REVIEW

Chemical Constituents of the Plants of the Genus *Calophyllum*

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

[a]) Department of Natural Product Chemistry, School of Pharmaceutical Sciences, Hebei Medical University, 361 Zhongshan East Road, Shijiazhuang 050017, Hebei Province, P. R. China (phone: +86-311-8626-5634; e-mail: shiqingwen@hebmu.edu.cn)

[b]) Syngenta Jealott's Hill International Research Centre, Bracknell, UK-Berkshire RG42 6EY

Contents

1. Introduction. – The genus *Calophyllum* of the Guttiferae family, a large group of tropical trees consisting of *ca.* 180–200 different species [1], is well-known as a rich and valuable source of bioactive xanthones and coumarins, especially since the isolation of the calanolides (= benzo-tripyranones), a unique subclass within the HIV-1 non-nucleoside reverse transcriptase inhibitors (NNRTIs), has been reported [2][3]. Chromanones are also distinctive compounds of this genus. A number of plants of this genus are used as traditional herbal medicines, such as being a diuretic [4], for the treatment of malaria, venereal diseases, and for blood pressure [5], rheumatism, varicose, haemorrhoids, and chronic ulcers [6], as well as skin infections, wounds,

leprous nephritis, pain, eye diseases, and inflammations [7]. The modern pharmacology research of genus *Calophyllum* has further revealed many activities, such as antiviral, antitumor-promoting, antimalarial, antibacterial, as well as cytotoxic activity.

To facilitate further research work, in this article, we review the structures and biological properties of the known constituents from *Calophyllum*.

2. Chemical Constituents. – The compounds of *Calophyllum* species were classified into four groups: coumarins, **1**–**84**, xanthones, **85**–**166**, chromanones, **167**–**211**, steroids and triterpenoids, **212**–**238**, and some other compounds, **239**–**243** (see the *Table*).

2.1. *Coumarins.* Natural coumarins isolated from the *Calophyllum* genus belong, from a biogenetic point of view, to a homogeneous group of naturally occurring heterocycles with a biosynthetic scheme related to that of neoflavonoids [76]. The known coumarins of the genus *Calophyllum* isolated over the past few decades include pyranocoumarins, **1**–**47**, furocoumarins, **48**–**65**, furo-pyranocoumarins, **66**–**69**, simple coumarins, **70**–**80**, and others, **81**–**84**. Individual members of the groups vary with respect to the substituent at C(4) of the lactone ring of the coumarins, where Me, Pr, or Ph groups may be encountered. In 1996, *McKee et al.* concluded three basic structural types of pyranocoumarins which are the most frequent coumarins (*Fig. 1*): *i*) tetracyclic dipyranocoumarins **A**, in which the *C* rings have a geminal dimethyl moiety, *e.g.*, compounds **1**–**18**; *ii*) tricyclic pyranocoumarins **B**, *e.g.*, compounds **19**–**32**; and *iii*) tetracyclic dipyranocoumarins **C** with reversed *C* and *D* pyran rings, *i.e.*, the geminal dimethyl groups are in the *D* ring, *e.g.*, as in compounds **33**–**35** [19].

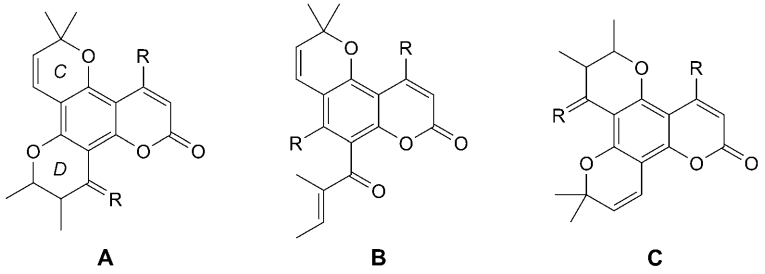


Fig. 1. *Three basic structural types of pyranocoumarins*

Compound **10** was firstly named as (−)-calanolide B [3]. *Fuller et al.* named compound **11** as costatolide [18]. But, *Spino et al.* recognized that (−)-calanolide B and costatolide were the same compound, *i.e.*, **10** [9]. Calanolide E (**26**) was first isolated from *C. lanigerum* [3]. *McKee et al.* isolated this compound and its diastereoisomer calanolide E2 (**27**) from the stem bark of the same plant. So, they renamed calanolide E as calanolide E_1, but the configurations of the two diastereoisomers were not defined [19]. Recedesolide (**31**) was isolated from *C. recedens* and *C. blancoi* with different structures [26][27]. Compounds **34** and **35** were first identified as shown in *Fig. 2*, with the names as calanolides C and D, respectively [3], but later, their structures were revised, and they were renamed as pseudocalanolides C and D (*Table*) [77][78]. Calophyllic acid (**36**) and isocalophyllic acid (**37**) belong to the pyranocoumarins of type A, but the lactone ring is cleaved.

Table. *Chemical Constituents from the Genus* Calophyllum

Compound	Name	Plant	Part	Ref.
1	Inophyllum C	*C. inophyllum*	leaf	[2][8]
			seed	[9]
			nut	[10]
		C. brasiliense	stem bark	[11]
		C. teysmannii var. *inophylloide*	bark	[12][13]
2	Inophyllum E	*C. inophyllum*	leaf	[2][8]
			seed	[9]
			nut	[10]
		C. brasiliense	stem bark	[11]
		C. teysmannii var. *inophylloide*	bark	[12]
3	Soulattrolone	*C. teysmannii* var. *inophylloide*	latex	[14][15]
4	Cordatolide A	*C. lanigerum* var. *austrocoriaceum*	latex	[15]
		C. cordato-oblongum	leaf	[16]
			twig, bud	[17]
5	Cordatolide B	*C. cordato-oblongum*	leaf	[16]
			twig, bud	[17]
6	12-Methoxycordatolide B	*C. cordato-oblongum*	twig, bud	[17]
7	(+)-Calanolide A	*C. lanigerum*	fruit, twig	[3]
		C. lanigerum var. *austrocoriaceum*	latex	[15]
		C. brasiliense	stem bark	[11]
8	12-Acetoxycalanolide A	*C. lanigerum*	fruit, twig	[3]
9	12-Methoxycalanolide A	*C. lanigerum*	fruit, twig	[3]
10	(−)-Calanolide B	*C. lanigerum*	fruit, twig	[3]
		C. teysmannii var. *inophylloide*	latex	[18]
11	Costatolide	*C. teysmannii* var. *inophylloide*	latex	[18]
		C. cerasiferum	seed	[9]
12	12-Methoxycalanolide B	*C. lanigerum*	fruit, twig	[3]
13	Calanolide F	*C. teysmannii* var. *inophylloide*	leaf, twig	[19]
14	Inophyllum A	*C. inophyllum*	leaf	[2]
		C. brasiliense	stem bark	[11]
		C. moonii	leaf	[20]
15	Soulattrolide	*C. teysmannii* var. *inophylloide*	latex	[14][15][18]
		C. moonii	leaf	[20]
		C. teysmannii	latex	[21]
16	Inophyllum B	*C. inophyllum*	leaf	[2]
			seed	[9]
17	Inophyllum P	*C. inophyllum*	leaf	[2]
18	Inophyllum D	*C. inophyllum*	leaf	[2]
		C. brasiliense	stem bark	[11]

Table (cont.)

Compound	Name	Plant	Part	Ref.
19	Calophyllolide	*C. inophyllum*	nut	[10]
			aerial part	[22]
			seed	[9][23]
		C. brasiliense	stem bark	[11]
20	Brasimarin A	*C. brasiliense*	stem bark	[11]
21	Calanone	*C. brasiliense*	stem bark	[11]
		C. teysmannii var. *inophylloide*	bark	[12][13]
			latex	[14][15]
		C. aff. *biflorum*	latex	[15]
22	Mammea A/BA cyclo D	*C. brasiliense*	leaf	[24]
23	5-Methoxy-2,2-dimethyl-6-(2-methyl-1-oxobut-2-enyl)-10-propyl-2*H*,8*H*-benzo[1,2-*b*:3,4-*b*′]dipyran-8-one	*C. brasiliense*	stem bark	[11]
24	Cordatolide E	*C. lanigerum* var. *austrocoriaceum*	stem bark	[19]
25	Oblongulide	*C. cordato-oblongum*	leaf	[16]
			twig, bud	[17]
26	Calanolide E (calanolide E1)	*C. lanigerum*	fruit, twig	[3]
		C. lanigerum var. *austrocoriaceum*	stem bark	[19]
27	Calanolide E2	*C. lanigerum* var. *austrocoriaceum*	stem bark	[19]
		C. polyanthum	seed	[25]
28	(−)-6-Benzoyl-3,4-dihydro-3,4,5-trihydroxy-2,2-dimethyl-10-phenyl-2*H*,8*H*-benzo[1,2-*b*:3,4-*b*′]-dipyran-8-one	*C. teysmannii* var. *inophylloide*	bark	[13]
29	Calopolyanolide C	*C. polyanthum*	seed	[25]
30	Calopolyanolide D	*C. polyanthum*	seed	[25]
31	Recedesolide	*C. recedens*	bark	[26]
		C. blancoi	seed	[27]
32	Isorecedensolide	*C. blancoi*	seed	[27]
33	Pseudocordatolide C	*C. lanigerum* var. *austrocoriaceum*	leaf	[19]
34	Pseudocalanolide C (Calanolide C)	*C. lanigerum*	fruit, twig	[3]
		C. brasiliense	stem bark	[11]
35	Pseudocalanolide D (Calanolide D)	*C. lanigerum*	fruit, twig	[3]
36	Calophyllic acid	*C. inophyllum*	leaf	[2]
37	Isocalophyllic acid	*C. inophyllum*	leaf	[2]
			aerial part	[22]
38	Teysmanone A	*C. teysmannii* var. *inophylloide*	bark	[12]
39	Apetatolide	*C. inophyllum*	aerial part	[22]
40	Calaustralin	*C. inophyllum*	nut	[10]
		C. austraiianum	bark	[28]
41	*O*-Methylisocalaustralin	*C. teysmannii* var. *inophylloide*	bark	[13]
42	*trans*-7,8-Dihydro-5-methoxy-7,8-dimethyl-10-(3-methylbut-2-enyl)-4-phenyl-2*H*,6*H*-benzo[1,2-*b*:5,4-*b*′]dipyran-2,6-dione	*C. teysmannii* var. *inophylloide*	bark	[13]

Table (cont.)

Compound	Name	Plant	Part	Ref.
43	Brasimarin C	*C. brasiliense*	stem bark	[11]
44	Calocoumarin A	*C. brasiliense*	stem bark	[11]
		C. inophyllum	aerial part	[22]
45	Teysmanone B	*C. teysmannii* var. *inophylloide*	bark	[12]
46	Isocalanone	*C. teysmannii* var. *inophylloide*	bark	[13]
47	Mammea A/AB cyclo E	*C. dispar*	stem bark	[29]
48	Calocoumarin B	*C. inophyllum*	aerial part	[22]
49	Mammea A/BA cyclo F	*C. dispar*	stem bark	[30]
50	Mammea A/BB cyclo F	*C. dispar*	stem bark	[30]
51	Mammea A/BC cyclo F	*C. dispar*	fruit	[30]
52	Mammea B/BA cyclo F	*C. brasiliense*	leaf	[24]
53	Mammea B/BB cyclo F	*C. brasiliense*	leaf	[24]
54	Isodisparfuran A	*C. dispar*	fruit	[30]
55	Brasimarin B	*C. brasiliense*	stem bark	[11]
56	(−)-9-Benzoyl-2,3-dihydro-2-(1-hydroxy-1-methylethyl)-4-methoxy-5-phenyl-7*H*-furo[3,2-*g*][1]benzopyran-7-one	*C. teysmannii* var. *inophylloide*	bark	[13]
57	(−)-9-Benzoyl-2,3-dihydro-3-hydroxy-2-(1-hydroxy-1-methylethyl)-4-methoxy-5-phenyl-7*H*-furo[3,2-*g*][1]benzopyran-7-one	*C. teysmannii* var. *inophylloide*	bark	[13]
58	(−)-6-Benzoyl-8,9-dihydro-5-hydroxy-8-(1-hydroxy-1-methylethyl)-4-phenyl-2*H*-furo[2,3-*h*][1]benzopyran-2-one	*C. teysmannii* var. *inophylloide*	bark	[13]
59	Disparfuran B	*C. dispar*	stem bark	[30]
60	Disparacetylfuran A	*C. dispar*	stem bark	[30]
61	Mammea A/AA deshydrocyclo F	*C. dispar*	stem bark	[30]
62	Mammea A/AA methoxycyclo F	*C. dispar*	stem bark	[30]
63	Mammea A/AA cyclo F	*C. dispar*	stem bark	[30]
64	Mammea A/AB cyclo F	*C. dispar*	stem bark	[30]
65	Mammea A/AC cyclo F	*C. dispar*	fruit	[30]
66	Inophyllum G-1	*C. inophyllum*	leaf	[2]
67	Inophyllum G-2	*C. inophyllum*	leaf	[2]
68	Calocoumarin C	*C. inophyllum*	aerial part	[22]
69	Mammea A/AB dioxalanocyclo F	*C. dispar*	stem bark	[29]
70	Mammea A/BA	*C. brasiliense*	leaf	[24]
71	Mammea A/BB	*C. brasiliense*	leaf	[24]
72	Mammea B/BA	*C. brasiliense*	leaf	[24]
73	Mammea B/BB	*C. brasiliense*	stem bark	[11]
		C. brasiliense	leaf	[24]
74	Mammea C/OA	*C. brasiliense*	leaf	[24]
75	Mammea C/OB	*C. brasiliense*	leaf	[24]
76	Isodispar B	*C. dispar*	fruit	[29]
77	Disparinol D	*C. dispar*	stem bark	[29]
78	Disparpropylinol B	*C. dispar*	stem bark	[29]
79	Disparinol B	*C. dispar*	stem bark	[29]
80	Dispardiol B	*C. dispar*	stem bark	[29]
81	Inocalophyllin A	*C. inophyllum*	seed	[23]

Table (cont.)

Compound	Name	Plant	Part	Ref.
82	Inocalophyllin A methyl ester	*C. inophyllum*	seed	[23]
83	Inocalophyllin B	*C. inophyllum*	seed	[23]
84	Inocalophyllin B methyl ester	*C. inophyllum*	seed	[23]
85	7-Hydroxy-8-methoxyxanthone	*C. caledonicum*	trunk bark	[4]
86	7,8-Dimethoxyxanthone	*C. caledonicum*	trunk bark	[4]
87	6-Hydroxy-5-methoxyxanthone	*C. caledonicum*	trunk bark	[4]
88	7-Hydroxy-5,6-dimethoxyxanthone	*C. caledonicum*	trunk bark	[4]
89	1,3,5-Trihydroxy-2-isoprenylxanthone	*C. austroindicum*	stem wood	[31]
90	1-Hydroxy-7-methoxyxanthone	*C. austroindicum*	stem wood	[31]
91	6-Hydroxy-l,3,5-trimethoxyxanthone	*C. austroindicum*	stem wood	[31]
92	3,6-Dihydroxy-l,5-dimethoxyxanthone	*C. austroindicum*	stem wood	[31]
93	1,3,6-Trihydroxy-5,7-dimethoxyxanthone	*C. austroindicum*	stem wood	[31]
94	2-Methoxyxanthone	*C. austroindicum*	bark	[31]
95	4-Hydroxyxanthone	*C. austroindicum*	bark	[31]
96	1,7-Dihydroxyxanthone	*C. austroindicum*	bark	[31]
		C. ramiflorum	heartwood	[32]
		C. inophyllum	heartwood	[33]
		C. tomentosum	heartwood	[34]
		C. teysmannii var. *inophylloide*	wood	[35]
97	1,5-Dihydroxyxanthone	*C. inophyllum*	root bark	[10][36]
		C. tomentosum	heartwood	[34]
98	1,5,6-Trihydroxyxanthone	*C. inophyllum*	heartwood	[33]
99	1,6-Dihydroxy-5-methoxyxanthone	*C. inophyllum*	heartwood	[33]
		C. tomentosum	heartwood	[34]
100	1,7-Dihydroxy-3,6-dimethoxyxanthone	*C. inophyllum*	timber	[37]
101	1-Hydroxy-6,7-dimethoxyxanthone	*C. ramiflorum*	heartwood	[32]
102	1,2,8-Trimethoxyxanthone	*C. teysmannii* var. *inophylloide*	wood	[35]
103	1,3,5,7-Tetramethoxyxanthone	*C. teysmannii* var. *inophylloide*	wood	[35]
104	2-Hydroxyxanthone	*C. austroindicum*	bark	[31]
		C. teysmannii var. *inophylloide*	wood	[38]
105	3-Hydroxy-2,4-dimethoxyxanthone	*C. teysmannii* var. *inophylloide*	wood	[38]
106	7-Hydroxy-1,2,8-trimethoxyxanthone	*C. teysmannii* var. *inophylloide*	wood	[38]
107	6-Hydroxy-1,2,5-trimethoxyxanthone	*C. teysmannii* var. *inophylloide*	wood	[38]
108	3,8-Dihydroxy-1,2,4-trimethoxyxanthone	*C. teysmannii* var. *inophylloide*	wood	[38]
109	1,7-Dihydroxy-3-methoxyxanthone	*C. teysmannii* var. *inophylloide*	wood	[38]
110	6-Methoxy-2-(methoxycarbonyl)xanthone	*C. teysmannii* var. *inophylloide*	wood	[38]
111	Caloxanthone E	*C. inophyllum*	root bark	[39]
112	1,3,8-Trihydroxy-7-methoxyxanthone	*C. inophyllum*	root bark	[39]
113	1,3-Dihydroxy-7,8-methoxyxanthone	*C. inophyllum*	root bark	[39]
114	6-Hydroxy-l,5-dimethoxyxanthone	*C. inophyllum*	root bark	[39]

Table (cont.)

Compound	Name	Plant	Part	Ref.
115	1,3,5-Trihydroxy-2-methoxyxanthone	*C. inophyllum*	root bark	[39]
		C. apetalum	stem wood	[40]
116	1,3-Dihydroxy-2,5-dimethoxyxanthone	*C. apetalum*	stem wood	[40]
117	3,8-Dihydroxy-1,2-dimethoxyxanthone	*C. apetalum*	stem wood	[40]
118	1,3,5-Trihydroxyxanthone	*C. apetalum*	stem wood	[40]
119	Teysmannic acid	*C. teysmannii* var. *inophylloide*	wood	[35]
120	Scriblitifolic acid	*C. teysmannii* var. *inophylloide*	wood	[35]
		C. cordato-oblongum	bark, timber	[41]
121	Caloxanthone H	*C. austroindicum*	stem wood	[31]
122	6-(3′,3′-Dimethylallyl)-1,5-dihydroxyxanthone; calophyllin B; guanandin	*C. austroindicum*	stem wood	[31]
		C. inophyllum	timber	[37]
		C. brasiliense	wood	[42]
		C. scriblitifolium	heartwood	[43]
123	1,5-Dihydroxy-6-(4-hydroxy-3-methylbutyl)xanthone	*C. scriblitifolium*	heartwood	[43]
124	l,5-Dihydroxy-6-(4-hydroxy-3-methylbut-2-enyl)xanthone	*C. scriblitifolium*	heartwood	[43]
125	8-(3′,3′-Dimethylallyl)-1,5-dihydroxy-xanthone	*C. brasiliense*	wood	[42]
126	2-(3,3-Dimethylallyl)-1,3,5-trihydroxy-xanthone	*C. inophyllum*	heartwood	[33][44]
127	l,3,5,6-Tetrahydroxy-2-(3-hydroxy-3-methylbutyl)xanthone	*C. inophyllum*	heartwood	[44]
128	2-(3,3-Dimethylallyl)-1,3,5,6-tetrahydroxyxanthone	*C. neo-ebudicum*	heartwood	[45]
		C. inophyllum	heartwood	[33][44][46]
129	6-Deoxy-γ-mangostin	*C. thwaitesii*	root bark	[47][48]
		C. caledonicum	root bark	[49]
130	Calocalabaxanthone	*C. calaba* var. *calaba*	bark	[50]
		C. bracteatum	root bark	[47]
131	Caledonixanthone D	*C. caledonicum*	trunk bark	[4]
132	1-Hydroxy-3,5,6-Trimethoxy-2-(3-methylbut-2-enyl)xanthone	*C. ramiflorum*	heartwood	[32]
133	Apetalinone A	*C. apetalum*	root	[40]
134	Osajaxanthone	*C. enervosum*	stem bark	[51]
135	Jacareubin	*C. austroindicum*	stem wood	[31]
		C. ramiflorum	heartwood	[32]
		C. tomentosum	heartwood	[34]
		C. cordato-oblongum	bark, timber	[41]
		C. brasiliense	wood	[42]
		C. neo-ebtuikum	heartwood	[45]
		C. inophyllum	timber	[37]
			heartwood	[33][44][46]

Table (cont.)

Compound	Name	Plant	Part	Ref.
136	6-Dehydroxyjacareubin	*C. austroindicum*	stem wood	[31]
		C. tomentosum	heartwood	[34]
		C. brasiliense	wood	[42]
		C. neo-ebudicum	heartwood	[45]
		C. inophyllum	heartwood	[33][44][46]
			timber	[37]
137	Caloxanthone A	*C. inophyllum*	root bark	[10][36]
138	Caloxanthone C	*C. caledonicum*	root bark	[49][52]
	(Inoxanthone)	*C. inophyllum*	root bark	[10]
	(Blancoxanthone)	*C. blancoi*	root	[53]
139	3-Hydroxyblancoxanthone (Macluraxanthone)	*C. blancoi*	root	[53]
		C. inophyllum	root bark	[10][36]
		C. caledonicum	root bark	[49]
140	Acetylblancoxanthone	*C. blancoi*	root	[53]
141	Trapezifolixanthone	*C. calaba* var. *calaba*	root bark	[47]
		C. thwaitesii	root bark	[48]
142	Calabaxanthone	*C. tomentosum*	bark	[34]
		C. bracteatum	root bark	[47]
143	Demethylcalabaxanthone	*C. thwaitesii*	root bark	[48]
		C. caledonicum	root bark	[49]
		C. walkeri	stem bark	[54]
144	Dombakinaxanthone	*C. caledonicum*	root bark	[49]
		C. moonii	root bark	[55]
145	Caledonixanthone B	*C. caledonicum*	trunk bark	[4]
146	Dehydrocycloguanandin	*C. brasiliense*	wood	[42]
147	Calothwaitesixanthone	*C. thwaitesii*	root bark	[47][48]
		C. caledonicum	root bark	[49]
148	Pyranojacaeubin	*C. blancoi*	root	[53]
149	Caloxanthone	*C. blancoi*	root	[53]
150	Thwaitesixanthone	*C. austroindicum*	bark	[31]
		C. thwaitesii	root bark	[47][48]
		C. walkeri	stem bark	[54]
151	Thwaitesixanthonol	*C. walkeri*	stem bark	[54]
152	11,12-Dihydrothwaitesixanthone	*C. thwaitesii*	root bark	[48]
153	Cordato-oblonguxanthone	*C. cordato-oblongum*	bark, timber	[41]
154	Caloxanthone G	*C. austroindicum*	stem wood	[31]
155	Caledonixanthone A	*C. caledonicum*	trunk bark	[4]
156	Caloxanthone B	*C. inophyllum*	root bark	[10][36]
157	Caloxanthone F	*C. austroindicum*	stem wood	[31]
158	Caledonixanthone C	*C. caledonicum*	trunk bark	[4]
159	2″-Isopropenyl-3″-hydroxydihydrofuranodemethylcalabaxanone	*C. walkeri*	stem bark	[54]
160	Caloxanthone D	*C. inophyllum*	root bark	[39]
161	Apetalinone B	*C. apetalum*	root	[40]
162	Calozeyloxanthone	*C. apetalum*	root	[40]
		C. moonii	root bark	[55]
		C. zeylanicum	bark	[56]
		C. caledonicum	root bark	[49]

Table (cont.)

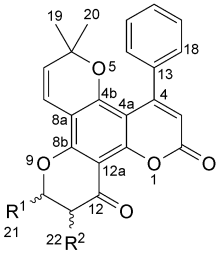
Compound	Name	Plant	Part	Ref.
163	Zeyloxanthonone	*C. apetalum*	root	[40]
164	Tomentonone	*C. apetalum*	stem bark	[40]
165	Apetalinone C	*C. apetalum*	root	[40]
166	Apetalinone D	*C. apetalum*	stem bark	[40]
167	(−)-Epicatechin	*C. austroindicum*	bark	[31]
		C. inophyllum	root bark	[36]
		C. enervosum	stem bark	[51]
168	(−)-Epiafzelechin	*C. apetalum*	stem wood	[40]
169	Myricetin	*C. inophyllum*	andraecium of flowers	[57]
170	Myricetin-7-glucoside	*C. inophyllum*	andraecium of flowers	[57]
171	Quercetin	*C. inophyllum*	andraecium of flowers	[57]
172	5,7,3′,4′-Tetrahydroxyisoflavone	*C. polyanthum*	seed	[25]
173	GB-1	*C. panciflorum*	stem bark	[58]
174	GB-2	*C. panciflorum*	stem bark	[58]
175	GB-1a	*C. panciflorum*	stem bark	[58]
176	GB-2a	*C. panciflorum*	stem bark	[58]
177	Pancibiflavonone	*C. panciflorum*	stem bark	[58]
178	Garcinianin	*C. panciflorum*	stem bark	[58]
179	GD-IV	*C. panciflorum*	stem bark	[58]
180	Amentoflavone	*C. brasiliense*	leaf	[24]
		C. calaba	leaf	[59]
181	Isocalolongic acid	*C. recedens*	bark	[26]
182	2,3-Dihydro-5-hydroxy-2,3,8,8-tetramethyl-2*H*-[l]benzopyran-6-(1-phenylethenyl)-4*H*,8*H*-benzo[1,2-*b:*3,4-b′]dipyran-4-one	*C. tomentosum*	leaf	[60]
183	(2*S*,3*R*)-2,3-Dihydro-5-hydroxy-2,3,8,8-tetramethyl-6-(1-phenylethenyl)-4*H*,8*H*-benzo[1,2-*b:*3,4-*b′*]dipyran-4-one	*C. inophyllum*	leaf	[61]
184	Inophynone ((2*R*,3*R*)-2,3-Dihydro-5-hydroxy-2,3,8,8-tetramethyl-6-(1-phenylethenyl)-4*H*,8*H*-benzo[1,2-*b:*3,4-*b′*]dipyran-4-one)	*C. inophyllum*	leaf	[61][62]
185	Isoinophynone	*C. inophyllum*	leaf	[62]
186	Papuanic acid	*C. papuanum*	bark resin	[63]
187	Isopapuanic acid	*C. papuanum*	bark resin	[63]
188	Recedensic acid	*C. recedens*	bark	[26]
189	Caloverticillic acid C	*C. verticillatum*	stem bark	[64]
190, **191**	Caloverticillic acid A, Caloverticillic acid B	*C. verticillatum*	stem bark	[64]
192	Brasiliensophyllic acid B	*C. brasiliense*	bark	[65]
193	Isobrasiliensophyllic acid B	*C. brasiliense*	bark	[65]
194	Brasiliensophyllic acid A	*C. brasiliense*	bark	[65]
195	Isobrasiliensophyllic acid A	*C. brasiliense*	bark	[65]
196	Brasiliensophyllic acid C	*C. brasiliense*	bark	[65]
197	Isobrasiliensophyllic acid C	*C. brasiliense*	bark	[65]
198	Calozeylanic acid	*C. walkeri*	leaf	[20]
		C. lankaensis	leaf	[66]
199	Calofloridé	*C. verticillatum*	seed	[67]

Table (cont.)

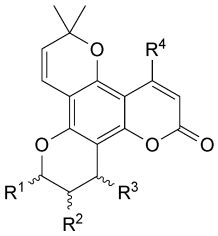
Compound	Name	Plant	Part	Ref.
200	Thwaitesic acid	*C. lankaensis*, *C. thwaitesis*	leaf	[66]
201	Isothwaitesic acid	*C. lankaensis*, *C. thwaitesis*	leaf	[66]
202	Apetalic acid	C. blancoi	seed	[27]
		C. macrocarpum, *C. walkeri*	stem bark	[54]
203	Isoapetalic acid	*C. blancoi*	seed	[27]
204	Apetalic acid methyl ester	*C. blancoi*	seed	[27]
205	Apetalic acid 5-*O*-acetate	*C. blancoi*	seed	[27]
206	Isoapetalic methyl ester	*C. blancoi*	seed	[27]
207	Isoapetalic acid 5-*O*-acetate	*C. blancoi*	seed	[27]
208	Chapelieric acid	*C. calaba*	leaf	[59]
209	Isochapelieric acid	*C. calaba*	leaf	[59]
210	Cordato-oblongic acid	*C. cordato-oblongum*	twig	[17]
			stem bark	[68]
211	Isocordato-oblongic acid	*C. cordato-oblongum*	stem bark	[68]
212	Friedelin	*C. cordato-oblongum*	leaf	[16]
			twig	[17]
		C. moonii	leaf	[20]
			root bark	[55]
		C. brasiliense	leaf	[24]
		C. inophyllum	root bark	[10]
			timber	[37]
			leaf	[69][62]
		C. walkeri	leaf	[20]
			stem bark	[54]
		C. tomentosum	branch timber, sapwood	[34]
			bark	[70]
		C. thwaitesii	root bark	[48]
			leaf	[66]
		C. calaba	leaf	[59]
		C. verticillatum	stem bark	[64]
		C. lankaensis	leaf	[66]
		C. apetalum	bark	[70]
		C. gracilipes	leaf	[71]
213	Canophyllol	*C. cordato-oblongum*	twig	[17]
		C. walkeri	leaf	[20]
		C. brasiliense	leaf	[24]
		C. calaba	leaf	[59]
		C. lankaensis, *C. thwaitesii*	leaf	[66]
		C. inophyllum	leaf	[69][62]
214	Canophyllal	*C. calaba*	leaf	[59]
		C. inophyllum	leaf	[69]
215	3-Oxo-27-hydroxyacetate friedelan-28-oic acid	*C. inophyllum*	leaf	[72]
216	Canophyllic acid	*C. inophyllum*	leaf	[69][62]
		C. calaba	leaf	[59]
217	Friedelan-3β-ol	*C. inophyllum*	timber	[37]
		C. tomentosum	branch timber, sapwood	[34]
			bark	[70]
		C. calaba	leaf	[59]

Table (cont.)

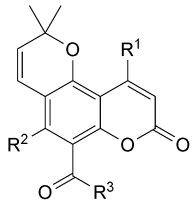
Compound	Name	Plant	Part	Ref.
218	Friedelane-3β,28-diol	*C. calaba*	leaf	[59]
219	27-Hydroxyacetate canophyllic acid	*C. inophyllum*	leaf	[72]
220	Ursolic acid	*C. polyanthum*	seed	[25]
221	Taraxerol	*C. moonii*	bark, branch, timber, sapwood	[34]
		C. tomentosum	root bark	[55]
222	Taraxerone	*C. moonii*	bark	[34]
		C. tomentosum	root bark	[55]
223	α-Amyrin	*C. verticillatum*	stem bark	[64]
224	β-Amyrin	*C. inophyllum*	timber	[37]
225	Betulinic acid	*C. tomentosum*	bark	[34]
		C. macrocarpum	stem bark	[54]
		C. apetalum	bark	[70]
		C. gracilipes	leaf	[71]
226	Lupeol	*C. gracilipes*	leaf	[71]
227	Lupenone	*C. gracilipes*	leaf	[71]
228	3β-Hydroxy-30-norlupan-20-one	*C. gracilipes*	leaf	[71]
229	Lupane-3β,20-diol	*C. gracilipes*	leaf	[71]
230	(20*R*)-3β-Hydroxylupan-29-oic acid	*C. gracilipes*	leaf	[71]
231	3,4-Secofriedelane-3,28-dioic acid	*C. inophyllum*	leaf	[72]
232	Apetalactone	*C. moonii*	leaf	[20]
		C. lankaensis	leaf	[67]
233	Squalene	*C. gracilipes*	leaf	[71]
234	Gracilipene	*C. gracilipes*	leaf	[71]
235	Sitosterol	*C. ordato-oblongum*	twig, bud	[17]
		C. moonii	leaf	[20]
			root bark	[55]
		C. polyanthum	seed	[25]
		C. ramiflorum	heartwood	[32]
		C. inophyllum	timber	[37]
			heartwood	[44]
		C. thwaitesii	root bark	[48]
		C. macrocarpum	stem bark	[54]
		C. apetalum	bark	[70]
		C. tomentosum	branch timber, sapwood	[34]
			bark	[70]
		C. gracilipes	leaf	[71]
236	β-Daucosterol	*C. polyanthum*	seed	[25]
237	Cholesterol	*C. inophyllum*	leaf	[62]
238	Stigmasterol	*C. macrocarpum*	stem bark	[54]
239	Enervosanone: 8,8-dimethyl-5-geranyl-1,7-bis(3-methylbut-2-enyl)bicyclo[3.3.1]-nonane-2,4,9-trione	*C. enervosum*	stem bark	[51][73]
240	Cambogin	*C. enervosum*	stem bark	[51]
241	Sundaicumone A	*C. sundaicum*	leaf	[74]
242	Sundaicumone B	*C. sundaicum*	leaf	[74]
243	Soulattrone A	*C. soulattri*	bark	[75]



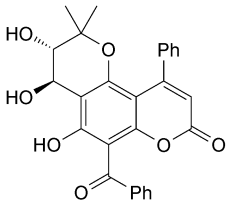
	R^1	R^2
1	β-Me	α-Me
2	β-Me	β-Me
3	α-Me	β-Me



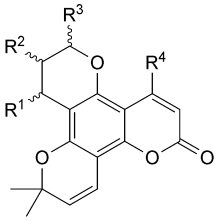
	R^1	R^2	R^3	R^4
4	β-Me	α-Me	β-OH	Me
5	β-Me	α-Me	α-OH	Me
6	β-Me	α-Me	α-MeO	Me
7	β-Me	α-Me	β-OH	Pr
8	β-Me	α-Me	β-AcO	Pr
9	β-Me	α-Me	β-MeO	Pr
10	β-Me	α-Me	α-OH	Pr
11	α-Me	β-Me	β-OH	Pr
12	α-Me	α-Me	α-MeO	Pr
13	α-Me	α-Me	β-OH	Pr
14	β-Me	β-Me	β-OH	Ph
15	α-Me	β-Me	β-OH	Ph
16	β-Me	α-Me	β-OH	Ph
17	β-Me	α-Me	α-OH	Ph
18	β-Me	β-Me	α-OH	Ph



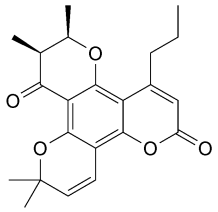
	R^1	R^2	R^3
19	Ph	MeO	(2*E*)-but-2-en-2-yl
20	Pr	OH	Ph
21	Ph	OH	Ph
22	Ph	OH	i-Bu
23	Pr	MeO	(2*E*)-but-2-en-2-yl
24	Me	OH	HOCH(Me)CH(Me)
25	Me	MeO	(2*Z*)-but-2-en-2-yl
26	Pr	OH	HOCH(Me)CH(Me)
27	Pr	OH	HOCH(Me)CH(Me)



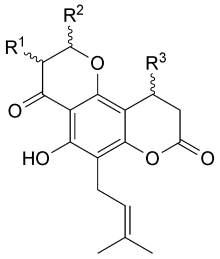
28



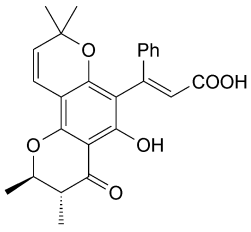
	R^1	R^2	R^3	R^4
33	α-OH	α-Me	α-Me	Me
34	β-OH	β-Me	β-Me	Pr



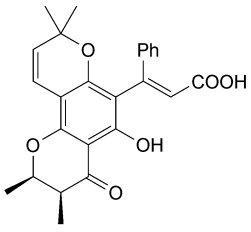
35



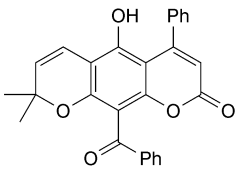
	R^1	R^2	R^3
29	β-Me	α-Me	α-Ph
30	α-Me	α-Me	α-Ph
31	β- or α-Me	α- or β-Me	Pr
32	β-Me	β-Me	Pr



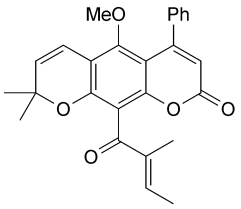
36



37



38



39

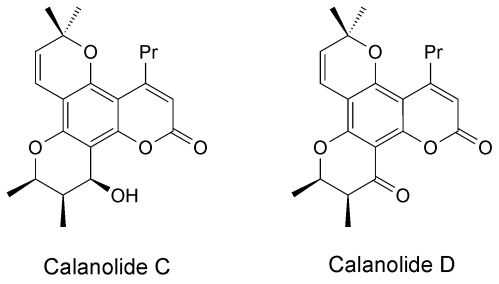


Fig. 2. *The primary structure of calanolides C and D*

As more coumarins were discovered in recent years, five new types of tricyclic pyranocoumarins were determined (*Fig. 3*): *a*) simple coumarins with a pyran ring fused at C(6)–C(7), which bear geminal dimethyl groups, (type **D**), *e.g.*, compounds **38** and **39**; *b*) simple coumarins with a pyran-4-one moiety fused at C(6)–C(7) (type **E**), *e.g.*, compounds **40**–**42**; *c*) tricyclic pyranocoumarins with a noncyclized equivalent of the *C* ring of the type **A** (type **F**) as represented by compounds **43**–**45**; *d*) tricyclic pyranocoumarins with a noncyclized equivalent of the *C* ring of the type **C** (type **G**), *e.g.*, compound **46**; *e*) tricyclic pyranocoumarins in which the C(11)=C(12) bond of the type **G** is hydrogenated (type **H**), compound **47**.

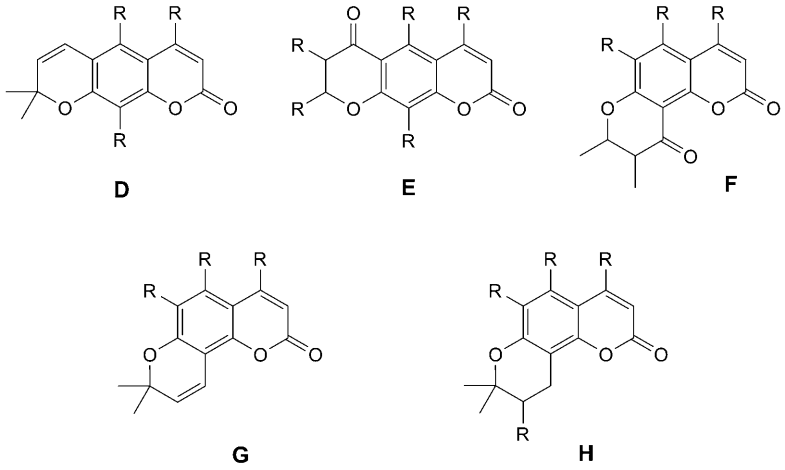
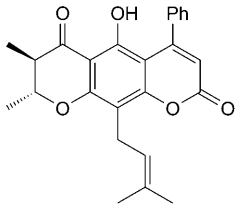
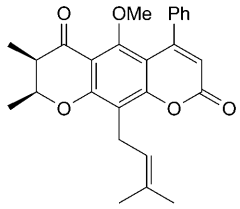


Fig. 3. *Five new structural types of pyranocoumarins*

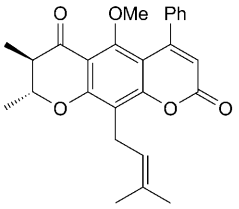
Compounds **48**–**65** belong to furocoumarins, in which the furan ring is fused at C(5)–C(6) (*i.e.*, **48**–**55**), C(6)–C(7) (*i.e.*, **56** and **57**), or C(7)–C(8) bonds (*i.e.*, **58**–**65**). Compounds **66**, **67**, and **68** possess a fused furan ring at C(5)–C(6) bond and a pyran ring at C(7)–C(8) bond. More specially, a 2-dimethylcyclopropane ring is fused to the furan ring. Mammea A/AB dioxalanocyclo F (**69**) isolated from *C. disar* has a fused furan ring with a fused dioxolane structure at the C(7)–C(8) bond.



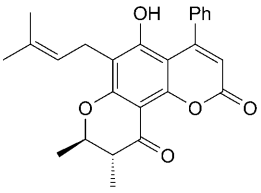
40



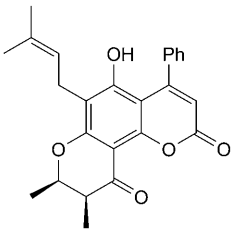
41



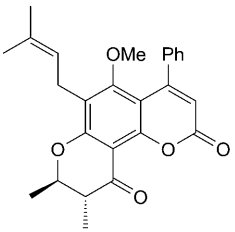
42



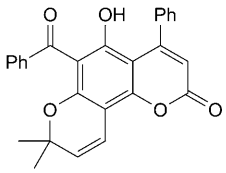
43



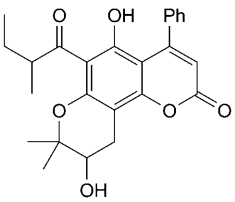
44



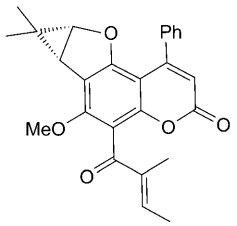
45



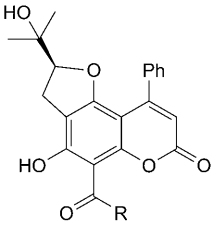
46



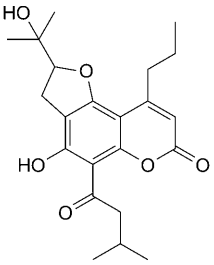
47



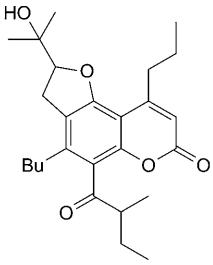
48



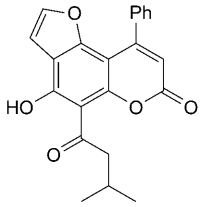
49 R = i-Bu
50 R = EtCH(Me)
51 R = Pr



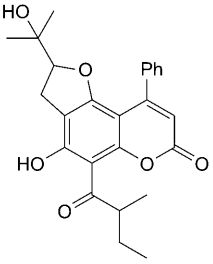
52



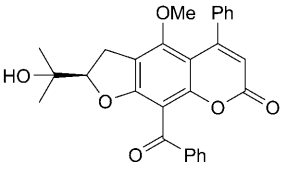
53



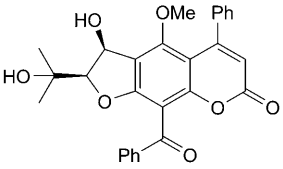
54



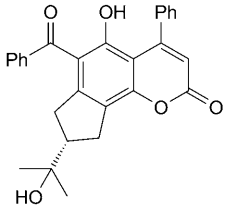
55



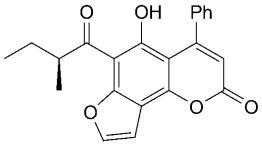
56



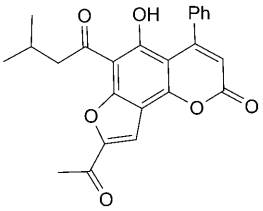
57



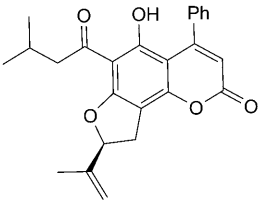
58



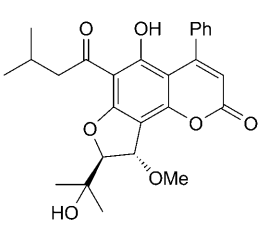
59



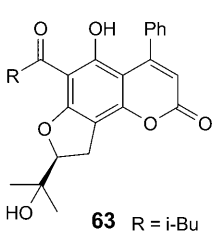
60



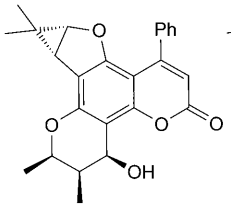
61



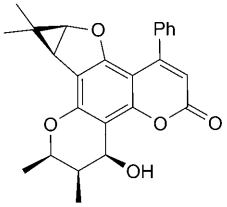
62



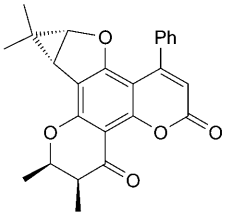
63 R = i-Bu
64 R = EtCH(Me)
65 R = Pr



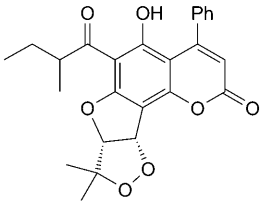
66



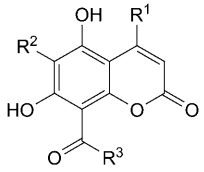
67



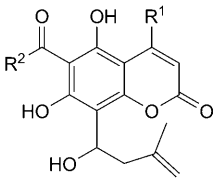
68



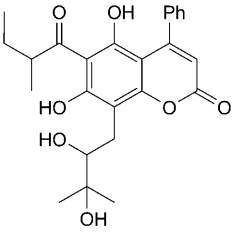
69



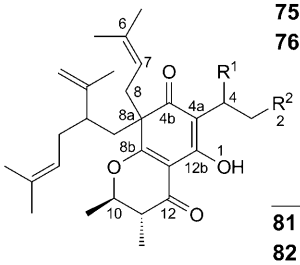
	R^1	R^2	R^3
70	Ph	isoprenyl	i-Bu
71	Ph	isoprenyl	EtCH(Me)
72	Pr	isoprenyl	i-Bu
73	Pr	isoprenyl	EtCH(Me)
74	pentyl	H	i-Bu
75	pentyl	H	EtCH(Me)
76	Ph	H	i-Bu



	R^1	R^2
77	Ph	i-Pr
78	Pr	EtCH(Me)
79	Ph	EtCH(Me)



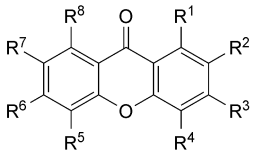
80

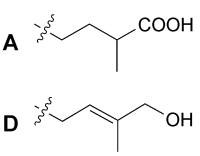


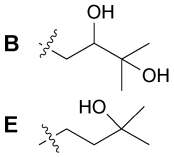
	R^1	R^2
81	Ph	COOH
82	Ph	COOMe
83	Pr	COOH
84	Pr	COOMe

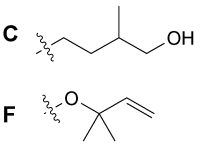
Compounds **70**–**80** are simple coumarins with differences at C(4), C(6), and C(8). Compounds **81**–**84** represent a new class of pyranocoumarin derivatives, which contain an isoprene unit and a monoterpene group at C(8a) of the unique pyranocoumarin ring system [23].

2.2. *Xanthones.* The genus *Calophyllum* is considered as a rich source of xanthone derivatives which are simply oxygenated and substituted with isoprenyl group(s) [79]. The xanthones with differences from C(1) to C(8), *i.e.*, **85**–**13** are listed in the *Table.* Besides OH, MeO, isoprenyl, and COOMe groups, the substituents also include some special groups such as 3-carboxybutyl (*i.e.*, **119** and **120**), 2,3-dihydroxy-3-methylbutyl (*i.e.*, **121**), 4-hydroxy-3-methylbutyl (*i.e.*, **123**), 4-hydroxy-3-methylbut-2-enyl (*i.e.*, **124**), and 1,1-dimethylprop-2-enyloxy (*i.e.*, **133**). The compound **122** is 1,5-dihydroxy-



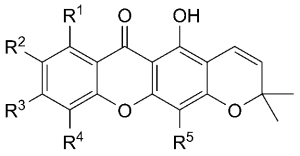




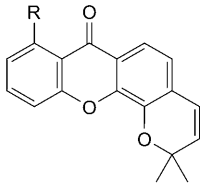


	R^1	R^2	R^3	R^4	R^5	R^6	R^7	R^8
85	H	H	H	H	H	H	OH	MeO
86	H	H	H	H	H	H	MeO	MeO
87	H	H	H	H	MeO	OH	H	H
88	H	H	H	H	MeO	MeO	OH	H
89	OH	isoprenyl	OH	H	OH	H	H	H
90	OH	H	H	H	H	H	MeO	H
91	MeO	H	MeO	H	MeO	OH	H	H
92	MeO	H	OH	H	MeO	OH	H	H
93	OH	H	OH	H	MeO	OH	MeO	H
94	H	MeO	H	H	H	H	H	H
95	H	H	H	OH	H	H	H	H
96	OH	H	H	H	H	H	OH	H
97	H	H	H	OH	H	H	H	OH
98	OH	H	H	H	OH	OH	H	H
99	OH	H	H	H	MeO	OH	H	H
100	OH	H	MeO	H	H	MeO	OH	H
101	OH	H	H	H	H	MeO	MeO	H
102	MeO	MeO	H	H	H	H	H	MeO
103	MeO	H	MeO	H	MeO	OH	MeO	H
104	H	OH	H	H	H	H	H	H
105	H	MeO	OH	MeO	H	H	H	H
106	MeO	MeO	H	H	H	H	OH	MeO
107	MeO	MeO	H	H	MeO	OH	H	H
108	MeO	MeO	OH	MeO	H	H	H	OH
109	OH	H	MeO	H	H	H	OH	H
110	H	COOMe	H	H	H	MeO	H	H
111	OH	H	OH	H	OH	OH	MeO	H
112	OH	H	OH	H	H	H	MeO	OH
113	OH	H	OH	H	H	H	MeO	MeO
114	MeO	H	H	H	MeO	OH	H	H
115	OH	MeO	OH	H	OH	H	H	H
116	OH	MeO	OH	H	MeO	H	H	H
117	MeO	MeO	OH	H	H	H	H	OH
118	OH	H	OH	H	OH	H	H	H
119	H	H	H	H	MeO	**A**	H	H
120	OH	H	H	H	MeO	**A**	H	H
121	OH	H	H	H	OH	**B**	H	H
122	OH	H	H	H	OH	isoprenyl	H	H
123	OH	H	H	H	OH	**C**	H	H
124	OH	H	H	H	OH	**D**	H	H
125	OH	H	H	H	OH	H	H	isoprenyl
126	OH	isoprenyl	OH	H	OH	H	H	H
127	OH	**E**	OH	H	OH	OH	H	H
128	OH	isoprenyl	OH	H	OH	OH	H	H
129	OH	isoprenyl	OH	H	H	H	OH	isoprenyl
130	OH	isoprenyl	OH	H	H	H	MeO	isoprenyl
131	OH	MeO	OH	isoprenyl	OH	H	H	H
132	OH	isoprenyl	MeO	H	MeO	MeO	H	H
133	OH	isoprenyl	OH	H	H	H	**F**	isoprenyl

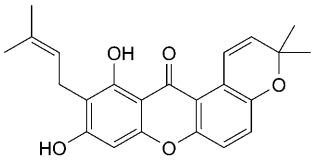
6-(3,3-dimethylbut-2-enyl)-1,5-dihydroxyxanthone, named as calophyllin B by *Jackson et al.* [46], while *Iinuma et al.* and *Gottlieb et al.* named it as guanandin [31][42]. Apetalinone A (**133**) was a novel xanthone with 1,1-dimethylprop-2-enyloxy ether moiety, which indicated a new biosynthetic pathway including *Claisen* rearrangement and *Diels–Alder* reaction. The occurrence of a xanthone with a 1,1-dimethylallyl group was reported for the first time in 1997 [40]. Compounds **134**–**147** were pyranoxanthones that possess a pyran ring at C(5)–C(6), C(6)–C(7), or C(7)–C(8). Two of them were named differently by different authors, compound **138** was named as caloxanthone C, inoxanthone, or blancoxanthone [10][49][53]; compound **139** was named as macluraxanthone and 3-hydroxyblancoxanthone [10][36][49][53]. Jacareubin (**135**) and 6-dehydroxyjacareubin (**136**) are very common constituents in genus *Calophyllum*. They have been found in *C. cordato-oblongum*, *C. tomentosum*, *C. neoebudicum*, *C. brasiliense*, *C. inophyllum*, *C. ramiflorum*, and *C. austroindicum* [31–34][37][41][42][44–46]. *C. moonii* afforded a trioxygenated diprenylated chromenxanthone, dombakinaxanthone (**144**) [55]. The pyranoxanthones **148**–**151** possess two pyran rings at C(2)–C(3) and C(6)–C(7) or C(7)–C(8). A 2,2-dimethyl-3,4-dihydropyrane ring was united in xanthones **152**–**155**, while a furan ring was united in xanthones **156**–**160**. Compounds **161**–**166** were isolated from *C. apetalum*. *Iinuma et al.* listed the biosynthesis of compounds **161**–**163** and **165** (*Schemes 1* and *2*) [40][56].



	R^1	R^2	R^3	R^4	R^5
134	H	OH	H	H	H
135	H	H	OH	OH	H
136	H	H	H	OH	H
137	H	OH	OH	isoprenyl	H
138	H	H	H	OH	CH_2=CHC(Me)$_2$
139	H	H	OH	OH	CH_2=CHC(Me)$_2$
140	H	H	H	AcO	CH_2=CHC(Me)$_2$
141	H	H	H	OH	isoprenyl
142	isoprenyl	MeO	H	H	H
143	isoprenyl	OH	H	H	H
144	isoprenyl	OH	H	H	isoprenyl



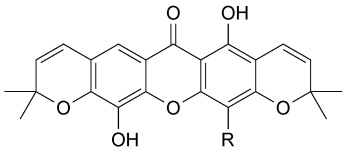
145 R = H
146 R = OH



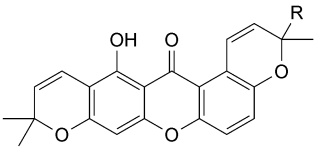
147

2.3. *Chromanones.* 2.3.1. *Flavonoids.* Compounds **157**–**171** are simple flavonoids obtained from genus *Calophyllum* [31][36][40][51][57]. The isoflavone **172** was isolated from *C. polyanthum* [25].

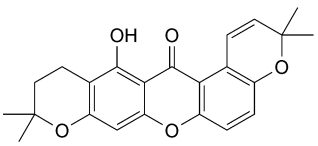
2.3.2. *Biflavonoids.* The types of biflavonoids isolated from *Calophyllum* species are: *a*) flavanone-flavonol, **173** and **174**; *b*) flavanone-flavanone, **175** and **176**; *c*) flavanone-flavonol, **177** and **178**; *d*) flavanone-flavone, **179**; and *e*) flavone-flavone, **180**) [24][58][59].



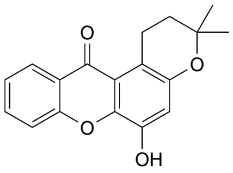
148 R = H
149 R = isoprenyl



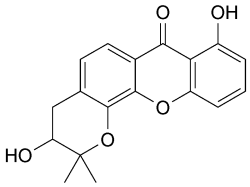
150 R = Me
151 R = $HOCH_2$



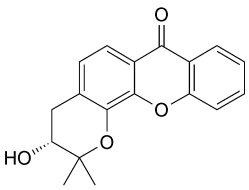
152



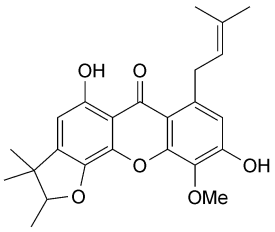
153



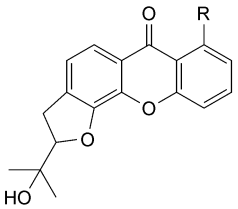
154



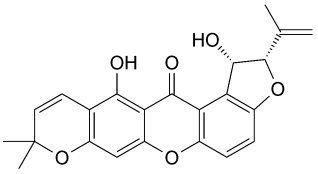
155



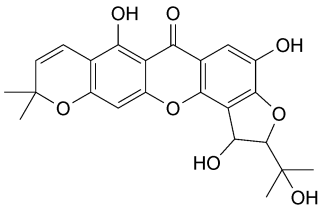
156



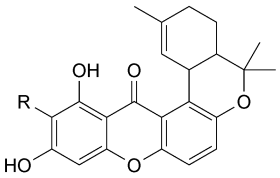
157 R = OH
158 R = H



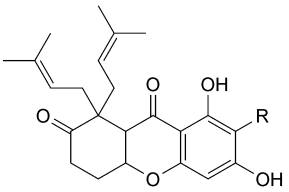
159



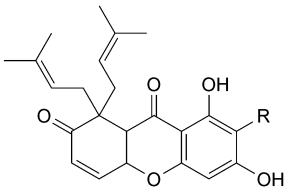
160



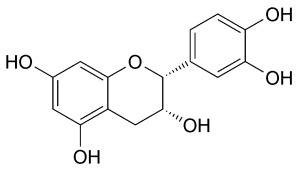
161 R = isoprenyl
162 R = H



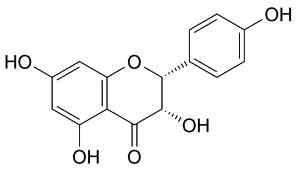
163 R = isoprenyl
164 R = H



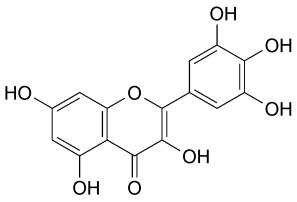
165 R = isoprenyl
166 R = H



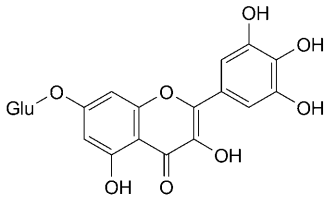
167



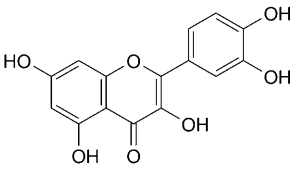
168



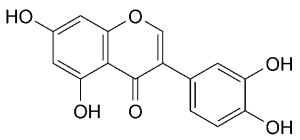
169



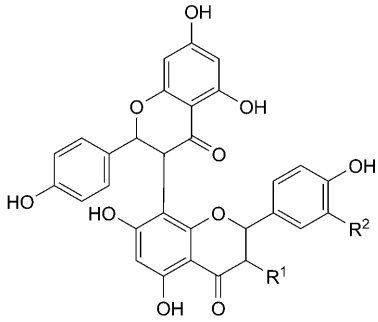
170



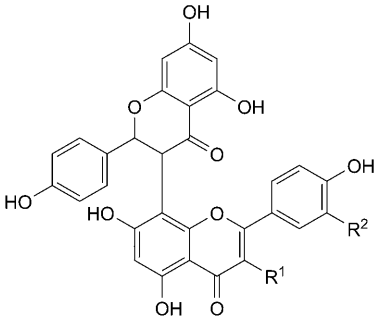
171



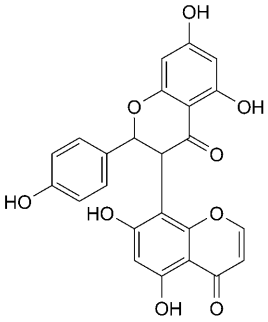
172



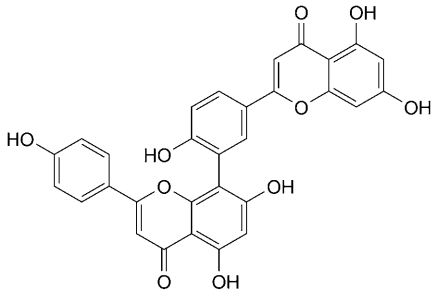
	R^1	R^2
173	OH	H
174	OH	OH
175	H	H
176	H	OH



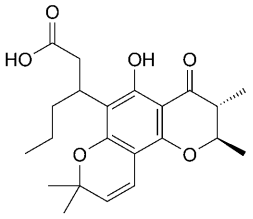
	R^1	R^2
177	OH	OH
178	OH	H



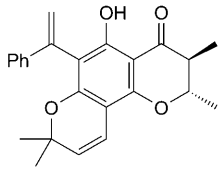
179



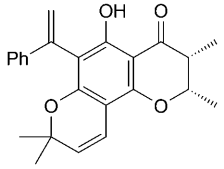
180



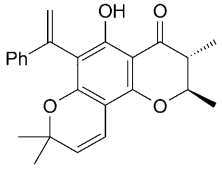
181



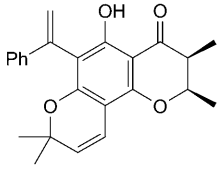
182



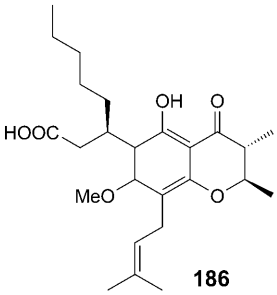
183



184

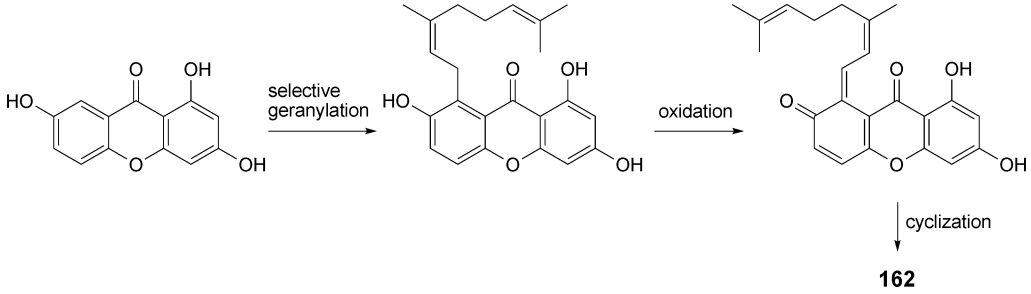


185

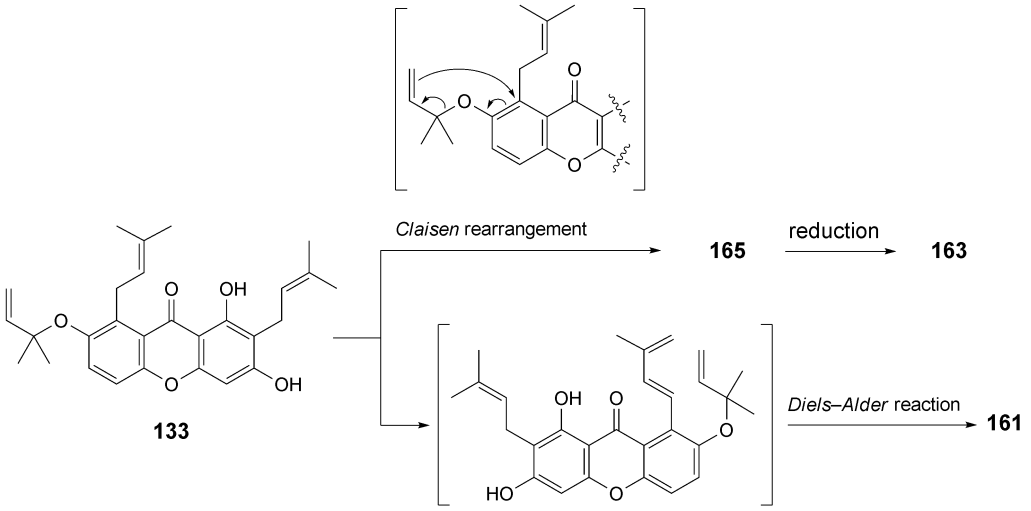


186

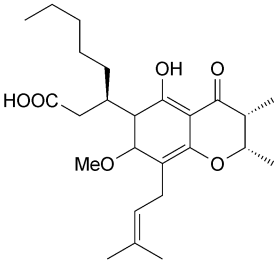
Scheme 1. *Hypothetical Biosynthesis of Compound* **162** *through a Geranylated Precursor* [56]



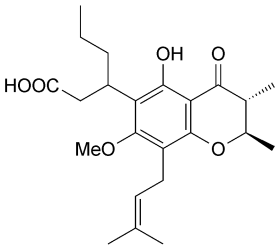
Scheme 2. *Possible Biosynthetic Pathways of Compounds* **161**, **163**, *and* **165** *Derived from* **133** [40]



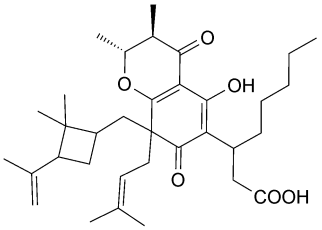
2.3.3. *Further Chromanone Derivatives.* Compounds **181**–**185** are five 1-benzopyran-4-one derivatives which possess an additional pyran ring fused at C(7)–C(8) bond. Papuanic and isopapuanic acids (**186** and **187**, resp.) represented the first pair of stereoisomeric products isolated from a species of *Calophyllum* [63]. Compounds **189**–**191** were isolated from *C. verticillatum* [64]. They have a rarely occurring cyclobutane moiety derived from the equally unusual lavandulyl chain. Compounds **190** and **191** are definitely distinct substances, since they can be easily separated on TLC plates. Small, but significant differences were also observed in the ^{1}H-NMR spectra, particularly in the chemical shifts of the signals for the two side chains. It was proposed that the absolute configuration at C(6) may differ in compounds **190** and **191**, although changes in the absolute configuration at C(22) and C(23) cannot be totally ruled out.



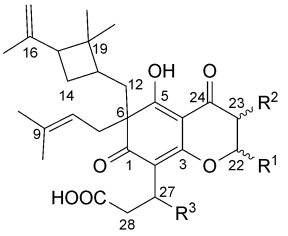
187



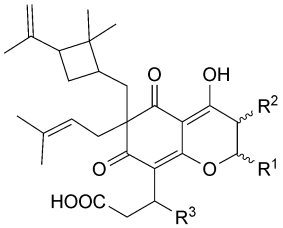
188



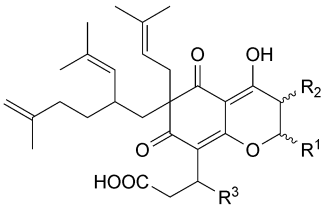
189



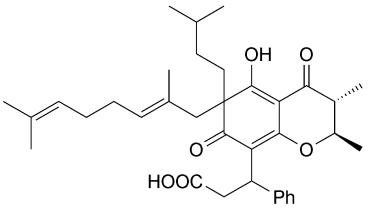
	R^1	R^2	R^3
190, **191**	β-Me	α-Me	pentyl
192	α-Me	β-Me	Ph
193	β-Me	β-Me	Ph



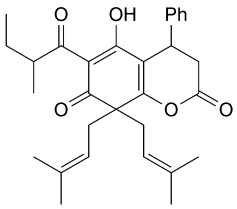
	R^1	R^2	R^3
194	α-Me	β-Me	Ph
195	β-Me	β-Me	Ph



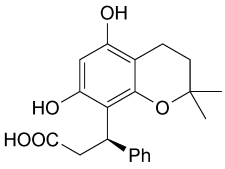
	R^1	R^2	R^3
196	α-Me	β-Me	Ph
197	β-Me	β-Me	Ph



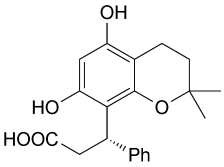
198



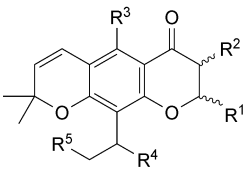
199



200



201

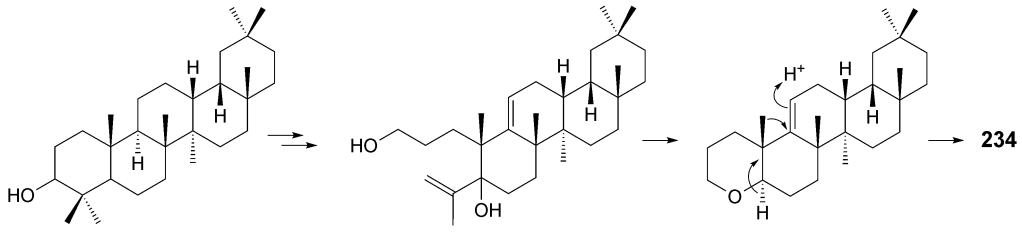


	R^1	R^2	R^3	R^4	R^5
202	β-Me	β-Me	OH	Pr	COOH
203	β-Me	α-Me	OH	Pr	COOH
204	β-Me	β-Me	OH	Pr	COOMe
205	β-Me	β-Me	AcO	Pr	COOH
206	β-Me	α-Me	OH	Pr	COOMe
207	β-Me	α-Me	AcO	Pr	COOH
208	α-Me	β-Me	OH	Ph	COOH
209	β-Me	β-Me	OH	Ph	COOH
210	α-Me	β-Me	OH	Me	COOH
211	β-Me	β-Me	OH	Me	COOH

Unfortunately, this point was not further investigated [64]. Compounds **192**–**197** were obtained from the bark of *C. brasiliense*. Four of them also exhibit an unusual cyclobutane ring (*i.e.*, **192**–**195**) [65]. Calozeylanic acid (**198**) appears to be the biogenetic precursor of chapelieric acid (**208**) found in the leaf extract of *C. calaba* [20]. In 1984, two neoflavonoids, thwaitesic acid (**200**) and isothwaitesic acid (**201**), were isolated from *C. thwaiteii* and *C. lankaensis*. The presence of the same acids in the leaves as well as in the bark of the same plant is of biogenetic significance [66]. Compounds **202**–**211** are ten pyranochromanone derivatives isolated from various *Calophyllum* species [27][54][59][68][17].

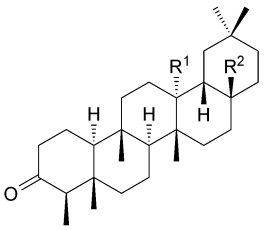
2.4. *Triterpenes and Steroids.* Among the triterpenes and steroids isolated from genus *Calophyllum*, friedelin (**212**), canophyllol (**213**), betulinic acid (**225**), and sitosterol (**235**) are most frequent. Compound **231** is a seco-triterpenoid. Apetalactone (**232**) from *C. lankaensis* and *C. moonii* possesses a lactone ring. Squalene (**233**) and gracilipene (**234**) were isolated from the leaves of *C. gracilipes*. Gracilipene (**234**) is a heterocyclic trisnor-triterpene that shows an unprecedented rearranged trisnor-seco-oleanane structure with a dihydropyran ring *A*. The possible biosynthesis of gracilipene (**234**) is depicted in *Scheme 3* [71].

Scheme 3. *Plausible Biosynthesis of Gracilipene* (**234**)

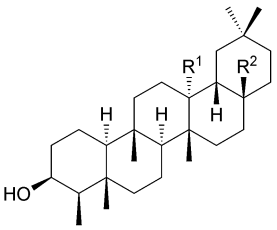


2.5. *Others.* In 2005, *Taher et al.* isolated two phloroglucinol derivatives, enervosanone (**239**) and cambogin (**240**), from the stem bark of *C. enervosum* [51]. Later, *Cao et al.* also isolated two similar compounds, **241** and **242**, from *C. sundaicum*, of which the structures contain a 3-propylpropanoic acid moiety not previously reported in other polyprenylated acylphloroglucinols [74]. The structure of soulattrone A (**243**), a C_{24} terpenoid isolated from the bark of *C. soulattri*, does not obey the terpene rules *sensu stricto*, but it might be considered as either a modified sesterterpene or a diprenyl-sesquiterpene derivative [75].

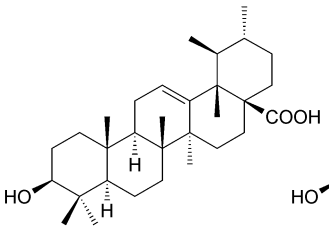
3. Biological Activity. – 3.1. *Antiviral Activities.* Five isolated pyranoxanthones, *i.e.*, blancoxanthone (**138**), 3-hydroxyblancoxanthone (**139**), acetylblancoxanthone (**140**), pyranojacaeubin (**148**), and caloxanthone (**149**), were tested against coronavirus *in vitro*. Compounds **138** and **148** exhibited viral inhibition with EC_{50} values of 3 and 15 μg/ml, respectively. This result suggested that compound **138** might be a potential candidate in the treatment of coronavirus infection [53].



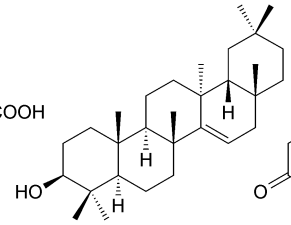
	R^1	R^2
212	Me	Me
213	Me	$HOCH_2$
214	Me	CHO
215	$AcOCH_2$	COOH



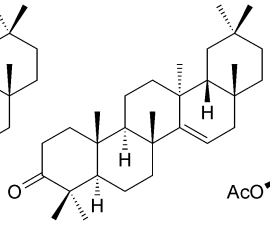
	R^1	R^2
216	Me	COOH
217	Me	Me
218	Me	$HOCH_2$
219	$AcOCH_2$	COOH



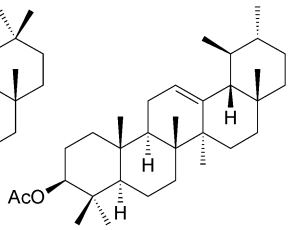
220



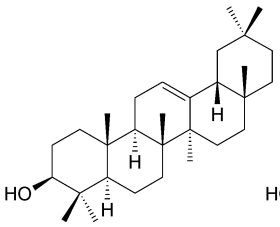
221



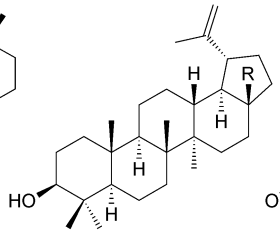
222



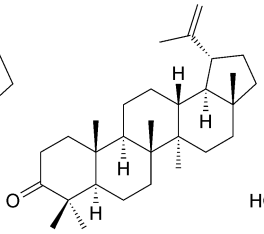
223



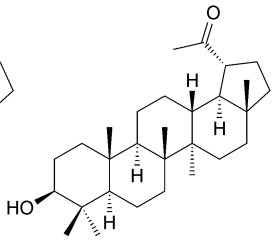
224



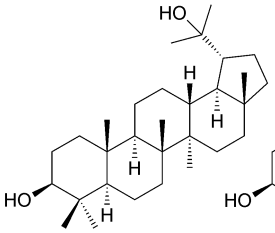
225 R = COOH
226 R = Me



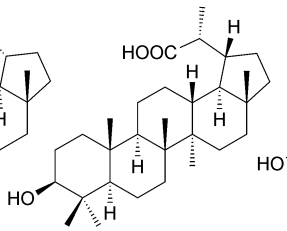
227



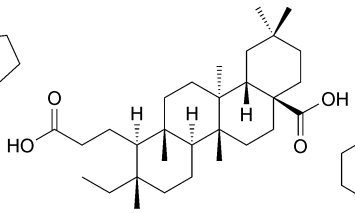
228



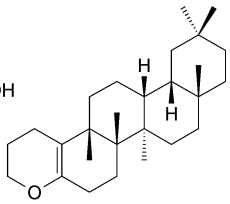
229



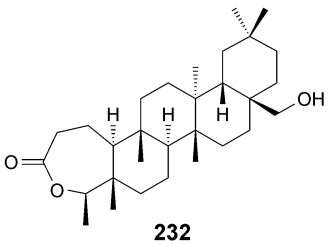
230



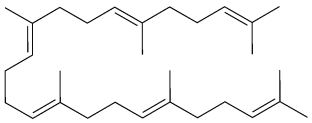
231



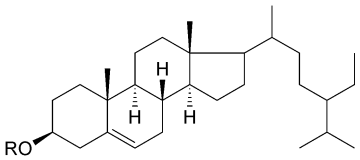
234



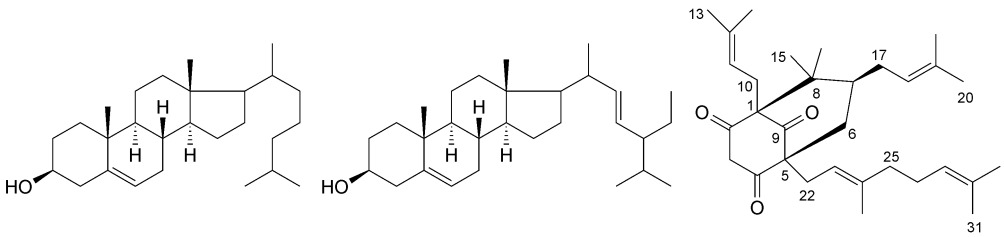
232



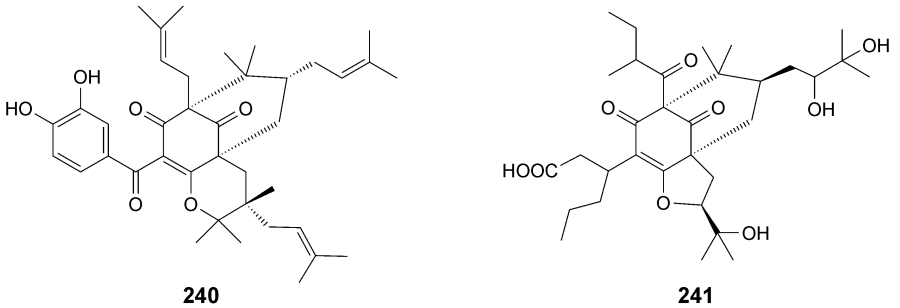
233



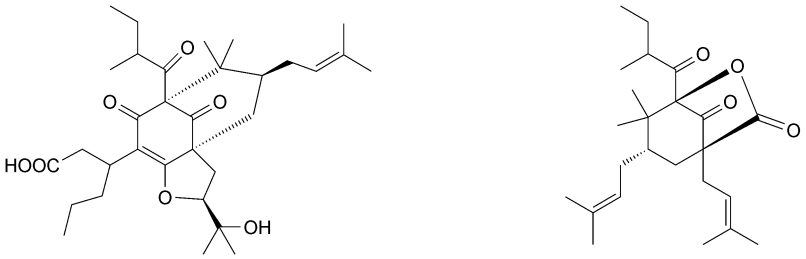
235 R = OH
236 R = Glu



237 **238** **239**



240 **241**



242 **243**

Besides, the highest attention was focused on anti-HIV activities. The calanolides and inophyllums, isolated from the genus *Calophyllum*, can be considered as NNRTIs, as they are primarily active against HIV-1 RT, but differ from the classical (synthetic) NNRTIs in their HIV sensitivity/resistance profile [80]. The following developments should be mentioned.

In 1992, eight coumarins, **7**–**10**, **12**, **26**, **34**, and **35**, isolated from *C. lanigerum* were evaluated for their anti-HIV activity [3]. Calanolides A and B (**7** and **10**, resp.) were completely protective against HIV-1 replication and cytopathicity (EC_{50} values of 0.1 and 0.4 μM, resp.). 12-Acetoxycalanolide A (**8**) was also active, albeit less potent (EC_{50} 2.7 μM). The apparent *in vitro* therapeutic indices (*TI*) for compounds **7**, **8**, and **10** were 200, 5, and 37, respectively. Studies with purified bacterial recombinant RT revealed that the calanolides are HIV-1-specific RT inhibitors distinct from any previously known pharmacologic class. Moreover, calanolide A (**7**) was active not only against AZT-resistant viral strains, as well as against the A 17 strain, which is known to be resistant to non-nucleoside RT inhibitors. Therefore, the pyranocoumarins provide a

new class of anti-HIV compounds [3]. In 1993, *Kashman et al.* tested compounds **1**, **2**, **14**, **16**–**19**, **36**, **37**, **66**, and **67** for their inhibitory activity against HIV-1 RT. Inophyllums B and P (**16** and **17**, resp.) inhibited HIV RT with IC_{50} values of 38 and 130 μM, respectively, and both were active against HIV-1 in cell culture (IC_{50} 1.4 and 1.6 μM, resp.). The configuration at C(12) is not critical, because **16** and **17** are both active at submicromolar concentrations, but the presence of a C=O group at this position lowered the activity significantly. The other compounds were much less active or inactive [2]. Soulattrolide (**15**), the enantiomer of inophyllum P (**17**), which was isolated from *C. teysmannii* latex, also found to be a potent inhibitor of HIV-1 RT with an IC_{50} value of 0.34 μM [21]. In 2003, *Yu et al.* reviewed the recent progress in the development of coumarin derivatives as potent anti-HIV agents [81]. For the coumarins isolated from genus *Calophyllum*, they determined the structure–activity relationship as well as the mechanism of action. First, bulky substituents are required at C(4); second, both calanolides and inophyllums require Me groups at C(10) and C(11) of the chromanol ring to be *trans*-diaxial; third, both calanolides and inophyllums require a H-bond acceptor at C(12). In case of calanolides, the configuration at C(12) should be (*S*), or C=O group can be present. The configuration at C(12) of inophyllums can be either (*S*) or (*R*), but a C=O group is not allowed.

3.2. *Antitumor-Promoting Activity.* In 2001, *Ito et al.* investigated the antitumor-promoting activity of ten natural 4-phenylcoumarins using the short-term *in vitro* assay of 12-*O*-tetradecanoylphorbol-13-acetate (TPA)-induced *Epstein–Barr* virus early antigen (EBV-EA) activation in *Raji* cells [82]. The compounds are tetracyclic (*i.e.*, **1**, **2**, **14**, and **18**), tricyclic (*i.e.*, **19**, **39**, and **44**), and dimethylcyclopropan fused (*i.e.*, **48** and **68**) 4-phenylcoumarins, and isocalophyllic acid (**37**), which were isolated from *C. inophyllum*. All tested compounds except for inophyllum C (**1**) and calocoumarin C (**68**) showed an inhibitory effect on EBV-EA activation, even at 1×10 mol ratio, and only weak cytotoxicity against *Raji* cells, even at 1×10^3 mol ratio. Calocoumarin A (**44**) showed more potent activity than any of the other compounds, suggesting that the prenyl side chain is decisive in increasing the antitumor-promoting effect [83]. Furthermore, calocoumarin A (**44**) exhibited a marked inhibitory effect on mouse skin tumor promotion in an *in vivo* two-stage carcinogenesis test. The results of the investigation by *Ito et al.* indicated that some of these 4-phenylcoumarins might be valuable as potential cancer chemopreventive agents (antitumor promoters) [82]. In 2005, *Ito et al.* also tested three 4-phenylcoumarins (*i.e.*, **21**, **43**, and **55**), and five 4-propylcoumarins (*i.e.*, **7**, **20**, **23**, **34**, and **73**), which were isolated from the stem bark of *C. brasiliense* [11]. All tested compounds showed inhibitory activity against EBV-EA without showing any cytotoxicity. The IC_{50} values of all tested compounds were lower than that of β-carotene. Among 4-propylcoumarins, **7**, **23**, and **73** showed more significant activities compared with 4-phenylcoumarins, **21**, **43**, and **55**. Mammea B/BB (**73**), 4-propylcoumarin with a prenyl side chain, exhibited the most potent inhibitory activity. Calanolide A (**7**) with *trans*-oriented 10,11-dimethyl groups was more potent than the corresponding *cis*-derivative, *i.e.*, calanolide C (**34**). These results are in accordance with the pattern of anti-HIV activity that the functional groups at C(10), C(11), and C(12), and their derivatives are critical for their anti-HIV activity [11].

Besides the coumarins, the antitumor-promoting activity of biflavonoids was also evaluated in the same way. Six biflavonoids, **173**–**178**, isolated from *C. panciflorum*,

along with two others from genus *Garcinia*, showed significant inhibitory effects at high concentrations (1×10^3 mol ratio) but weak cytotoxicities in assays of *Raji* cells. Among these compounds, garcinianin (**178**) showed the most significant inhibitory effect on EBV-EA activation (100% inhibition of activation at 1×10^3 mol ratio/TPA) [58].

3.3. *Inhibition of the Multidrug Transporter P-glycoprotein. Raad et al.* studied the structure–activity relationship of natural and synthetic coumarins originated from the genus *Calophyllum* inhibiting the multidrug transporter P-glycoprotein. Results showed a favorable electrostatic and steric volume, like the (1-hydroxy-1-methylethyl)dihydrofuran moiety, fused at the C(5)–C(6) or C(7)–C(8) bond. In addition, the analysis revealed an important hydrophobic, neutral-charge group, like Ph, at C(4) of the coumarin ring [76].

3.4. *Cytotoxic Activity.* The coumarins isolated from *C. brasiliense* were cytotoxic against K562, U251, and PC3 human tumor cell lines. The highest activity was exhibited by mammea A/BA (**70**; IC_{50} 0.04 to 0.59 μM). The mixtures of mammea A/BA + A/BB (**70** and **71**), mammea B/BA + B/BB (**72** and **73**), and mammea C/OA + C/OB (**74** and **75**) were also highly active ($IC_{50} < 4.05$ μM). In contrast, mammea B/BA cyclo F (**52**) pure or in mixture with mammea B/BB cyclo F (**53**) were less potent with IC_{50} values of 5.0–63 μM. The above data suggest that a Pr, pentyl, or Ph group at C(4) (*i.e.*, **70**–**75**) is relevant for high cytoxic activity. On the other hand, a 6-prenyl chain (*i.e.*, **70**–**75**) increases cytotoxicity, but this effect decreases if this substituent is cyclized to a dihydrofuran or a pyran ring (*i.e.*, **52** and **53**) [24]. GUT-70, characterized as a tricyclic coumarin, 5-methoxy-2,2-dimethyl-6-(2-methyl-1-oxobut-2-enyl)-10-propyl-2*H*,8*H*-benzo[1,2-*b*;3,4-*b*′]dipyran-8-one (**23**), was tested on six human leukemic cell lines, BV173, K562, NALM6, HL60, SEM, and the colorectal adenocarcinoma cell line HCT116, including a P-glycoprotein over-expressing cell line. It significantly inhibited the growth of leukemic cells by inducing caspase-mediated and p53-independent apoptosis, and can overcome multidrug resistance [84]. The cytotoxic effect against KB cell of a number of known compounds isolated from genus *Calophyllum* was evaluated. Calophyllolide **19** displayed the most significant cytotoxic activity against KB cells with an IC_{50} value of 3.5 μg/ml. Other compounds such as caloxanthone A (**139**), with an IC_{50} value of 7.4 μg/ml, was considered, in addition to calaustralin (**40**) and inophyllum E (**2**), as inactive [10]. The furanocoumarins mammea A/BA cyclo F (**49**), mammea A/AA cyclo F (**63**), mammea A/AB cyclo F (**64**), mammea A/AC cyclo F (**65**), together with other coumarins, isodispar B (**76**), disparpropylinol B (**78**), and disparinol B (**79**), which were all isolated from *C. dispar*, also exhibited significant activities in this assay, since these compounds inhibited 50% of the cellular growth at concentration ranging from 5 to 9 and 4 to 8 μg/ml, respectively [29][30].

3.5. *Antimalarial Activity. Hay et al.* tested the activity on a chloroquino-resistant strain of *Plasmodium falciparum* of seven xanthones, **129**, **138**, **139**, **143**, **144**, **147**, and **162**, which were obtained from *C. caledonicum*. They showed IC_{50} values from 0.8 to 4.4 μg/ml. Regarding the structure–activity relationship, the authors concluded that *1*) the position of the OH groups appears to be important; *2*) the substitution by a 1,1-dimethylallyl chain, or the presence of an additional pyran ring appear to be factors for good activity, as well as the substitution with two isopentenyl chains, or the combination of one isopentenyl chain and a pyranic ring; and *3*) hydroxylation of the prenyl side chain is not required for higher activity [49].

3.6. *Antibacterial Activity.* The MeOH extracts of leaves, root, and stem barks of *C. soulattri* were partitioned with petroleum ether, CH_2Cl_2, and AcOEt. All extracts showed a range of activity against all the tested bacteria and protozoan. Fractionation improved the level of activity, particularly the petroleum ether fraction of the root bark [5]. Besides the extracts, the antibacterial activity of several constituents were also evaluated. Six chromanone acids, *i.e.*, **192**–**197**, isolated from *C. brasiliense* showed moderate-to-strong antibacterial activity against the *Gram*-positive bacteria *Bacillus cereus* and *Staphylococcus epidermidis*. Compounds **194** and **195** were most active against *B. cereus*, while compounds **196** and **197** are less active. Thus, the presence of a cyclobutane ring in compounds **192**–**195** most probably contributes to the strong antibacterial activity [65]. Mammea A/BA + A/BB (**70** + **71**), and mammea C/OA + C/OB (**74** + **75**) inhibited the growth of *S. aureus*, *S. epidermidis*, and *B. subtilis* [24]. The inhibition of *S. aureus* was also observed with calozeyloxanthone. The *MIC* values of calozeyloxanthone (**162**) for *S. aureus* ranged from 4.1 to 8.1 μg/ml. Hence, **162** appears to hold promise as an antimicrobial agent in the treatment of infections with *S. aureus* [85]. In 2004, *Yimdjo et al.* also evaluated the isolated compounds for their antimicrobial and potency against representative *Gram*-positive (*S. aureus*, *Vibrio anguillarium*) and *Gram*-negative (*Escherichia coli*) bacteria, and yeast, and *Candida tropicalis* organisms, in agar well diffusion assays. At the dose of 20 μg/disc, caloxanthone A (**137**), calophyllolide (**19**), and inophyllum C (**1**) and E (**2**) were found to exhibit significant inhibitory activity against *S. aureus*, but not against other microorganisms [21].

3.7. *Activity in Gastrointestinal Affections. Sartori et al.* investigated the pharmacological basis for the ethnomedicinal use of stem bark extracts of *C. brasiliense* in gastrointestinal affections. This study examined the effects of a CH_2Cl_2 fraction, obtained from the hexane extract of bark, on EtOH, indomethacin, and hypothermic restraint stress-induced gastric lesions in mice and rats, respectively. Oral administration of CH_2Cl_2 fraction at doses ranging from 12.5 to 250 μg/kg significantly inhibited the development of gastric lesions in all three test models. It caused significant decreases of the pyloric-ligation and bethanechol-stimulated gastric secretion, and also the free and total acidities. Besides, CH_2Cl_2 fraction offered protection against EtOH-induced depletion of stomach-wall mucus and reduction in nonprotein sulfhydryl concentration. The results indicate that CH_2Cl_2 fraction from *C. brasiliense* possesses antisecretory, antiulcer, and cytoprotective properties [6].

3.8. *Inhibition of Sulfotransferases.* Four xanthones, **127**, **128**, **135**, and **136**, and two coumarins, **70** and **74**, which were obtained from *C. brasiliense*, were tested as substrates and inhibitors for two recombinant sulfotransferases (SULTs). Assays were performed using recombinant phenolsulfotransferase (SULT1A1) and hydroxysteroidsulfotransferase (SULT2A1). Two xanthones, **135** and **136**, and two coumarins, **70** and **74**, tested were substrates for SULT1A1, while the coumarin mammea A/BA (**70**) was a substrate for SULT2A1. The xanthones **127**, **128**, **135**, and **136** reversibly inhibited SULT1A1 with IC_{50} values ranging from 1.6 to 7.4 μM. Both coumarins **70** and **74** inhibited SULT1A1 with IC_{50} values of 47 and 185 μM, and SULT2A1 with IC_{50} values of 16 and 31 μM. The results indicate that SULT1A1, but not SULT2A1, is highly sensitive to inhibition by xanthones. The potency of this inhibition depends on the position and number of OH

groups. Conversely, SULT2A1 is 3–6 times more sensitive to coumarins than SULT1A1 [86].

4. Conclusions. – The plants of the genus *Calophyllum* are well known as rich sources of bioactive xanthones and coumarins. Biflavonoids and neoflavonoids are also distinctive constituents in this genus. The studies on chemical constituents in recent years have disclosed many different activities of the isolated compounds, such as antiviral activity, antitumor-promoting activity, inhibition of the multidrug transporter P-glycoprotein, cytotoxic activity, antimalarial activity, antibacterial activity, activity in gastrointestinal affections, and inhibition of sulfotransferases, especially anti-HIV activity of calanolides and inophyllums. The possible biosynthetic pathways of several compounds are also reviewed in this article. Nevertheless, there are still many plants of this genus that have not yet received enough attention. This review might provide some motivation for further investigations on genus *Calophyllum*.

REFERENCES

[1] S. Crane, G. Aurore, H. Joseph, Z. Mouloungui, P. Bourgeois, *Phytochemistry* **2005**, *66*, 1825.
[2] A. D. Patil, A. J. Freyer, D. S. Eggleston, R. C. Haltiwanger, M. F. Bean, P. B. Taylor, M. J. Caranfa, A. L. Breen, H. R. Bartus, R. K. Johnson, R. P. Hertzberg, J. W. Westly, *J. Med. Chem.* **1993**, *36*, 4131.
[3] Y. Kashman, K. R. Gustafson, R. W. Fuller, J. H. Cardellina II, J. B. McMahon, M. J. Currens, R. W. Buckheit Jr., S. H. Hughes, G. M. Cragg, M. R. Boyd, *J. Med. Chem.* **1992**, *35*, 2735.
[4] C. Morel, D. Séraphin, J. M. Oger, M. Litaudon, T. Sévenet, P. Richomme, J. Bruneton, *J. Nat. Prod.* **2000**, *63*, 1471.
[5] M. R. Khan, M. Kihara, A. D. Omoloso, *Fitoterapia* **2002**, *73*, 741.
[6] N. T. Sartori, D. Canepelle, P. T. Sousa Jr., D. T. O. Martins, *J. Ethnopharmacol.* **1999**, *67*, 149.
[7] N. Y. Chiu, K. H. Chang, 'The Illustrated Medicinal Plants of Taiwan', Institute of Chinese Pharmaceutical Science, China Medical College, Taichung, Taiwan, 1995, Vol. 4, p. 117.
[8] K. Kawazu, H. Ohigashi, T. Mitsui, *Tetrahedron Lett.* **1968**, *9*, 2383.
[9] C. Spino, M. Dodier, S. Sotheeswaran, *BioMed. Chem. Lett.* **1998**, *8*, 3475.
[10] M. C. Yimdjo, A. G. Azebaze, A. E. Nkengfack, A. M. Meyer, B. Bodo, Z. T. Fomum, *Phytochemistry* **2004**, *65*, 2789.
[11] C. Ito, M. Itoigawa, Y. Mishina, V. C. Filho, F. Enjo, H. Tokuda, H. Nishino, H. Furukawa, *J. Nat. Prod.* **2003**, *66*, 368.
[12] S. G. Cao, K. Y. Sim, J. Pereira, S. H. Goh, *Phytochemistry* **1998**, *47*, 773.
[13] S. G. Cao, X. H. Wu, K. Y. Sim, B. H. K. Tan, J. J. Vittal, J. T. Pereira, S. H. Gob, *Helv. Chim. Acta* **1998**, *81*, 1404.
[14] K. R. Gustafson, H. R. Bokesch, R. W. Fuller, J. H. Cardellina, M. R. Kadushin, D. D. Soejarto, M. R. Boyd, *Tetrahedron Lett.* **1994**, *35*, 5821.
[15] T. C. McKee, C. D. Covington, R. W. Fuller, H. R. Bokesch, S. Young, J. H. Cardellina II, M. R. Kadushin, D. D. Soejarto, P. F. Stevens, G. M. Cragg, M. R. Boyd, *J. Nat. Prod.* **1998**, *61*, 1252.
[16] H. R. W. Dharmaratne, S. Sotheeswaran, S. Balasubramaniam, E. S. Waight, *Phytochemistry* **1985**, *24*, 1553.
[17] H. R. W. Dharmaratne, J. R. D. M. Sajeevani, G. P. K. Marasinghe, E. M. H. G. S. Ekanayake, *Phytochemistry* **1998**, *49*, 995.
[18] R. W. Fuller, H. R. Bokesch, K. R. Gustafson, T. C. McKee, J. H. Cardellina II, J. B. McMahon, G. M. Cragg, D. D. Soejarto, M. R. Boyd, *BioMed. Chem. Lett.* **1994**, *4*, 1961.
[19] T. C. McKee, R. W. Fuller, C. D. Covington, J. H. Cardellina II, R. J. Gulakowski, B. L. Krepps, J. B. McMahon, M. R. Boyd, *J. Nat. Prod.* **1996**, *59*, 754.

[20] B. M. R. Bandara, H. Ranjith, W. Dharmaratne, S. Sotheeswaran, S. Balasubramaniam, *Phytochemistry* **1986**, *25*, 425.
[21] T. Pengsuparp, *J. Nat. Prod.* **1996**, *59*, 839.
[22] C. Ito, Y. Mishina, M. Ohta, H. Furukawa, H. Tan, H. Tokuda, H. Nishino, The 119th Annual Meetings of the Pharmaceutical Society of Japan, Tokushima, March 1999, Abstract II, p. 156.
[23] Y. C. Shen, M. C. Hung, L. T. Wang, C. Y. Chen, *Chem. Pharm. Bull.* **2003**, *51*, 802.
[24] R. Reyes-Chilpa, E. Estrada-Muñiz, T. R. Apan, B. Amekraz, A. Aumelas, C. K. Jankowski, M. Vázquez-Torres, *Life Sci.* **2004**, *75*, 1635.
[25] C. H. Ma, B. Chen, H. Y. Qi, B. G. Li, G. L. Zhang, *J. Nat. Prod.* **2004**, *67*, 1598.
[26] E. Guerreiro, G. Kunesch, J. Polonsky, *Phytochemistry* **1973**, *12*, 185.
[27] Y. C. Shen, L. T. Wang, A. T. Khalil, Y. H. Kuo, *Chem. Pharm. Bull.* **2004**, *52*, 402.
[28] G. D. Breck, G. H. Stout, *J. Org. Chem.* **1969**, *34*, 4203.
[29] D. Guilet, D. Séraphin, D. Rondeau, P. Richomme, J. Bruneton, *Phytochemistry* **2001**, *58*, 571.
[30] D. Guilet, J. J. Hélesbeux, D. Séraphin, T. Sévenet, P. Richomme, J. Bruneton, *J. Nat. Prod.* **2001**, *64*, 563.
[31] M. Iinuma, H. Tosa, N. Toriyama, T. Tanaka, T. Ito, V. Chelladurai, *Phytochemistry* **1996**, *43*, 681.
[32] S. Bhanu, F. Scheinmann, A. Jefferson, *Phytochemistry* **1975**, *14*, 298.
[33] F. S. A. Jeboury, H. D. Locksley, *Phytochemistry* **1971**, *10*, 603.
[34] S. Karunanayake, S. Sotheeswaran, M. Uvais, S. Sultanbawa, S. Balasubramaniam, *Phytochemistry* **1981**, *20*, 1303.
[35] A. Kijjoa, M. J. Gonzalez, C. M. Afonso, M. M. M. Pinto, C. Anantachoke, W. Herz, *Phytochemistry* **2000**, *53*, 1021.
[36] M. Iinuma, H. Tosa, T. Tanaka, S. Yonemori, *Phytochemistry* **1994**, *35*, 527.
[37] V. Kumar, S. Ramachandran, M. U. S. Sultanbawa, *Phytochemistry* **1976**, *15*, 2016.
[38] A. Kijjoa, M. J. Gonzalez, M. M. M. Pinto, A. M. S. Silva, C. Anantachoke, W. Herz, *Phytochemistry* **2000**, *55*, 833.
[39] M. Iinuma, H. Tosa, T. Tanaka, S. Yonemori, *Phytochemistry* **1995**, *38*, 725.
[40] M. Iinuma, T. Ito, H. Tosa, T. Tanaka, R. Miyake, V. Chelladurai, *Phytochemistry* **1997**, *46*, 1423.
[41] S. P. Gunasekera, M. U. S. Suhanbawa, *J. Chem. Soc., Perkin Trans. 1* **1975**, *1*, 2215.
[42] O. R. Gottlieb, M. T. Magalhães, M. O. S. Pereira, A. A. L. Mesquita, D. D. B. Corrêa, G. G. Oliveira, *Tetrahedron* **1968**, *24*, 1601.
[43] B. Jackson, H. D. Locksley, F. Scheinmann, *Tetrahedron* **1968**, *24*, 3059.
[44] S. H. Goh, I. Jantan, *Phytochemistry* **1991**, *30*, 366.
[45] F. Scheinmann, N. A. Sripong, *Phytochemistry* **1971**, *10*, 1331.
[46] B. Jackson, H. D. Locksley, F. Scheinmann, *Phytochemistry* **1969**, *8*, 927.
[47] H. R. W. Dharmaratne, S. Sotheeswaran, S. Balasubramaniam, J. Reisch, *Phytochemistry* **1986**, *25*, 1957.
[48] H. R. W. Dharmaratne, W. M. A. R Wanigasekera, *Phytochemistry* **1996**, *42*, 249.
[49] A. E. Hay, J. J. Hélesbeux, O. Duval, M. LabaRed, P. Grellier, P. Richomme, *Life Sci.* **2004**, *75*, 3077.
[50] V. Kumar, S. Sotheeswaran, S. Surendrakumar, S. Balasubramaniam, *Phytochemistry* **1982**, *21*, 807.
[51] M. Taher, M. S. Idris, F. Ahmad, D. Arbain, *Phytochemistry* **2005**, *66*, 723.
[52] M. Iinuma, H. Tosa, T. Tanaka, S. Yonemori, *Heterocycles* **1994**, *37*, 833.
[53] Y. C. Shen, L. T. Wang, A. T. Khalil, L. C. Chiang, P. W. Cheng, *Chem. Pharm. Bull.* **2005**, *53*, 244.
[54] S. A. Ampofo, P. G. Waterman, *Phytochemistry* **1986**, *25*, 2617.
[55] H. R. W. Dharmaratne, W. M. N. M. Wuesinghe, *Phytochemistry* **1997**, *46*, 1293.
[56] S. P. Gunasekera, S. Sotheeswaran, U. S. Sultanbawa, *J. Chem. Soc., Perkin Trans. 1* **1981**, *1*, 1831.
[57] S. S. Subramanian, A. G. R. Nair, *Phytochemistry* **1971**, *10*, 1679.
[58] C. Ito, M. Itoigawa, Y. Miyamoto, K. S. Rao, J. Takayasu, Y. Okuda, T. Mukainaka, H. Tokuda, H. Nishino, H. Furukawa, *J. Nat. Prod.* **1999**, *62*, 1668.
[59] A. A. L. Gunatilaka, A. M. Y. J. D. Silva, S. Sotheeswaran, S. Balasubramaniam, M. I. M. Wazeer, *Phytochemistry* **1984**, *23*, 323.
[60] V. Babu, R. Arya, M. Ilyas, K. T. Nasim, *Phytochemistry* **1994**, *35*, 507.

[61] N. U. D. Khan, N. Parveen, M. P. Singh, R. Singh, B. Achari, P. P. G. Dastidar, P. K. Dutta, *Phytochemistry* **1996**, *42*, 1181.
[62] M. S. Ali, S. Mahmud, S. Perveen, V. U. Ahmad, G. H. Rizwani, *Phytochemistry* **1999**, *50*, 1385.
[63] G. H. Stout, G. K. Hickernell, K. D. Sears, *J. Org. Chem.* **1968**, *33*, 4191.
[64] B. Ravelonjato, N. Kunesch, J. E. Poisson, *Phytochemistry* **1987**, *26*, 2973.
[65] F. Cottiglia, B. Dhanapal, O. Sticher, J. Heilmann, *J. Nat. Prod.* **2004**, *67*, 537.
[66] H. R. W. Dharmaratne, S. Sotheeswaran, S. Balasubramaniam, *Phytochemistry* **1984**, *23*, 2601.
[67] F. Ramiandrasoa, N. Kunesch, J. Poisson, G. Kunesch, *Tetrahedron* **1983**, *23*, 3923.
[68] H. R. W. Dharmaratne, D. S. C. Perera, G. P. K. Marasinghe, J. Jamie, *Phytochemistry* **1999**, *51*, 111.
[69] T. R. Govindachari, N. Viswanathan, B. R. Pai, U. R. Rao, M. Srinivasan, *Tetrahedron* **1967**, *23*, 1901.
[70] S. K. Nigam, C. R. Mitra, *Phytochemistry* **1969**, *8*, 323.
[71] S. G. Cao, K. Y. Sire, S. H. Goh, F. Xue, T. C. W. Mak, *Tetrahedron Lett.* **1997**, *38*, 4783.
[72] F. Laure, G. Herbette, R. Faure, J. P. Bianchini, P. Raharivelomanana, B. Fogliani, *Magn. Reson. Chem.* **2005**, *43*, 65.
[73] M. Taher, M. S. Idris, F. Ahmad, D. Arbain, *Phytochemistry* **2006**, *67*, 1048.
[74] S. G. Cao, K. N. Low, R. P. Glover, S. C. Crasta, S. Ng, A. D. Buss, M. S. Butler, *J. Nat. Prod.* **2006**, *69*, 707.
[75] S. K. Nigam, R. Banerji, S. Rebuffat, M. Cesario, C. Pascard, B. Bodo, *Phytochemistry* **1988**, *27*, 527.
[76] I. Raad, R. Terreux, P. Richomme, E. L. Matera, C. Dumontet, J. Raynaud, D. Guilet, *Bioorg. Med. Chem.* **2006**, *14*, 6979.
[77] C. J. Palmer, J. L. Josephs, *Tetrahedron Lett.* **1994**, *35*, 5363.
[78] T. C. McKee, J. H. Cardellina II, G. B. Dreyer, M. R. Boyd, *J. Nat. Prod.* **1995**, *58*, 916.
[79] G. J. Bennet, H. Lee, *Phytochemistry* **1989**, *28*, 967.
[80] E. D. Clercq, 'Chemotherapy of Human Immunodeficiency Virus (HIV) Infection', 2000, p. 323.
[81] D. L. Yu, M. Suzuki, L. Xie, S. L. Morris-Natschke, K. H. Lee, *Med. Res. Rev.* **2003**, *23*, 322.
[82] M. Itoigawa, C. Ito, H. T. W. Tan, M. Kuchide, H. Tokuda, H. Nishino, H. Furukawa, *Cancer Lett.* **2001**, *169*, 15.
[83] C. Ito, M. Itoigawa, H. Furukawa, H. Tokuda, Y. Okuda, T. Mukainaka, M. Okuda, H. Nishino, *Cancer Lett.* **1999**, *138*, 87.
[84] S. Kimura, C. Ito, N. Jyoko, H. Segawa, J. Kuroda, M. Okada, S. Adachi, T. Nakahata, T. Yuasa, V. C. Filho, H. Furukawa, T. Maekawa, *Int. J. Cancer* **2005**, *113*, 158.
[85] H. R. W. Dharmaratne, W. M. N. M. Wijesinghe, V. Thevanasem, *J. Ethnopharmacol.* **1999**, *66*, 339.
[86] S. Mesía-Vela, R. I. Sánchez, E. Estrada-Muñiz, D. Alavez-Solano, C. Torres-Sosa, M. Jiménez-Estrada, R. Reyes-Chilpa, F. C. Kauffman, *Phytomedicine* **2001**, *8*, 481.

Received October 30, 2007