*B activation in murine macrophage RAW264.7 cells transfected with NF-*κ*B-mediated reporter gene construct, and on nitric oxide (NO) production in LPS-stimulated RAW264.7 cells [28]. Celastrol (**111**) was the most active, while compounds orbiculins D, H, and I (**42**, **46**, and **47**, resp.), and celaphanol A (**96**) showed moderate inhibition in both NF-*κ*B activation and NO production. The results also suggested that the furoyloxy groups at C(6) and C(9) (orbiculins H, I, and D) are important structural factors of dihydro-*β*-agarofuran sesquiterpenes in the modulation of NF-*κ*B activity. Investigating MDR-reversing activity, *S. E. Kim et al.* discovered that orbiculin A (**39**), celafolin A-1 (**48**), and celorbicol ester (**49**) partially or completely reversed resistance to adriamycin (ADR), vinblastine (VLB), and paclitaxel (TX) of multidrug-resistant KB-V1 and MCF7/ADR cells [27]. Compound **37**, ejap-2 (**38**), orbiculin A (**39**), orbiculin E (**43**), orbiculin F (**44**), and triptogelin C-1 (**50**) turned out to be more active than verapamil in reversing vinblastine resistance in multidrug-resistant KB-V1 cells [26]. Orbiculin A (**39**), orbiculin E (**43**), and triptogelin C-1 (**50**), which have an AcO group at C(2), showed strong reversal activity; orbiculin F (**44**) with a furoyloxy at C(2) was half active compared to orbiculin E (**43**); orbiculin G (**45**) with a benzoyloxy at C(2) was the weakest; compounds **37** and **38**, which have two AcO groups at C(1) and C(13), exhibited strong activity irrespective of the presence of an ester group at C(2). These results suggest that the polarity of C(1)/C(2) or C(1)/C(13) is an important factor in



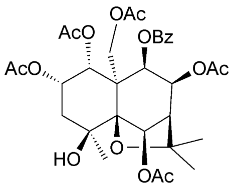
	R1	R9	R13
1	Nic	Fu	iBut
2	Nic	Fu	Hang
3	Nic	Fu	Ac
4	Nic	Bz	Ac



	R1	R2	R6	R8	R9	R13
5	Cin	Ac	Ac	Ac	Ac	Ac
6	Ac	Ac	H	iBut	Bz	Hang
7	Ac	Ac	H	Fu	Bz	iBut
8	Ac	Ac	H	iBut	Bz	iBut
9	Ac	iBut	H	Nic	Bz	Ac



	R2	R6	R8	R9	R13
10	Fu	Ac	iBut	Nic	iBut
11	Ac	Ac	iBut	Fu	iBut
12	Ac	Ac	Fu	Fu	Hang
13	Ac	H	iBut	Bz	Ac
14	Ac	Ac	Fu	Fu	iBut
15	Ac	Ac	Ac	Bz	iBut
16	Ac	Ac	Fu	Bz	iBut
17	Ac	Ac	iBut	Fu	Hang
18	Ac	Ac	iBut	Bz	iBut
19	Ac	Ac	iBut	Bz	Hang



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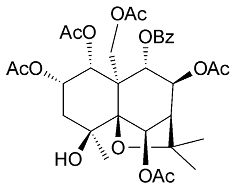

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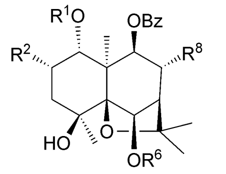
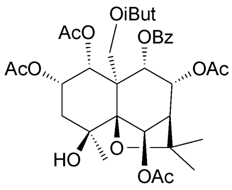


	R1	R2	R6	R8
23	Bz	H	Ac	H
24	Bz	H	Bz	H
25	Ac	OBz	H	OBz
26	Ac	OFu	H	OBz
27	Ac	OHang	H	OBz



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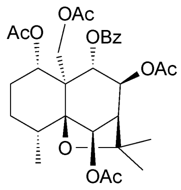

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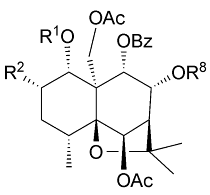
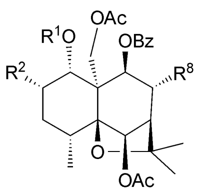
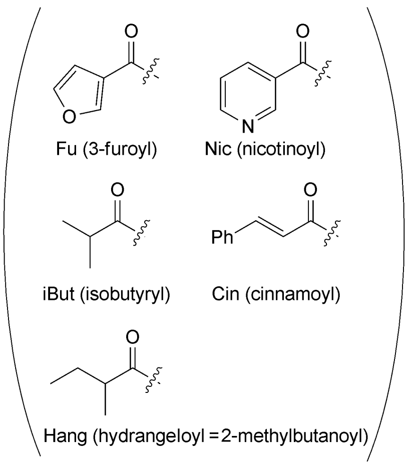
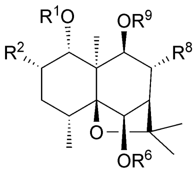


	R1	R2	R8
29	Ac	OH	Ac
30	Bz	OAc	Nic
31	H	OAc	Nic
32	Ac	H	Ac

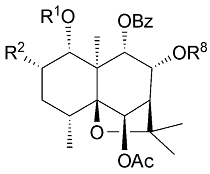


	R1	R2	R8
33	Ac	H	OAc
34	Ac	OAc	H
35	H	OAc	H
36	Ac	OAc	OBz
37	Ac	OBz	H
38	Ac	H	H

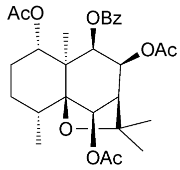




	R^1	R^2	R^6	R^8	R^9
39	Ac	OAc	Bz	H	Bz
40	Ac	H	Fu	H	Bz
41	Ac	H	Bz	H	Fu
42	Ac	H	Fu	H	Fu
43	Ac	OAc	Fu	H	Bz
44	Ac	OFu	Fu	H	Bz
45	Ac	OBz	Bz	H	Bz
46	Ac	H	Fu	OAc	Fu
47	Ac	OFu	Fu	H	Fu
48	Ac	H	Cin	H	Bz
49	Ac	H	Bz	H	Bz
50	Ac	OAc	Ac	H	Bz
51	Ac	H	Ac	H	Bz
52	Ac	H	Ac	OAc	Bz
53	H	H	H	H	H
54	Ac	OHang	H	OBz	Bz
55	Ac	OHang	H	OFu	Bz
56	Ac	OAc	Bz	H	Cin
57	Ac	H	Ac	OAc	Fu



	R^1	R^2	R^8
58	Ac	H	Cin
59	H	OH	Bz
60	Ac	H	Bz
61	Bz	H	Bz
62	Bz	H	Hang
63	Bz	H	H
64	Ac	H	Ac



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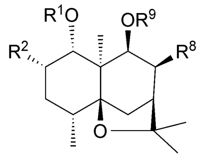
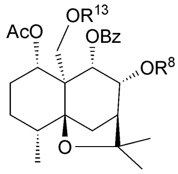
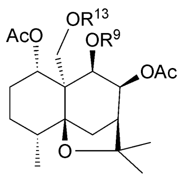


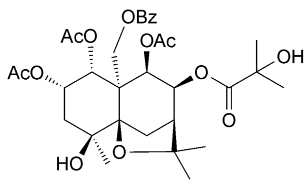
	R^1	R^2	R^8	R^9
66	H	OAc	H	Cin
67	Ac	OAc	H	Cin
68	Ac	OH	H	Cin
69	Ac	OBz	H	Cin
70	Ac	H	H	Cin
71	H	H	H	H
72	Ac	OAc	OAc	Cin
73	Ac	Cin	H	Cin
74	Ac	OAc	H	EpCin
75	Ac	OBz	H	EpCin
76	Ac	OBut	H	EpCin
77	Ac	H	H	EpCin



	R^8	R^{13}
89	Bz	Nic
90	Ac	Ac



	R^9	R^{13}
91	Nic	Bz
92	Fu	Ac



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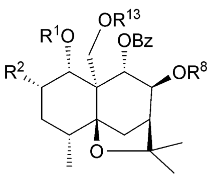
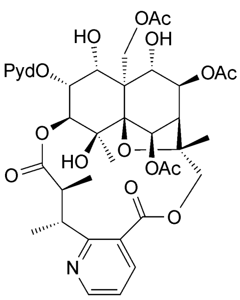


	R^1	R^2	R^8	R^{13}
78	Ac	H	Ac	Nic
79	Ac	OAc	Ac	Nic
80	Ac	OAc	Ac	Pic
81	Ac	OAc	Ac	Ac
82	Ac	H	Ac	Ac
83	Ac	H	Ac	Pic
84	iBut	H	Ac	Nic
85	Prp	H	Ac	Nic
86	Ac	H	H	Nic
87	Ac	H	Hang	Nic
88	Ac	H	iBut	Nic



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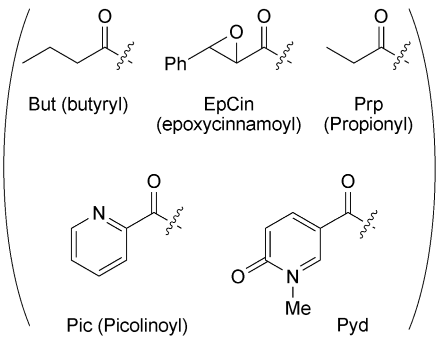
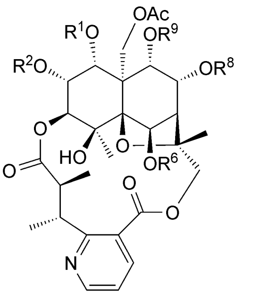
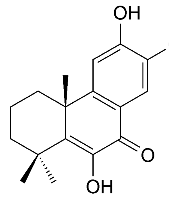




	R^1	R^2	R^6	R^8	R^9
95	Ac	Nic	Ac	iBut	Ac
96	Bz	Ac	Bz	Ac	Bz
97	Ac	Pyd	Ac	Ac	Ac



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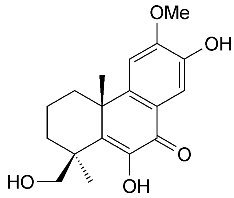

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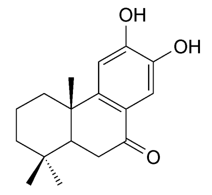

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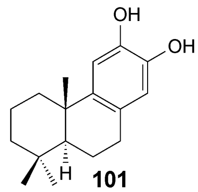

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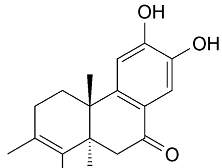

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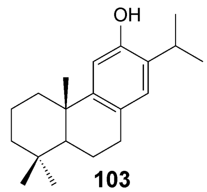

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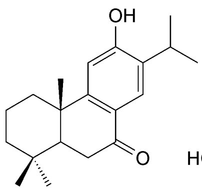

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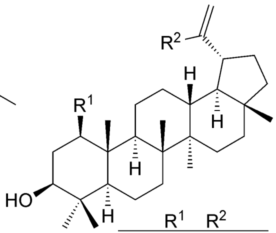
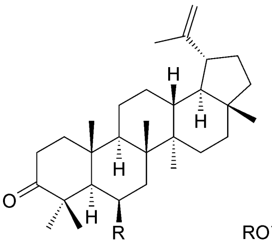
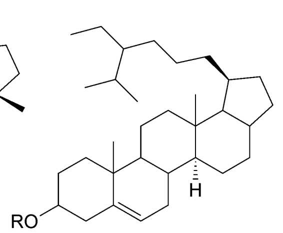


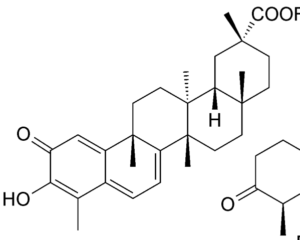
	R^1	R^2
105	H	$HOCH_2$
106	OH	Me



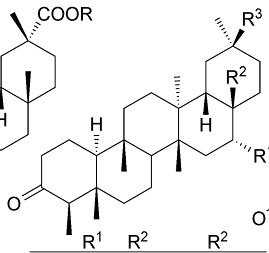
107 R = OH
108 R = H



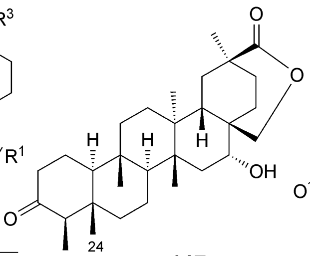
109 R = Glc
110 R = H



111 R = H
112 R = Me



	R^1	R^2	R^2
113	OH	Me	$HOCH_2$
114	OH	$HOCH_2$	Me
115	H	Me	Me
116	H	$HOCH_2$	Me



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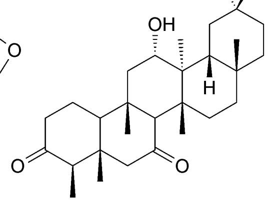

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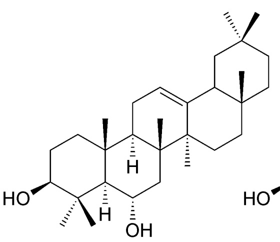

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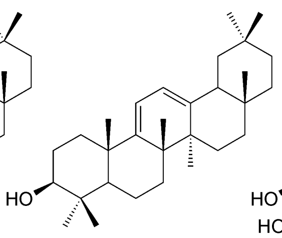

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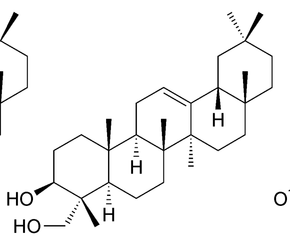

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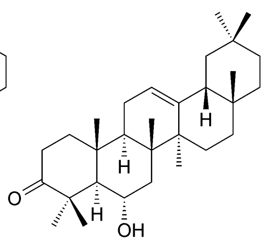

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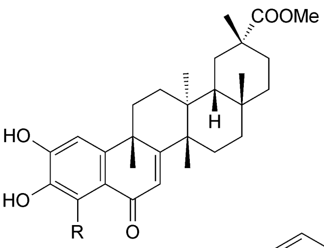
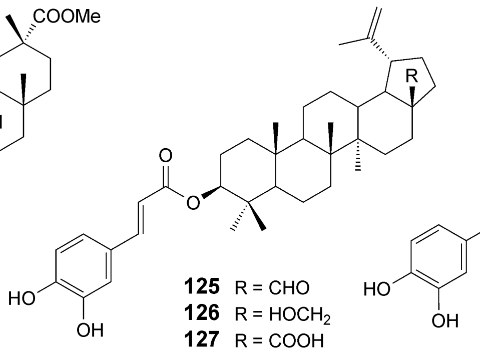
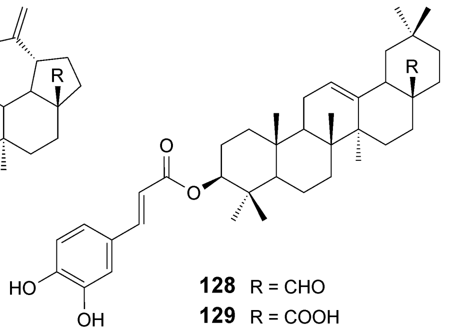


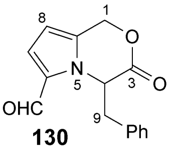
123 R = COOH
124 R = CHO



125 R = CHO
126 R = $HOCH_2$
127 R = COOH



128 R = CHO
129 R = COOH



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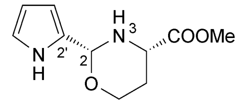

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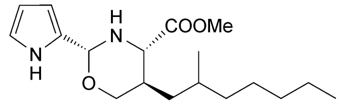

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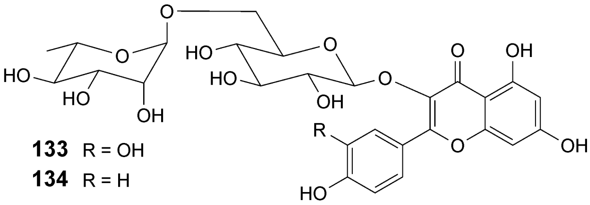
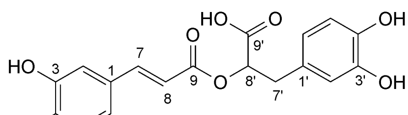


133 R = OH
134 R = H



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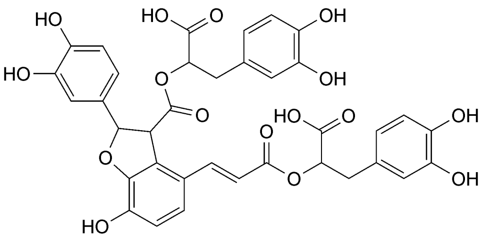

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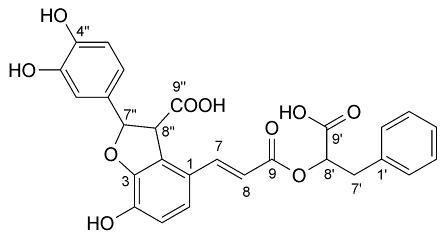

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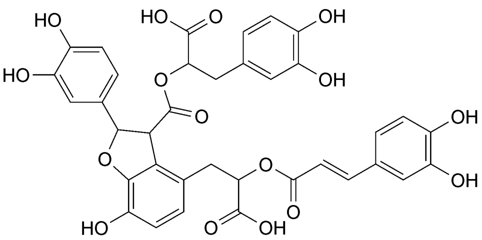

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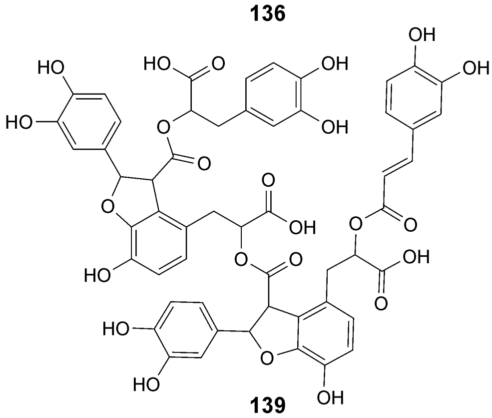

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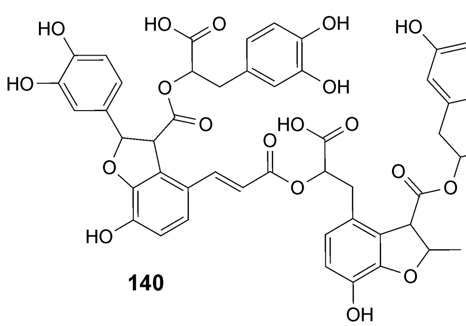

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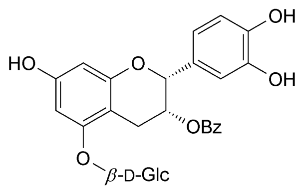

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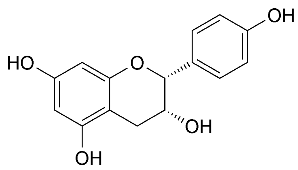

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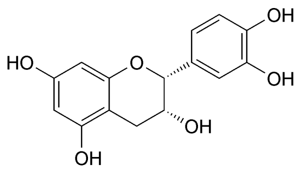

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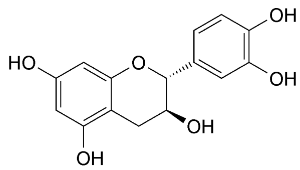

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MDR-reversal activity [26]. In addition, compounds **49**–**52**, **63**, and **66**–**67** were also examined for the inhibitory tendency on the EBV-EA (*Epstein*–*Barr* virus early antigen) activation. The inhibitory effects of compounds **63** and **66** on the activation of early antigen and the viabilities of *Raji* cell were stronger than those of other compounds [29]. Compounds **53**–**58** were isolated from *C. orbiculatus*, *C. rosthornianus*, *C. hindsii*, and *C. paniculatus.* Angulatueoid G (**59**) and angulatueoid H (**60**) were obtained from the seeds of *C. angulatus* (*Table*). Angulatueoid G (**59**; 100 ppm) showed insect antifeedant effect against *Aulacophora femoralis* (73.2% antifeedant rate) and *Piutella xylostella* (87.7% antifeedant rate) [34]. The plant *C. orbiculatus* also contained the sesquiterpene isocelorbicol **71** and **72**. Celastrine B (**73**) was obtained from *C. flagellaris.* The seed oil of *C. gemmatus* was the source of compounds **74**–**77**. The investigation of the seeds and seed oil of *C. angulatus* led to the isolation of **78**–**91**. Besides **28**, **57**, and **58**, compound **92** was also isolated from *C. paniculatus.* Compound **93**, which was obtained from the leaves of *C. angulatus*, showed strong nonselective cytotoxicity against four of the NCl panel cell lines (leukemia (PRMI-8226), CNS cancer (U251), prostate cancer (PC-3), and breast cancer (MDA-MB-231/ATCC)) through preliminary biological study on antitumor activity [41]. The more special compounds are **94**–**97**, which were isolated from *C. gemmatus* and *C. hindsii.* Besides the 6/6/5 rings, C(3) and C(14) also form another large ring with a fused pyridine ring.

2.2. *Diterpenes* **98**–**104**. In 1999, *Chen et al.* isolated three diterpenes, **98**–**100**, from the stem of *C. stephanotifolius* (*Table*). Celaphanol A (**98**) was also obtained from *C. orbiculatus. Xiong et al.* reported the isolation and synthesis of (+)-7-deoxynimbidiol (**101**) in 2006. In the same year, *Wang et al.* isolated three diterpenes, *i.e.*, celahypodiol (**102**), furreginol (**103**), and suigol (**104**), together with three triterpenes, **107**, **108**, and **119**, from *C. hypoleucus.* Celahypodiol (**102**) and (3β)-olean-12-ene-3,23-diol (**119**)

Table. *Chemical Constituents from the Genus* Celastrus

Compound	Name	Plant	Part	Ref.
1	2α,6β-Diacetoxy-9β-(3-furoyloxy)-13-(isobutyryloxy)-1α-(nicotinoyloxy)-β-dihydroagarofuran-4β-ol	*C. angulatus*	Root bark	[9]
2	2α,6β-Diacetoxy-9β-(3-furoyloxy)-13-[(2-methylbutanoyl)oxy]-1α-(nicotinoyloxy)-β-dihydroagarofuran-4β-ol	*C. angulatus*	Root bark	[9]
3	2α,6β,13-Triacetoxy-9β-(3-furoyloxy)-1α-(nicotinoyloxy)-β-dihydroagarofuran-4β-ol	*C. angulatus*	Root bark	[9]
4	2α,6β,13-Triacetoxy-9β-(benzoyloxy)-1α-(nicotinoyloxy)-β-dihydroagarofuran-4β-ol	*C. angulatus*	Root bark	[9]
5	2α,6β,8β,9α,13-Pentaacetoxy-1α-(cinnamoyloxy)-β-dihydroagarofuran-4β-ol	*C. angulatus*	Leaf	[10]
6	1α,2α-Diacetoxy-9α-(benzoyloxy)-8β-(isobutyryloxy)-13-[(2-methylbutanoyl)oxy]-β-dihydroagarofuran-4β,6β-diol	*C. angulatus*	Root bark	[11]
7	1α,2α-Diacetoxy-9α-(benzoyloxy)-8β-(3-furoyloxy)-13-(isobutyryloxy)-β-dihydroagarofuran-4β,6β-diol	*C. angulatus*	Root bark	[11]
8	Angulatin A	*C. angulatus*	Root bark	[12]
9	1α,13-Diacetoxy-9α-(benzoyloxy)-2α-(isobutyryloxy)-8β-(nicotinoyloxy)-β-dihydroagarofuran-4β,6β-diol	*C. angulatus*	Root bark	[13]
10	1α,6β-Diacetoxy-2α-(3-furoyloxy)-8α,13-bis(isobutyryloxy)-9β-(nicotinoyloxy)-β-dihydroagarofuran-4β-ol	*C. angulatus*	Root bark	[13]
11	1α,2α,6β-Triacetoxy-9β-(3-furoyloxy)-8α,13-bis(isobutyryloxy)-β-dihydroagarofuran-4β-ol	*C. angulatus*	Root bark	[14]
12	1α,2α,6β-Triacetoxy-8α,9β-bis(3-furoyloxy)-13-[(2-methylbutanoyl)oxy]-β-dihydroagarofuran-4β-ol	*C. angulatus*	Root bark	[14]
13	1α,2α,13-Triacetoxy-9β-(benzoyloxy)-8α-(isobutyryloxy)-β-dihydroagarofuran-4β,6β-diol	*C. angulatus*	Root bark	[14]
14	Celangulin II: 1α,2α,6β-triacetoxy-8α,9β-bis(3-furoyloxy)-13-(isobutyryloxy)-β-dihydroagarofuran-4β-ol	*C. angulatus*	Root bark	[14][15]
15	Celangulin III	*C. angulatus*	Root bark	[15]
16	1α,2α,6β-Triacetoxy-9β-(benzoyloxy)-8α-(3-furoyloxy)-13-(isobutyryloxy)-β-dihydroagarofuran-4β-ol	*C. angulatus*	Root bark	[16]
17	1α,2α,6β-Triacetoxy-9β-(3-furoyloxy)-8α-(isobutyryloxy)-13-[(2-methylbutanoyl)oxy]-β-dihydroagarofuran-4β-ol	*C. angulatus*	Root bark	[16]
18	1α,2α,6β-Triacetoxy-9β-(benzoyloxy)-8α,13-bis(isobutyryloxy)-β-dihydroagarofuran-4β-ol	*C. angulatus*	Root bark	[16]
19	1α,2α,6β-Triacetoxy-9β-(benzoyloxy)-8α-(isobutyryloxy)-13-[(2-methylbutanoyl)oxy]-β-dihydroagarofuran-4β-ol	*C. angulatus*	Root bark	[16]
20	1α,2α,6β,8β,13-Pentaacetoxy-9β-(benzoyloxy)-β-dihydroagarofuran-4β-ol	*C. angulatus*	Root bark	[16]
21	Celangulin	*C. angulatus*	Root bark	[2]

Table (cont.)

Compound	Name	Plant	Part	Ref.
22	Celangulin IV	*C. angulatus*	Root bark	[15]
23	6β-Acetoxy-1α,9β-bis(benzoyloxy)-β-dihydro-agarofuran-4β-ol	*C. paniculatus*, subsp. *paniculatus*	Seed	[17]
24	1α,6β,9β-Tris(benzoyloxy)-β-dihydroagaro-furan-4β-ol	*C. paniculatus*, subsp. *paniculatus*	Seed	[17]
25	1α-Acetoxy-2α,8α,9β-tris(benzoyloxy)-β-dihydroagarofuran-4β,6β-diol	*C. rosthornianus*	Root bark	[18]
26	1α-Acetoxy-8α,9β-bis(benzoyloxy)-2α-(3-furoyl-oxy)-β-dihydroagarofuran-4β,6β-diol	*C. rosthornianus*	Root bark	[18]
27	1α-Acetoxy-8α,9β-bis(benzoyloxy)-2α-[(2-methyl-butanoyl)oxy]-β-dihydroagarofuran-4β,6β-diol	*C. rosthornianus* *C. hindsii*	Root bark Stem	[19] [20]
28	1α,6β,8β,13-Tetraacetoxy-9α-(benzoyloxy)-β-dihydroagarofuran	*C. paniculatus*	Whole plant Seed	[21] [22]
29	1α,6β,8α,13-Tetraacetoxy-9α-(benzoyloxy)-β-dihydroagarofuran-2α-ol	*C. angulatus*	Root bark	[11]
30	2α,6β,13-Triacetoxy-1α,9α-bis(benzoyloxy)-8α-(nicotinoyloxy)-β-dihydroagarofuran	*C. angulatus*	Leaf	[23]
31	2α,6β,13-Triacetoxy-9α-(benzoyloxy)-8α-(nicotinoyloxy)-β-dihydroagarofuran-1α-ol	*C. angulatus*	Leaf	[23]
32	Celastrine A	*C. flagellaris*	Seed oil	[24]
33	Ejap-3	*C. flagellaris*	Seed oil	[24]
34	Celahin B	*C. hindsii*	Stem	[25]
35	Celahin C	*C. hindsii*	Stem	[25]
36	Celahin D	*C. hindsii*	Stem	[20]
37	1α,6β,13-Triacetoxy-2α,9β-bis(benzoyloxy)-β-dihydroagarofuran	*C. orbiculatus*	Root	[26]
38	Ejap-2	*C. orbiculatus*	Root	[26]
39	Orbiculin A	*C. orbiculatus*	Root	[27]
40	Orbiculin B	*C. orbiculatus*	Root	[26]
41	Orbiculin C	*C. orbiculatus*	Root	[26]
42	Orbiculin D	*C. orbiculatus*	Root	[26]
43	Orbiculin E	*C. orbiculatus*	Root	[26]
44	Orbiculin F	*C. orbiculatus*	Root	[26]
45	Orbiculin G	*C. orbiculatus*	Root	[26]
46	Orbiculin H	*C. orbiculatus*	Root	[28]
47	Orbiculin I	*C. orbiculatus*	Root	[28]
48	Celafolin A-1	*C. stephanotiifolius* *C. orbiculatus*	Seed Root	[29] [27]
49	1α-Acetoxy-6β,9β-bis(benzoyloxy)-β-dihydro-agarofuran	*C. stephanotiifolius* *C. orbiculatus*	Seed Root	[29] [27]
50	Triptogelin C-1	*C. orbiculatus* *C. stephanotiifolius*	Root Seed	[26] [29]
51	1α,6β-Diacetoxy-9β-(benzoyloxy)-β-dihydro-agarofuran	*C. stephanotiifolius*	Seed	[29]
52	Celafolin C-1	*C. stephanotiifolius*	Seed	[29]
53	Celorbicol	*C. orbiculatus*	Seed oil	[30]
54	1α-Acetoxy-8α,9β-bis(benzoyloxy)-2α-[(2-methyl-butanoyl)oxy]-β-dihydroagarofuran-6β-ol	*C. rosthornianus* *C. hindsii*	Root bark Stem	[31] [20]
55	1α-Acetoxy-9β-(benzoyloxy)-8α-(3-furoyloxy)-2α-[(2-methylbutanoyl)oxy]-β-dihydroagarofuran-6β-ol	*C. rosthornianus*	Root bark	[31]

Table (cont.)

Compound	Name	Plant	Part	Ref.
56	1α,2α-Diacetoxy-6β-(benzoyloxy)-9β-(cinnamoyl-oxy)-β-dihydroagarofuran	*C. orbiculatus*	–	[32]
57	1α,6β,8α-Triacetoxy-9β-(3-furoyloxy)-β-dihydro-agarofuran	*C. paniculatus*	Seed oil	[33]
58	1α,6β-Diacetoxy-9α-(benzoyloxy)-8α-(cinnamoyl-oxy)-β-dihydroagarofuran	*C. paniculatus*	Seed oil	[33]
59	Angulatueoid G	*C. angulatus*	Seed	[34]
60	Angulatueoid H	*C. angulatus*	Seed	[34]
61	Celafolin D-1	*C. angulatus*	Seed oil	[35]
		C. stephanotiifolius	Seed	[29]
62	Celafolin D-3	*C. stephanotiifolius*	Seed	[29]
63	Celafolin D-2	*C. stephanotiifolius*	Seed	[29]
64	1α,6β,8α-Triacetoxy-9α-(benzoyloxy)-β-dihydroagarofuran	*C. paniculatus*	Seed	[22]
65	1α,6β,8β-Triacetoxy-9β-(benzoyloxy)-β-dihydroagarofuran	*C. paniculatus*	Seed	[22]
66	Celafolin B-2	*C. stephanotiifolius*	Seed	[29]
67	1α,2α-Diacetoxy-9β-(cinnamoyloxy)-β-dihydroagarofuran	*C. stephanotiifolius*	Seed	[29]
		C. flagellaris	Seed oil	[24]
68	Celafolin B-1	*C. stephanotiifolius*	Seed	[29]
69	Celafolin B-3	*C. stephanotiifolius*	Seed	[29]
		C. flagellaris	Seed oil	[24]
70	1α-Acetoxy-9β-(cinnamoyloxy)-β-dihydro-agarofuran	*C. stephanotiifolius*	Seed	[29]
71	Isocelorbicol	*C. orbiculatus*	Seed oil	[30]
72	1α,2α,8β-Triacetoxy-9β-(cinnamoyloxy)-β-dihydroagarofuran	*C. orbiculatus*	–	[32]
73	Celastrine B	*C. flagellaris*	Seed oil	[24]
74	1α,2α-Diacetoxy-9β-[(2,3-epoxy-3-phenylpro-panoyl)oxy]-β-dihydroagarofuran	*C. gemmatus*	Seed oil	[7]
75	1α-Acetoxy-2α-(benzolyloxy)-9β-[(2,3-epoxy-3-phenylpropanoyl)oxy]-β-dihydroagarofuran	*C. gemmatus*	Seed oil	[7]
76	1α-Acetoxy-2α-(butanoyloxy)-9β-[(2,3-epoxy-3-phenylpropanoyl)oxy]-β-dihydroagarofuran	*C. gemmatus*	Seed oil	[7]
77	1α-Acetoxy-9β-[(2,3-epoxy-3-phenylpropano-yl)oxy]-β-dihydroagarofuran	*C. gemmatus*	Seed oil	[7]
78	1α,8β-Diacetoxy-9α-(benzoyloxy)-13-(nicotinoyl-oxy)-β-dihydroagarofuran	*C. angulatus*	Seed	[36]
79	1α,2α,8β-Triacetoxy-9β-(benzoyloxy)-13-(nicotin-oyloxy)-β-dihydroagarofuran	*C. angulatus*	Seed	[37]
80	Angulatueoid A	*C. angulatus*	Seed	[38]
81	Angulatueoid B	*C. angulatus*	Seed	[38]
82	Angulatueoid C	*C. angulatus*	Seed	[38]
		C. paniculatus	Seed	[22]
83	Angulatueoid D	*C. angulatus*	Seed	[38]
84	Angulatueoid E	*C. angulatus*	Seed	[39]
85	Angulatueoid F	*C. angulatus*	Seed	[39]
86	1α-Acetoxy-9α-(benzoyloxy)-13-(nicotinoyl-oxy)-β-dihydroagarofuran-8β-ol	*C. angulatus*	Seed oil	[40]

Table (cont.)

Compound	Name	Plant	Part	Ref.
87	1α-Acetoxy-9α-(benzoyloxy)-8β-[(2-methylbutanoyl)oxy]-13-(nicotinoyloxy)-β-dihydroagarofuran	*C. angulatus*	Seed oil	[40]
88	1α-Acetoxy-9α-(benzoyloxy)-8β-(isobutyryloxy)-13-(nicotinoyloxy)-β-dihydroagarofuran	*C. angulatus*	Seed oil	[40]
89	1α-Acetoxy-8α,9α-bis(benzoyloxy)-13-(nicotinoyloxy)-β-dihydroagarofuran	*C. angulatus*	Seed oil	[40]
90	1α,8α,13-Triacetoxy-9α-(benzoyloxy)-β-dihydroagarofuran	*C. angulatus*	Seed oil	[35]
91	1α,8β-Diacetoxy-13-(benzoyloxy)-9β-(nicotinoyloxy)-β-dihydroagarofuran	*C. angulatus*	Seed	[36]
92	1α,8β,13-Triacetoxy-9β-(3-furoyloxy)-β-dihydroagarofuran	*C. paniculatus*	Whole plant	[21]
93	1α,2α,9β-Triacetoxy-13-(benzoyloxy)-8β-[(2-hydroxy-2-methylpropanoyl)oxy]-β-dihydroagarofuran-4β-ol	*C. angulatus*	Leaf	[41]
94	Emarginatine E	*C. hindsii*	Stem	[20]
95	Angulatamine	*C. gemmatus*	Root bark	[42]
96	Celahinine A	*C. hindsii*	Stem	[43]
97	Emarginatine A	*C. hindsii*	Stem	[43]
98	Celaphanol A	*C. stephanotifolius*	Stem	[44]
		C. orbiculatus	Root	[28]
99	Celaphanol B	*C. stephanotifolius*	Stem	[44]
100	Nimbidiol	*C. stephanotifolius*	Stem	[44]
101	(+)-7-Deoxynimbidiol	*C. hypoleucus*	Stalk	[45]
102	Celahypodiol	*C. hypoleucus*	Stalk	[46]
103	Furreginol	*C. hypoleucus*	Stalk	[46]
104	Suigol	*C. hypoleucus*	Stalk	[46]
105	Lup-29(30)-ene-3β,29-diol	*C. hypoleucus*	Stalk	[46]
106	Lup-20(29)-ene-1β,3β-diol	*C. hypoleucus*	Stalk	[46]
107	6β-Hydroxy-3-oxolup-20(29)-ene	*C. angulatus*	Root bark	[47]
108	Lupenone	*C. hindsii*	Stem	[20]
109	Sitosterin 3-glucoside	*C. angulatus*	Root bark	[47]
110	Sitosterol	*C. angulatus*	Root bark	[47]
		C. hypoleucus	Stalk	[48]
111	Celastrol	*C. orbiculatus*	Root	[28]
		C. paniculatus	Root outer bark	[49]
		C. hypoleucus	Root	[50]
112	Pristimerin	*C. paniculatus*	Root outer bark	[49]
		C. hypoleucus	Root	[50]
113	Celasdin A	*C. hindsii*	Stem	[51]
114	Celasdin B	*C. hindsii*	Stem	[51]
115	Friedelin	*C. hindsii*	Stem	[51]
116	Canophyllol	*C. hindsii*	Stem	[51]
117	Maytenfolone-A	*C. hindsii*	Stem	[51]
118	Celasdin C	*C. hindsii*	Stem	[51]
119	Olean-12-ene-3β,6α-diol	*C. hypoleucus*	Stalk	[46]

Table (cont.)

Compound	Name	Plant	Part	Ref.
120	3β-Hydroxyoleana-9(11),12-diene	*C. angulatus*	Root bark	[47]
121	(3β)-Olean-12-ene-3,23-diol	*C. hypoleucus*	Stalk	[48]
122	6α-Hydroxyolean-12-en-3-one	*C. hypoleucus*	Stalk	[48]
123	Zeylasterone	*C. paniculatus*	Root outer bark	[49]
124	Zeylasteral	*C. paniculatus*	Root outer bark	[49]
125	28-Oxolup-20(29)-en-3β-yl caffeate	*C. stephanotifolius*	Stem	[44]
126	28-Hydroxylup-20(29)-en-3β-yl caffeate	*C. stephanotifolius*	Stem	[44]
127	Betulin	*C. stephanotifolius*	Stem	[44]
128	28-Oxoolean-3β-yl caffeate	*C. stephanotifolius*	Stem	[44]
129	3β-Caffeoylolean-28-oic acid	*C. stephanotifolius*	Stem	[44]
130	3-Oxo-4-benzyl-3,4-dihydro-1*H*-pyrrolo[2,1-*c*]-oxazine-6-carbaldehyde	*C. orbiculatus*	Fruit	[52]
131	Chinese bittersweet alkaloid I	*C. angulatus*	Seed	[53] [54]
132	Chinese bittersweet alkaloid II	*C. angulatus*	Seed	[53] [54]
133	Quercetin 3-β-D-rutinoside (rutin)	*C. hindsii*	Leaf	[55]
134	Kaempferol 3-β-D-rutinoside	*C. hindsii*	Leaf	[55]
135	Rosmarinic acid	*C. hindsii*	Leaf	[55]
136	Lithospermic acid	*C. hindsii*	Leaf	[55]
137	Lithospermic acid B	*C. hindsii*	Leaf	[55]
138	4-{2-[2-Carboxy-3-(3,4-dihydroxyphenyl)-1-oxo-2-propenoxy]ethyl}-2-(3,4-dihydroxy-phenyl)-7-hydroxy-2,3-dihydrobenzofuran-3-carboxylic acid 1-carboxy-2-(3,4-dihydroxy-phenyl)ethyl ester	*C. hindsii*	Leaf	[55]
139	4-{2-[2-Carboxy-3-(3,4-dihydroxyphenyl)-1-oxo-2-propenoxy]ethyl}-2-(3,4-dihydroxy-phenyl)-2,3-dihydro-7-hydroxybenzofuran-3-carboxylic acid 1-carboxy-2-[2-(3,4-di-hydroxyphenyl)-7-hydroxy-2,3-dihydrobenzo-furan-3-carboxylic acid 1-carboxy-2-(3,4-dihydroxyphenyl)ethoxycarbonyl]ethyl ester	*C. hindsii*	Leaf	[55]
140	4-{3-[2-(3-{[1-carboxy-2-(3,4-dihydroxy-phenyl)ethoxy]carbonyl}-7-hydroxy-2-methyl-2,3-dihydrobenzofuran-4-yl)-1-carboxyethoxy]-3-oxoprop-1-enyl}-2-(3,4-dihydroxyphenyl)-7-hydroxy-2,3-dihydro-benzofuran-3-carboxylic acid 1-carboxy-2-(3,4-dihydroxyphenyl)ethyl ester	*C. hindsii*	Leaf	[55]
141	(−)-5-*O*-β-D-Glucosyl-3-*O*-benzoylepicatechin	*C. orbiculatus*	Aerial part	[56]
142	(−)-Epiafzelechin	*C. orbiculatus*	Aerial part	[56]
143	(−)-Epicatechin	*C. angulatus*	–	[57]
		C. orbiculatus	Aerial part	[56]
144	(+)-Catechin	*C. angulatus*	Root bark	[47]
			–	[57]

showed moderate antitumor activity against human mammary carcinoma (Bcap 37), human colon carcinoma (RKO), human hepatocellular carcinoma (SMMC 7721), and human erythroleukemia (K 562) with the IC_{50} values from 11.21 to 38.03 μg/ml [46].

2.3. *Triterpenes* **105**–**129**. Compounds **105**–**110** are the 6/6/6/6/5-ring triterpenes, which have been isolated from *C. angulatus*, *C. paniculatus*, *C. hypoleucus*, and *C. hindsii* (*Table*). Celastrol (**111**) and pristimerin (**112**), occurring in *C. hypoleucus*, *C. paniculatus*, and *C. orbiculatus*, exhibited inhibitory effects against diverse phytopathogenic fungi. They were found to inhibit the mycelial growth of *Rhizoctonia solani* Kühn and *Glomerella cingulata* (Stonem) Spauld and Schrenk *in vitro*. In addition, pristimerin (**112**) and celastrol (**111**) showed good preventive and curative effects against wheat powdery mildew *in vivo* [50]. From the stem of *C. hindsii*, seven triterpenes, **113**–**118**, were isolated. Biological evaluation showed that celasdin B (**114**) exhibited an anti-HIV replication activity in H9 lymphocyte cells with an EC_{50} value of 0.8 μg/ml and toxicity at 5.5 μg/ml, and maytenfolone-A (**117**) an EC_{50} value of 1.8 μg/ml and a lower toxicity at 7.0 μg/ml [51]. Compound **117** also demonstrated cytotoxicity against hepatoma (ED_{50} 2.3 μg/ml) and nasopharynx carcinoma (ED_{50} 3.8 μg/ml) [51]. Compound **120** was obtained from *C. angulatus*. The stalk of *C. hypoleucus* yielded two triterpenes, **121** and **122**. Compound **121** showed moderate antitumor activity against human cervical squamous carcinoma cells, with an IC_{50} value of 28.9 μg/mg relative to 5.6 μg/mg for cisplatin used as a positive control [48]. Zeylasterone (**123**) and zeylasteral (**124**) were isolated from *C. paniculatus*. The OH groups at C(3) of compounds **125**–**129**, which were obtained from the stem of *C. stephanotifolius*, were esterified by a β-caffeic acid.

2.4. *Alkaloids* **130**–**132**. From the fruit of *C. orbiculatus*, an alkaloid, **130**, was isolated (*Table*). Both **131** and **132**, which were isolated from the seeds of *C. angulatus*, contain a 1,3-oxazine moiety, which displayed a novel skeleton, so far not found in the natural products. Chinese bitter-sweet alkaloid II (**132**) demonstrated moderate cytotoxicity against non-small lung cancer (NCL-H23) cell line at concentrations of 3.0×10^{-5} mM (GI_{50}) by the *National Cancer Institute in vitro* cytotoxicity screen [54].

2.5. *Flavonoids* **133**–**144**. In 2006, eight phenolic compounds, **133**–**140**, were obtained from *C. hindsii* (*Table*). They were the five known compounds **133**–**137** and three novel oligomers of rosmarinic acid, *i.e.*, a dimer, **138**, and two trimers, **139** and **140**. The major components in the extract were rosmarinic acid (**135**) and lithospermic acid B (**137**). These compounds could suppress the autoxidation of methyl linoleate in bulk phase and the radical-initiated peroxidation of soybean phosphatidylcholine in liposomes. Therefore, the extract of *C. hindsii* is expected to be a source of natural antioxidants [55]. Compounds **141**–**143** were obtained from *C. orbiculatus*. The (−)-epicatechin (**143**) was also isolated from *C. angulatus* together with (+)-catechin (**144**). Compound **141**–**143** exhibited antioxidant activity with IC_{50} values of 25, 7.5, and 8.5 μg/ml, respectively [56]. (−)-Epicatechin (**143**) also exhibited a dose-dependent inhibition on COX activity with an IC_{50} value of 15 μM and significant anti-inflammatory activity on carrageenin-induced mouse paw edema, when the compound (100 mg/kg) was orally administrated 1 h before carrageenin treatment [58].

2.6. *Crude Extract.* Along with the compounds mentioned, the pharmacological activities of extracts were also discussed. Ethanolic extract of *C. aculeatus* was shown to have anti-inflammatory and analgesic activity [59]. Aqueous extracts of *C. paniculatus* seed exhibited free-radical-scavenging capacity, and protected cultured rat neuronal cell (FBNC) cultures from H_2O_2-induced oxidative injury and glutamate-induced toxicity by modulating glutamate receptor function [60][61]. Also, the seed oil of *C. paniculatus* showed similar activities, and the authors presumed that the activity of protecting neuronal cells against H_2O_2-induced toxicity is in part due to their antioxidant properties, and their ability to induce antioxidant enzymes [62]. Regarding the activity of enhancing cognition, aqueous extracts of seed have been reported to improve learning and memory in rats. Aqueous extracts of *C. paniculatus* seed reduced oxidative stress in the brain by increasing endogenous antioxidant enzymes [63]. Rats treated with the seed oil of *C. paniculatus* for 15 days exhibited a significant decrease in the levels of norepinephrine, dopamine, and serotonin, and their respective metabolites in both brain and urine. It indicated that the seed oil of *C. paniculatus* caused an overall decrease in the turnover of all the three central monoamines, and implicates the involvement of these aminergic systems in the learning and memory process [64].

3. Outlook. – The plants of the genus *Celastrus* are widespread in China. The studies on chemical constituents in recent years have disclosed that β-dihydroagarofuran sesquiterpenes and triterpenes are the important active components. Along with the use as natural insecticides and insect-feeding deterrents, the plants of genus *Celastrus* still offer wide-reaching interesting and applicable prospects, such as anti-inflammatory and antitumor activity, modulability of multidrug resistance, and antioxidation. The activity-screening and structure–activity relationship studies of triterpenes of this genus are to be continued to search for new medicines.

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