

Natural products from true mangrove flora: source, chemistry and bioactivities

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The mangrove flora is a diverse group of salt-tolerant plants growing in tropical and subtropical intertidal estuarine zones. This review summarizes the source, chemistry and bioactivities of natural products from true mangrove species worldwide. It includes 349 metabolites and 150 references. The molecular phylogeny and chemotaxonomy of true mangrove plants is discussed.

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1 Introduction

The word “Mangrove” is derived from a combination of the Portuguese word “*Mangue*”, which means tree, and the English word “*grove*”, which means a stand of trees. Mangroves are composed of a large group of different salt-tolerant plants growing in tropical and subtropical intertidal estuarine zones. This review not only outlines the source, chemistry, and biological evaluations of natural products from the true mangrove flora worldwide that have appeared in the literature from 1913 to February 2008, but also discusses the molecular phylogeny and chemotaxonomy of true mangrove plants.

The habitats of mangrove plants are often referred as mangrove forests or “tide forests”, which have important ecological and social-economic values to *Homo sapiens*. For instance, mangrove plants provide timber for construction, firewood, charcoal, fishing poles, pulp, and tannin. These plants, constantly subjected to tidal flushing with the ability to live in salt water, have specially adapted their own morphological structures and physiological mechanisms to the harsh natural surroundings. Pneumatophores supporting stilt roots and buttresses, salt-excreting glands in the leaves, and viviparous propagules are some of the several highly specialized and collectively well-known adaptations of this group.¹

Mangrove plants are usually categorized into two subgroups, true mangrove and semi-mangrove plants. True mangrove plants are restricted to the typical intertidal mangrove habitats where seawater salinity is often 17.0–36.4. Usually, they are not found in the terrestrial marginal zones, which are subjected only to spring or storm high tides. In general, true mangrove plants are distinguished from their terrestrial relatives at the generic level and the subfamily or family level. Semi-mangrove plants grow on the landward fringe of mangrove habitats or in the terrestrial

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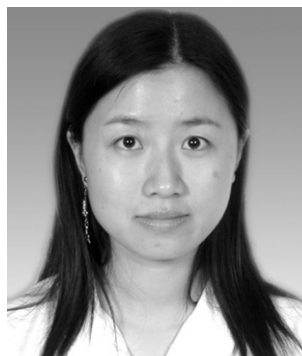
marginal zones subjected to irregular high tides. At the generic level, they are mostly different from their terrestrial relatives. However, mangrove-associated plants, halophilous and halotolerant terrestrial plants, are occasionally found on the landward edge of mangrove habitats, where they are submerged or flushed only by the irregular high tides. Hence, they are called fringe species or non-typical species of mangrove. In fact, mangrove-associated plants, including herbs, liana, parasitic plants and epiphytes, should not be considered as true mangrove or semi-mangrove plants, though their habitats are constrained to mangrove habitats.²

Global mangrove plants are distributed across the tropical and subtropical forests and are predominantly found in tropical regions. The majority of mangrove communities occur in tropical and subtropical areas where the water temperature is higher than 24 °C in the warmest month and the annual rainfall exceeds 1250 mm. Asia and Australia have the greatest diversity and distribution of mangrove species in the world. For example, among 18 million hectares of mangrove forests, more than 40% are found along the Asian coasts. The largest mangrove formations are found in Bangladesh, Brazil, Indonesia, India, and Thailand.^{3,4} The mangrove plants of the world can be mainly



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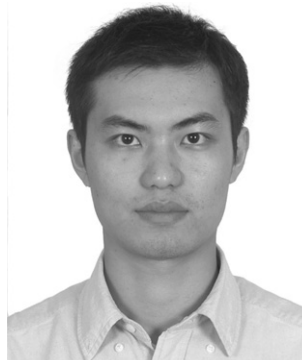
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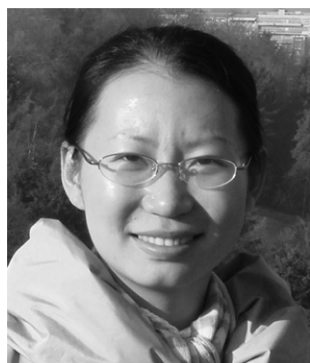
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divided into two main groups, the eastern group and the western group. The eastern group covers the region from west and central Pacific to the southern end of Africa. The western group covers the west coast of Africa and coastal regions of Caribbean, North and South America. In mangrove species, the eastern group is the majority, while the western group is the minority. Specifically, as far as the species are concerned, the number in the eastern group is five times than that of the western group.⁵ According to the statistics, the eastern group is made up of seventy four species (including twelve varieties) belonging to eighteen genera and fourteen families, however, the western group consists of only ten species belonging to six genera and five families. In total, global mangrove plants have eighty four species belonging to twenty four genera and sixteen families. Among them, seventy species are true mangroves pertaining to sixteen genera and eleven families (Table 1), and fourteen species are semi-mangrove belonging to eight genera and five families (Table 2). True mangrove families include Avicenniaceae, Bombacaceae, Combretaceae, Maliaceae, Myrtaceae, Myrsinaceae, Pellicieraceae, Plumbaginaceae, Rhizophoraceae, Rubiaceae, and Sonneratiaceae, while semi-mangrove families comprise Acanthaceae, Euphorbiaceae, Lythraceae, Palmae and Sterculiaceae.²

Table 1 True mangrove species worldwide^a

Avicenniaceae	Myrsinaceae
<i>Avicennia africana</i>	<i>Aegiceras corniculatum</i>
<i>A. alba</i>	<i>A. floridum</i>
<i>A. alba</i> var. <i>latifolia</i>	Pellicieraceae
<i>A. balanophora</i>	<i>Pelliciera rhizophora</i>
<i>A. bicolor</i>	Plumbaginaceae
<i>A. germinans</i>	<i>Aegialitis annulata</i>
<i>A. integra</i>	<i>A. rotundifolia</i>
<i>A. lanata</i>	Rhizophoraceae
<i>A. marina</i>	<i>Bruguiera cylindrica</i>
<i>A. marina</i> var. <i>acutissima</i>	<i>B. exaristata</i>
<i>A. marina</i> var. <i>anomala</i>	<i>B. gymnorrhiza</i>
<i>A. marina</i> var. <i>australasoca</i>	<i>B. hainensis</i>
<i>A. marina</i> var. <i>eucalyptifolia</i>	<i>B. parviflora</i>
<i>A. marina</i> var. <i>intermedia</i>	<i>B. sexangula</i>
<i>A. marina</i> var. <i>resinifera</i>	<i>B. sexangula</i> var. <i>rhynchopetala</i>
<i>A. marina</i> var. <i>typica</i>	<i>Ceriops decandra</i>
<i>A. officinalis</i>	<i>C. tagal</i>
<i>A. rumphiana</i>	<i>C. tagal</i> var. <i>australasica</i>
<i>A. schaueriana</i>	<i>C. tagal</i> var. <i>typical</i>
<i>A. tomentosa</i>	<i>Kandelia candel</i>
Bombacaceae	<i>Rhizophora apiculata</i>
<i>Camptostemon philippinensis</i>	<i>R. harrisonii</i>
<i>C. schultzei</i>	<i>R. lamarkii</i>
Combretaceae	<i>R. mangle</i>
<i>Conocarpus erectus</i>	<i>R. mucronata</i>
<i>Laguncularia racemosa</i>	<i>R. racemosa</i>
<i>Lumnitzera littorea</i>	<i>R. samoensis</i>
<i>L. littorea</i> var. <i>lutea</i>	<i>R. selala</i>
<i>L. racemosa</i>	<i>R. stylosa</i>
<i>L. rosea</i>	Rubiaceae
Maliaceae	<i>Scyphiphora hydrophyllacea</i>
<i>Xylocarpus gangeticus</i>	Sonneratiaceae
<i>X. granatum</i>	<i>Sonneratia alba</i>
<i>X. mekongensis</i>	<i>S. apetala</i>
<i>X. minor</i>	<i>S. caseolaris</i>
<i>X. moluccensis</i>	<i>S. griffithii</i>
<i>X. parvifolius</i>	<i>S. guilgai</i>
Myrtaceae	<i>S. hainanensis</i>
<i>Osbornia octodonta</i>	<i>S. ovata</i>
	<i>S. paracaseolaris</i>

^a T: true mangrove (70 species).

Table 2 Semi-mangrove species worldwide^a

Acanthaceae	Palmae
<i>Acanthus ebracteatus</i>	<i>Mauritia flexuosa</i>
<i>A. ilicifolius</i>	<i>Nypa fruticans</i>
<i>A. volubilis</i>	<i>Phoenix paludosa</i>
<i>A. xiamenensis</i>	<i>Oncosperma tigllarium</i>
Euphorbiaceae	Sterculiaceae
<i>Excoecaria agallocha</i>	<i>Heritiera littoralis</i>
<i>E. indica</i>	<i>H. fomes</i>
Lythraceae	<i>H. globosa</i>
<i>Pemphis acidula</i>	

^a Semi: semi-mangrove (14 species).

Twenty eight mangrove species (including one variety), belonging to fifteen genera and twelve families, are recorded in China. They contribute to about 38% of the total mangrove species in the eastern group and 33% in the world. *Sonneratia hainanensis*, *Sonneratia paracaseolaris*, *Bruguiera sexangula* var. *rhynchopetala*, and *Acanthus xiamenensis*, are the four endemic mangrove species found in China. Though its terrestrial area does not exceed 34 thousand square kilometres, Hainan island has the richest diversity of mangrove species in China. According to the statistics, twenty five species are recorded in this tropical island.⁶

The first investigation on the chemistry of mangrove plants can be traced back to 1913, when Bournot characterized lapachol from the wood of the Indian and West African *Avicennia tomentosa*.⁷ Then Rao and Bose isolated a triterpene named genin-A from the bark of the Indian *Aegiceras corniculatum* in 1959.⁸ And in 1965, from the timber of the East African *Xylocarpus granatum*, Taylor obtained a limonoid named gedunin,⁹ which was first isolated from the timber of the West African *Entandrophragma angolense* and identified by chemical methods.^{10,11} Its crystal structure, however, was determined later.¹² From 1970 to 2000, Australian, Indian, and Japanese scientists intermittently investigated natural products of some mangrove plants, including *Acanthus ilicifolius*, *Bruguiera gymnorrhiza*, *Heritiera littoralis*, and *Excoecaria agallocha*. During the last decade of the 20th century, a highlight of the research into the chemistry and bioactivities of diterpenoids of *E. agallocha* has been carried out by Indian and Japanese scientists. Four labdane and beyerane diterpenes obtained from this plant exhibited strong *in vitro* anti-tumor activities.^{13,14} Since the beginning of this century, a remarkable upsurge in the research of natural products from mangrove plants has sprung up in China due to the increase of financial support from some special Chinese research programs, such as the National High Technology Research and Development Program of China (863 Program). Since 2001, a number of phytochemical investigations have been undertaken on Chinese true mangrove plants. In 2004, two highly oxidized 8,9,30-phragmalin orthoesters, named xylocensins O and P, were isolated from the barks of the Chinese *X. granatum* by our group as a new type of orthoester of phragmalin. Their structures were elucidated by spectroscopic and single-crystal X-ray diffraction techniques.¹⁵ In the same year, an unusual novel macrocyclic polydisulfide possessing an unprecedented carbon skeleton, named gymnorrhizol, characterized as a 15-membered macrocycle that was composed of three repeated 1,3-dimercaptopropan-2-ol units, was isolated from

stems and leaves of the Chinese mangrove *Bruguiera gymnorrhiza* by Sun and Guo coworkers.¹⁶ Its structure was determined by extensive spectroscopic studies. The structure of gymnorrhizol was further confirmed by X-ray crystallography and total synthesis later.^{17,18} Recently, thirteen limonoids with a new carbon skeleton, named xylogranatins F–R, have been isolated from the seeds of the Chinese mangrove *X. granatum* by our group. Their structures were elucidated on the basis of spectroscopic data and chemical methods. The absolute configurations of these compounds were determined by the modified Mosher MTPA ester method and quantum chemical circular dichroism calculations. The structures of these compounds suggested a new biogenetic pathway to tetranortriterpenoids. Xylogranatins F, G and R were found to exhibit marked antifeedant activity against the third instar larvae of *Mythimna separata* (Walker), a pest to wheat in the north of China, at a concentration of 1 mg mL⁻¹.¹⁹ Based on these discoveries, a new tide of research on natural products of Chinese mangrove plants has been triggered in China.

2 Avicenniaceae

2.1 *Avicennia*

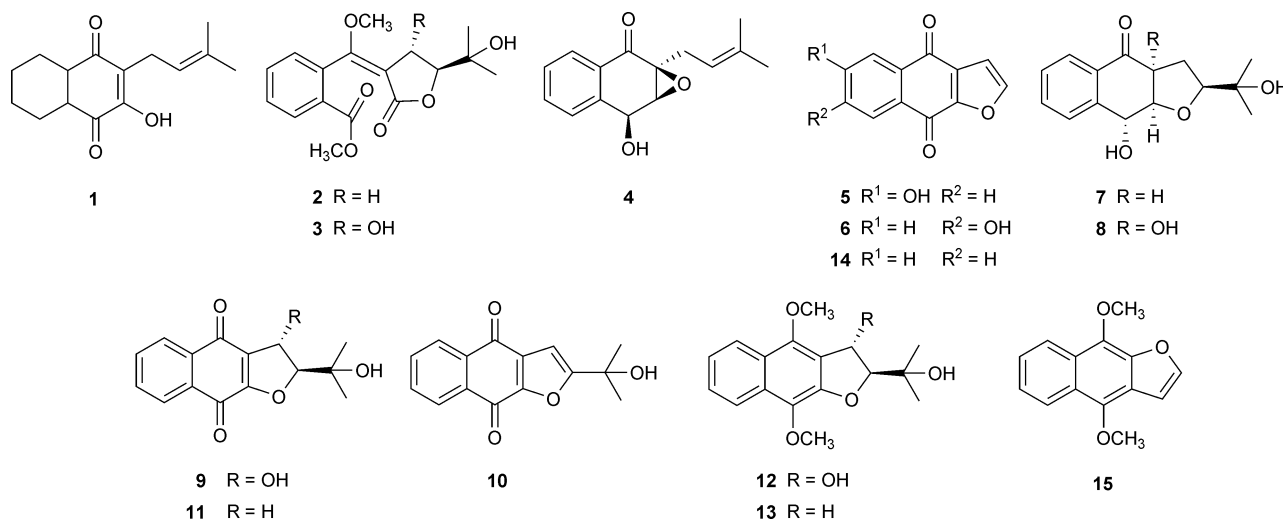
Avicennia is the only mangrove genus of Avicenniaceae. It comprises twelve species and eight varieties which derive from *A. alba* and *A. marina*. The first chemical investigation on it can be traced back to 1913, when Bournot characterized lapachol (**1**) from the wood of the Indian and West African *A. tomentosa*.⁷ To date, betain, triacontane, triacontan-1-ol, a flavone, a megastigmane glucoside, two lignans, three phenylpropanoid glycosides, five sterols, eight diterpenes, nine triterpenes, fifteen naphthoquinones, and sixteen iridoid glucosides, have been reported from the leaves, roots, stem bark, and twigs of the genus *Avicennia*.

2.1.1 Naphthoquinones. Fifteen naphthoquinones (**1**–**15**) were reported from *A. marina*, *A. alba* and *A. officinalis*. An investigation on the twigs of the Chinese Xiamen *A. marina* led to the isolation of twelve naphthoquinones, including avicennones

A–G (**2**–**8**), avicequinones A (**9**), C (**10**), stenocarpoquinone B (**11**), and avicenols A (**12**), C (**13**).²⁰ The mixture of avicennones E–F (**5**–**6**), avicequinone C (**10**), and stenocarpoquinone B (**11**) showed strong antiproliferative activities against L-929 (mouse fibroblasts) and K562 (human chronic myeloid leukemia) cell lines. However, these naphthoquinones were less cytotoxic against the HeLa (human cervix carcinoma) cell line.²⁰ The *p*-dione of the naphthoquinone core is an essential structural element for the antiproliferative activities and the α,β -unsaturated quinone system for the cytotoxicity of these naphthoquinones. Avicequinone A (**9**), C (**10**), stenocarpoquinone B (**11**), and the mixture of avicennones E–F (**5**–**6**) also exhibited significant antimicrobial activities against *Candida albicans*, *Mycobacterium smegmatis*, *Mycobacterium aurum*, *Mycobacterium vaccae*, *Mycobacterium fortuitum*, and *Staphylococcus aureus*.²⁰

From the stem bark of *A. alba* collected in Singapore, Ito and his coworkers characterized six naphthoquinones, avicequinones A (**9**), B (**14**), C (**10**), and avicenols A (**12**), B (**15**), C (**13**).²¹ Avicenol C (**13**), given another name avicennol, was obtained again by Anjaneyulu and his coworkers from the roots of *A. officinalis* collected from the Indian Sunderban islands.²²

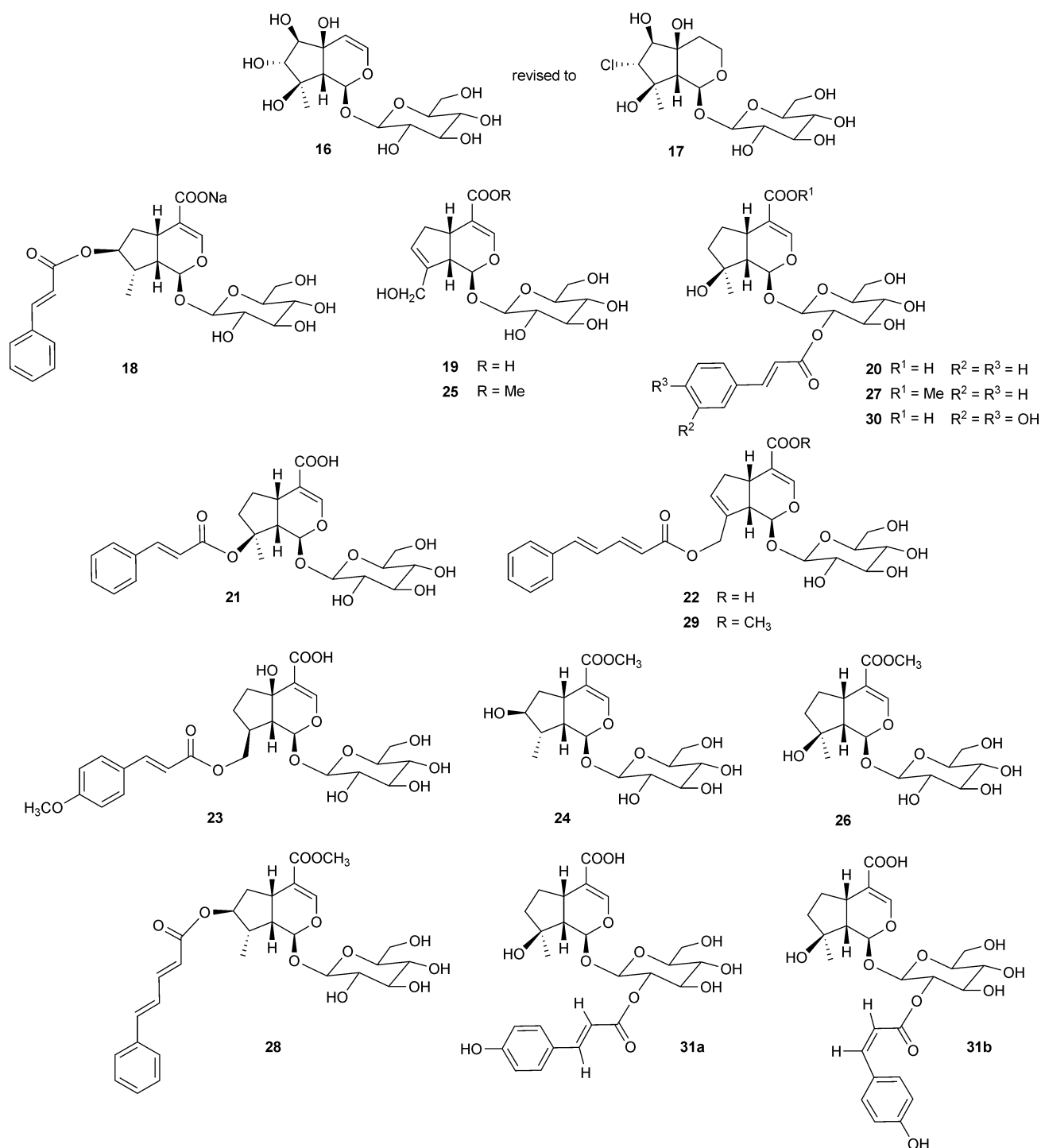
2.1.2 Iridoid glucosides. Fifteen iridoid glucosides (**17**–**31**) were isolated from *A. officinalis* and *A. germinans*. König and his coworkers isolated avicennioside (**16**), 7-*O*-cinnamoyl-8-epiloganic acid sodium salt (**18**), geniposidic acid (**19**), 2'-cinnamoyl-mussaenosidic acid (**20**), from the air-dried leaves of the Sri Lanka *A. officinalis*.²³ The structure of avicennioside (**16**) was revised to linarioside (**17**) later.^{24,25} Pandey and Garg obtained four iridoid glucosides, 8-*O*-cinnamoylmussaenosidic acid (**21**), 10-*O*-(5-phenyl-2,4-pentadienyl)geniposidic acid (**22**), 5-hydroxy-10-*O*-(*p*-methoxycinnamoyl)adoxosidic acid (officinosidic acid) (**23**), and loganin (**24**), from the leaves of the Indian *A. officinalis* Linn.²⁶ Five iridoid glucosides, geniposide (**25**), mussaenoside (**26**), 2'-cinnamoyl-mussaenoside (**27**), 7-*O*-(5-phenyl-2,4-pentadienyl)-8-epiloganin (**28**), 10-*O*-(5-phenyl-2,4-pentadienyl)-geniposide (**29**), were reported from a methanol extract of the leaves of the Sri Lanka *A. marina*.²⁷ 2'-Caffeoyl-mussaenosidic acid (**30**), along with 2'-cinnamoyl-mussaenosidic acid (**20**), were identified from the leaves of the Guyana *A. germinans*.²⁸ They

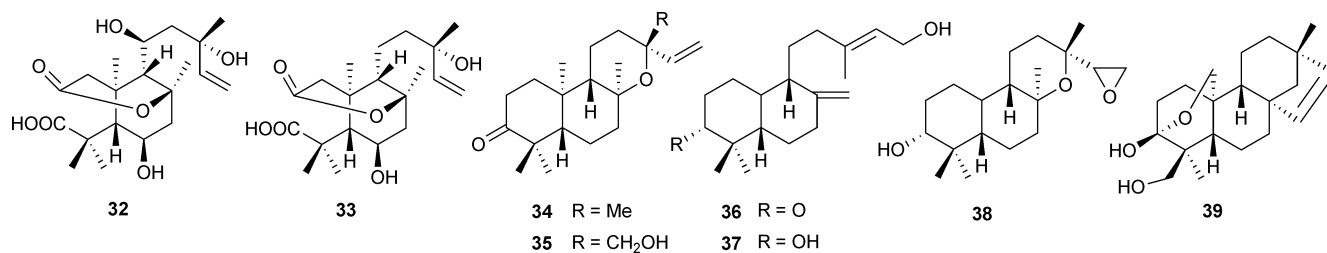


were reported again by Fauvel and his coworkers from the leaves of *A. germinans*, collected at Libreville in Gabon.²⁹ Concentrations of them in different populations of several *Avicennia* species were measured as well. Those results seem to confirm the recognition of infraspecific taxa in *A. marina* and *A. germinans*.³⁰ 2'-Coumaroyl-mussaenosidic acid (**31**) was obtained from the leaves of the Libreville *A. germinans*. Its two isomeric forms (**31a** and **31b**), differing from each other on the geometry of the double bond of the 2'-coumaroyl group, were analyzed and confirmed by their NMR spectra and molecular models.³¹

2.1.3 Diterpenoids. Seven labdanes, viz. rhizophorin-A (**32**), *ent*-(13*S*)-2,3-*seco*-14-labden-2,8-olide-3-oic acid (**33**), ribenone (**34**), *ent*-16-hydroxy-3-oxo-13-*epi*-manoyl oxide (**35**), *ent*-15-hydroxy-labda-8(17),13*E*-dien-3-one (**36**), *ent*-3 α ,15-dihydroxy-labda-8(17),13*E*-diene (**37**), excoecarin A (**38**), and an *ent*-beyerane, rhizophorin-B (**39**), were identified from the roots of the Indian *Avicennia officinalis* Linn.³²

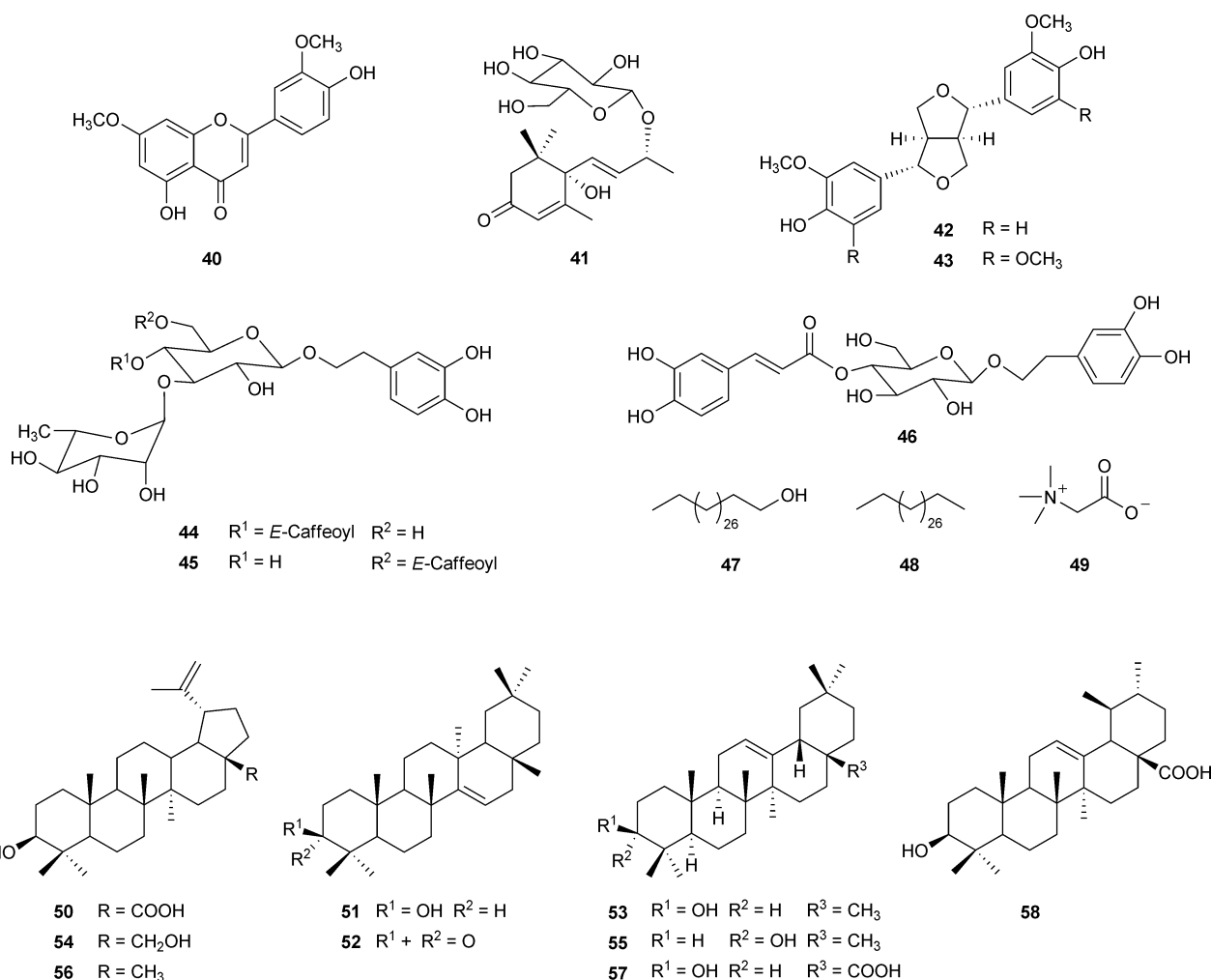
2.1.4 Miscellaneous. A flavone, velutin (**40**), was isolated from the defatted leaves of the Indian *A. officinalis*.³³ A

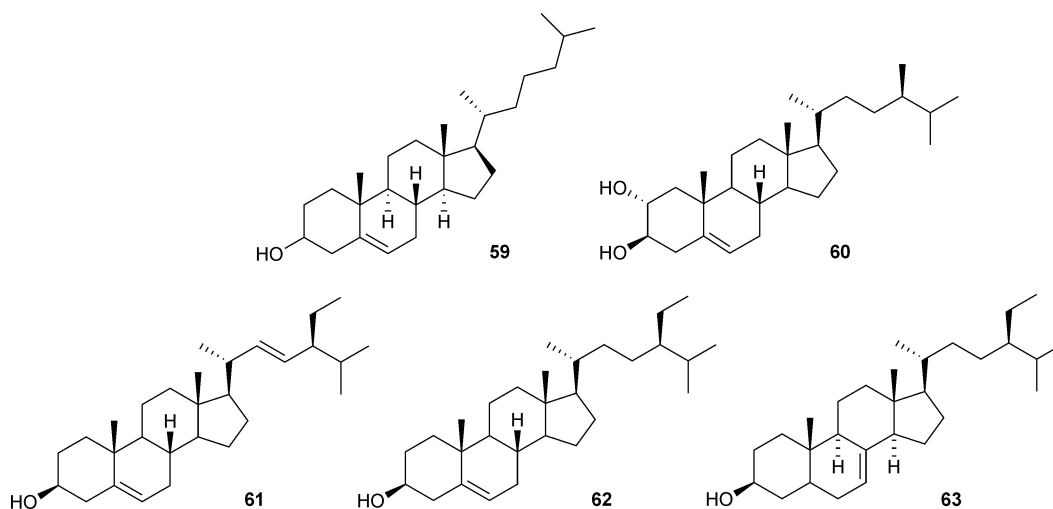




megastigmane glucoside, vomifoliol 9-*O*-β-D-glucopyranoside [(6*S*,9*R*)-roseoside] (**41**), was obtained from the leaves of *A. germinans*, collected at Libreville in Gabon.³⁰ Two lignans, pinoresinol (**42**) and syringaresinol (**43**), were identified from the Costa Rica *A. germinans*.³⁴ Three phenylpropanoid glycosides, verbascoside (acteoside) (**44**), isoverbascoside (**45**), and derhamnosylverbascoside (**46**), were characterized from the leaves of *A. marina* collected from Java.³⁵ Triacontan-1-ol (**47**) was isolated from the roots of the Indian *A. officinalis* Linn.,³² and triacotane (**48**) obtained from *A. marina*, collected at Newcastle in Australia.³⁶ A high concentration of betain (**49**) was found in the aerial parts of *A. marina*, collected in the United Arab Emirates.³⁷

Three triterpenes, betulinic acid (**50**), taraxerol (**51**), taraxerone (**52**), were identified from *A. marina*, collected at Newcastle in Australia.³⁶ From the stem bark and leaves of the Indian *A. officinalis* and *A. tomentosa*, betulinic acid (**50**), taraxerol (**51**), taraxerone (**52**), β-amyryl (**53**), and betulin (**54**) were identified.³⁸ From those of the Indian *A. alba*, betulinic acid (**50**), taraxerol (**51**), β-amyryl (**53**), and betulin (**54**) were characterized again.³⁸ Six triterpenes, β-amyryl (**53**), betulin (**54**), α-amyryl (**55**), lupeol (**56**), oleanolic acid (**57**), ursolic acid (**58**) and five sterols, cholesterol (**59**), campesterol (**60**), stigmasterol (**61**), β-sitosterol (**62**), stigmaster-7-en-3β-ol (**63**), were characterized from the leaves of the Indian *A. officinalis*.³⁹ Hydrocarbons, sterols, alcohols, monobasic, α,ω-dibasic and ω-hydroxy acids of the fresh and





decayed leaves and pneumatophores of the Australian *A. marina* were reported.⁴⁰ From the quantitative comparisons, relative changes in the lipid classes occurring during leaf decay can be highlighted.⁴⁰ Compositions of total lipids, hydrocarbons, wax esters, sterol esters, triglycerides, sterols, and terpenes in the leaves of the Indian *A. officinalis* growing normally and under tidal water were analyzed.⁴¹

3 Combretaceae

3.1 *Lumnitzera*

The mangrove family of Combretaceae consists of five species, viz. *Conocarpus erectus*, *Laguncularia racemosa*, *Lumnitzera littorea*, *L. racemosa*, *L. rosea*, and one variety, viz. *L. littorea* var. *lutea*. However, only the chemical ingredients for *L. racemosa* have been investigated. Specifically, triacontanol (**47**), taraxerol (**51**), β -amyrin (**53**), betulin (**54**), β -sitosterol (**62**) and friedelin (**64**) were characterized by Majumdar and Patra from the leaves and barks of the Indian *L. racemosa*, collected from Sundarban and Kakinada.⁴² 3-(4-Hydroxyphenyl)-propyl-3'-(3,4-dihydroxyphenyl)-propionate (**65**), an aromatic ester, was identified from the stems of the Indian Bhiravapalem Island *L. racemosa*, together with betulinic acid (**50**), betulin (**54**) and friedelin (**64**).⁴³ Eleven tannins, castalagin (**66**), corilagin (**67**), chebulagic acid (**68**), chebulinic acid (**69**), neochebulinic acid (**70**), 2,3-di-*O*-galloyl- β -D-glucopyranose (**71**), 1,2,3,6-tetra-*O*-galloyl- β -D-glucopyranose (**72**), 2,3,4,6-*O*-galloyl- β -D-glucopyranose (**73**), 1,2,3,4,6-penta-*O*-galloyl- β -D-glucopyranose (**74**), 2,3-(*S*)-HHDP- β -D-glucose (**75**) and punicalagin (**76**), were reported from the leaves of the Taiwan *L. racemosa*, which existed in Kaohsiung Bay. Among them, castalagin (**66**), corilagin (**67**), and chebulinic acid (**69**) were regarded as the promising candidates for antihypertensive lead compounds.⁴⁴ Moreover, ten compounds, including 2-methyl-1,3-dihydroxy-5-tridecylbenzene (**77**), 1,3-dihydroxy-5-undecylbenzene (**78**), ergosta-7,22-dien-3 β -ol (**79**), emodin (**80**), kaempferol (**81**), quercetin (**82**), quercitrin (**83**), isoquercitrin (**84**), (–)-epigallocatechin (**85**), and gallic acid (**86**), were identified from stems and leaves of the Chinese Beihai *L. racemosa*.⁴⁵

4 Maliaceae

4.1 *Xylocarpus*

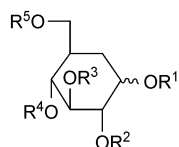
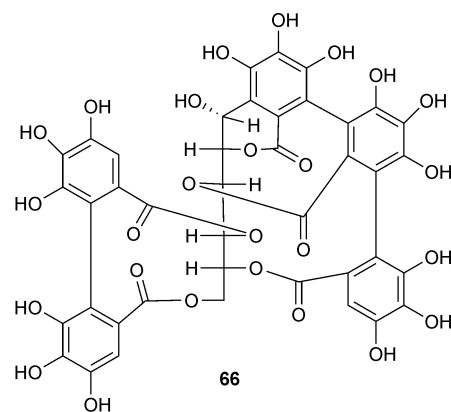
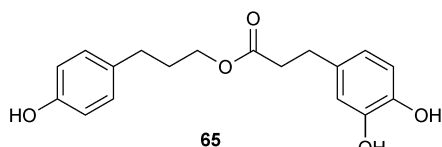
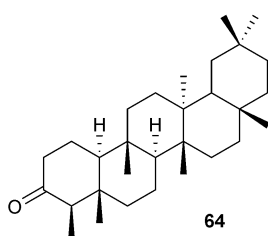
It was reported that the genus of mangrove *Xylocarpus* has six species, *X. gangeticus*, *X. granatum*, *X. mekongensis*, *X. minor*, *X. moluccensis*, and *X. parvifolius*.² However, *X. gangeticus*, *X. mekongensis* and *X. moluccensis* may be the same species, though they were given three different names. The taxonomy and nomenclature of these species still need to be clarified in the future.

A flavonone, a monoterpene, a sterol glucoside, two phenolic acids, three alkaloids, five protolimonoids, and eighty three limonoids, have been reported from the stem bark, timber, fruits, and seeds of *X. moluccensis* and *X. granatum*. Obviously, limonoids are the main secondary metabolites of this genus.

4.1.1 Limonoids. The limonoids, obtained from *X. moluccensis* and *X. granatum*, consist of one andirobin, an obacunol, three gedunins, forty two mexicanolides, twenty three phragmalins, and thirteen recently identified limonoids with new skeletons.

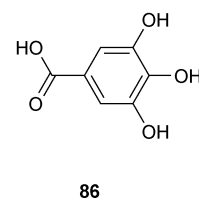
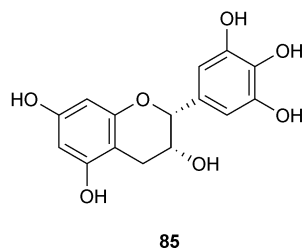
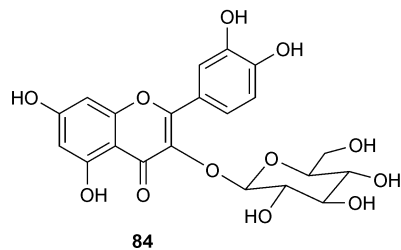
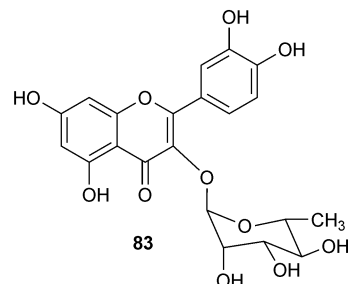
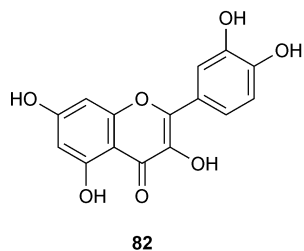
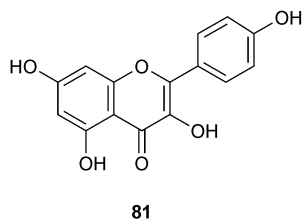
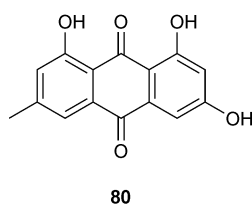
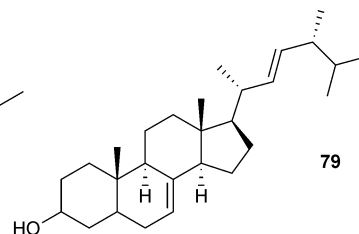
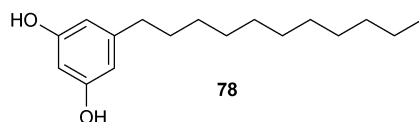
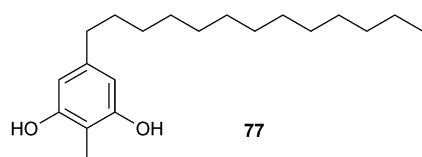
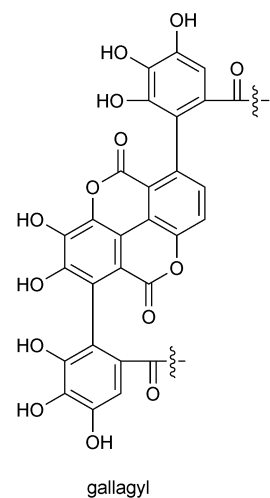
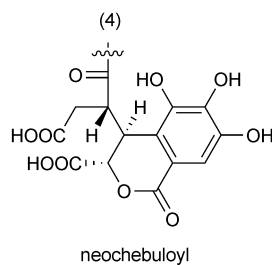
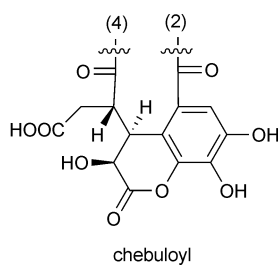
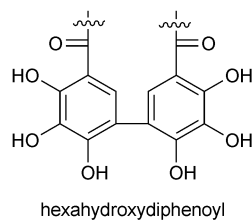
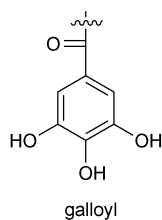
4.1.1.1 Andirobins. Methyl angolensate (**87**) was identified by Taylor and his coworkers from the timber of the African *X. moluccensis*.⁴⁶ It is the only limonoid of andirobin group isolated from the genus *Xylocarpus*.

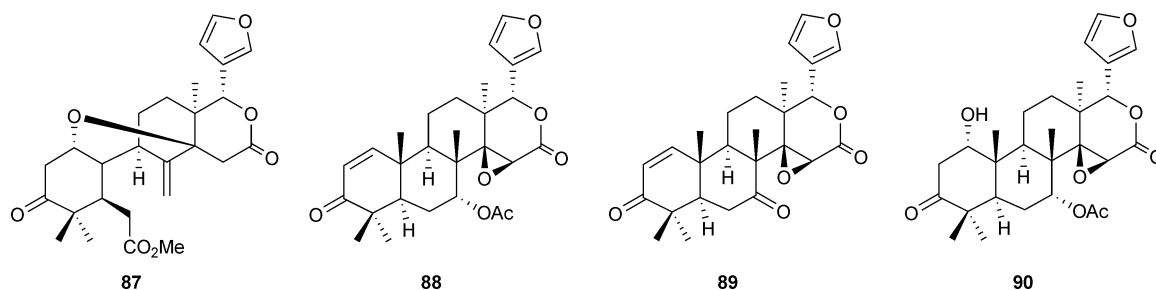
4.1.1.2 Gedunins. Three limonoids of the gedunin group, gedunin (**88**) and 7-oxogedunin (**89**), 1 α -hydroxy-1,2-dihydrogedunin (**90**), were isolated from the genus *Xylocarpus*. Gedunin (**88**), the first limonoid from the genus *Xylocarpus*, was identified by Taylor and his coworkers from the timber of the east African *X. granatum*.^{9,10} 7-Oxogedunin (**89**), isolated by Taylor and his coworkers from the timber of the Kenya *X. moluccensis*⁴⁷ and seeds of the Australian *X. moluccensis*,⁴⁸ has been recently obtained again from the seeds of the southern Thailand *X. granatum*. Its crystal structure was further analyzed by single-crystal X-ray study.⁴⁹ Recently, 1 α -hydroxy-1,2-dihydrogedunin (**90**) has been identified from the bark of the Bangladeshi *X. granatum*, together with gedunin (**88**).⁵⁰



	R ¹	R ²	R ⁴	R ³	R ⁵
67	G	H	H	HHDP	
68	G	CHEB		HHDP	
69	G	CHEB		G	G
70	G	NECH		G	G
71	H	G	H	G	H
72	G	G	H	G	G
73	H	G	G	G	G
74	G	G	G	G	G
75	H	HHDP		H	H
76	H	HHDP		GALA	

G = galloyl
 HHDP = hexahydroxydiphenoyl
 CHEB = chebuloyl
 NECH = neochebuloyl
 GALA = gallagyl

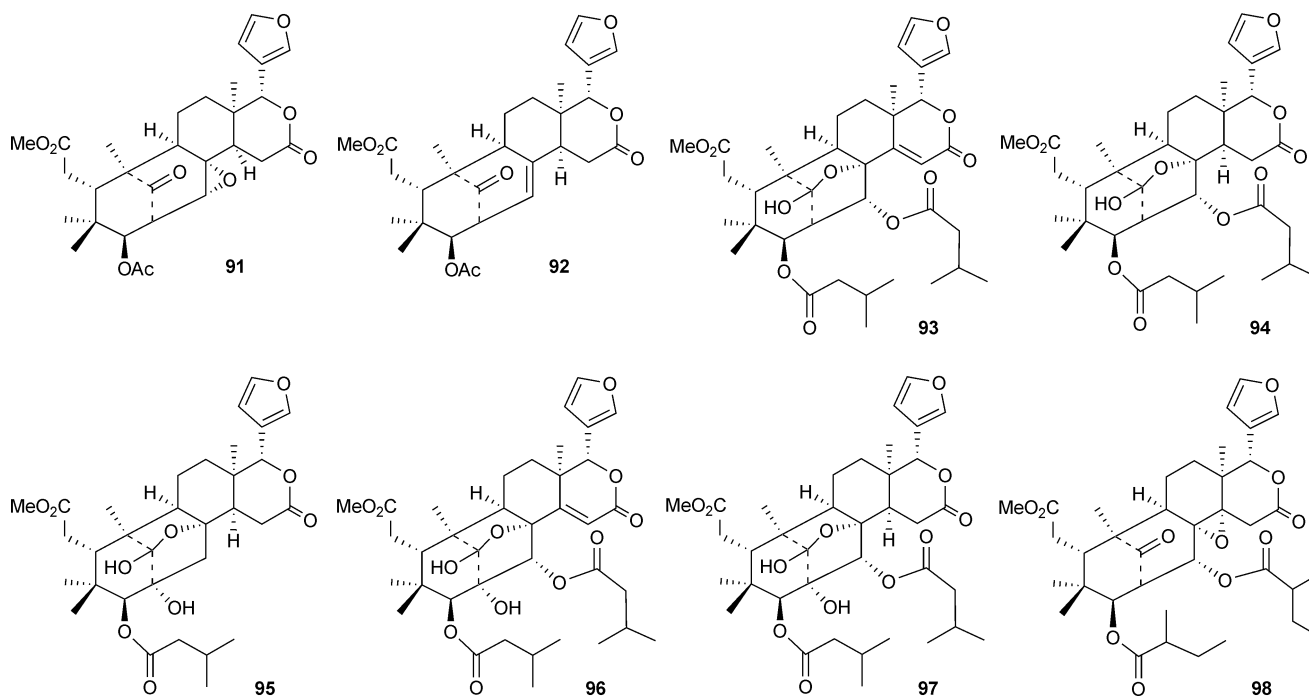


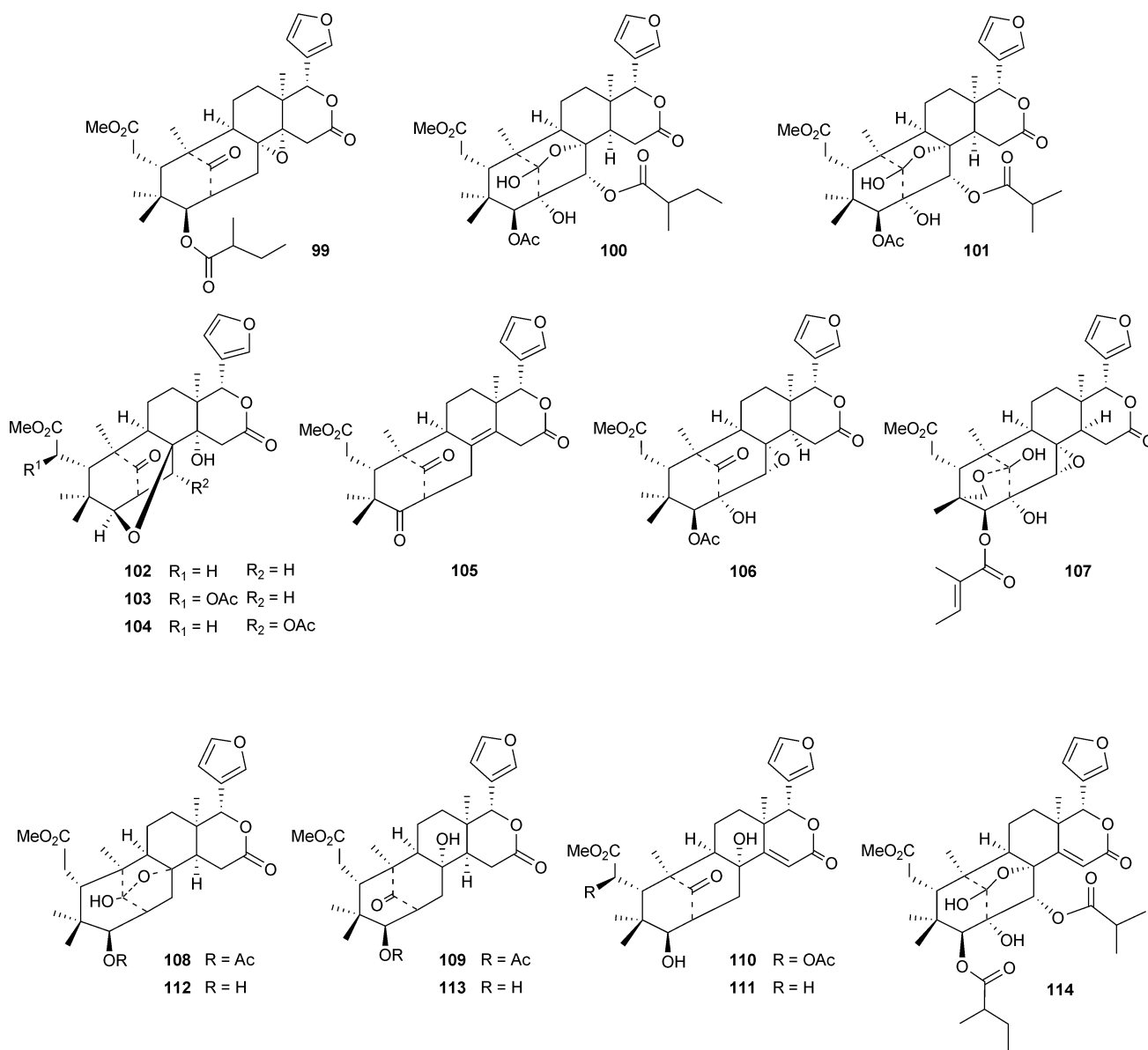


Gedunin (**88**), isolated from the bark of the Bangladeshi *X. granatum*, inhibited the growth of caco-2 colon cancer cell line *in vitro*. Its IC_{50} value was found to be $16.83 \mu M$.⁵⁰ The insect growth inhibitory activity of gedunin was well known.^{51,52} The acetylcholinesterase inhibitory and insecticidal activities of gedunin (**88**) were demonstrated by Calderó and his coworkers.⁵³ Gedunin (**88**) also showed mosquitocidal and antimalarial properties.^{54–58} Gedunin (**88**), isolated from *Cedrela odorata*, was investigated for its *in vivo* antimalarial efficacy in CD-1 mice infected with *Plasmodium berghei*. Oral doses of gedunin (**88**) at $50 \text{ mg kg}^{-1} \text{ day}^{-1}$ for 4 days suppressed the parasitemia level by 44%.⁵⁵ The antifungal property of gedunin (**88**) was early found by Sundarasivarao and his coworkers.⁵⁹ Recently, the anti-allergic activity of gedunin (**88**) has been reported. The oral pretreatment with it was found to inhibit the total leukocyte and eosinophil accumulation in pleural cavities of C57BL/10 mice 24 hours after the intrathoracic injection with ovalbumin.⁶⁰

4.1.1.3 Mexicanolides. To date, 42 limonoids of the mexicanolide group have been isolated from *X. moluccensis* and *X. granatum*. Xylocarpin (**91**) and 3 β -acetoxy-6-deoxy-swietenine (**92**) were first isolated from the seeds of *X. granatum*.⁶¹ Then they were acquired again from the timber and seeds of the Australian

and African *X. moluccensis*.^{46,48} Xylococcins A–D (**93–96**),⁴⁶ F (**97**),⁴⁶ G–I (**98–100**),⁴⁷ were identified from the timber of the African *X. moluccensis*. Xylococcin J (**101**) was isolated from the fruits of the Fijian *X. moluccensis* and *X. granatum*,⁶² together with xylococcin I. Xylococcin K (**102**), a 3 β ,8 β -epoxy mexicanolide, was obtained from the seeds of the Thailand *X. granatum*.⁶³ The other two 3 β ,8 β -epoxy mexicanolides, 6-acetoxycedrodorin (**103**) and xylococcin W (**104**), were identified by spectroscopic analysis from the fruit of the Chinese *X. granatum*.⁶⁴ Mexicanolide (**105**) was isolated from the seeds of *X. granatum*⁶⁵ and the timber of the African *X. moluccensis*.⁴⁷ Humilin B (**106**) was obtained from the seeds of the Australian *X. moluccensis*.⁴⁸ Xylococcin L (**107**), the first mexicanolide with an oxygen bridge between C₁ and C₂₉, was identified from the stem bark of the Chinese *X. granatum*,⁶⁶ together with xylococcins M (**108**) and N (**109**).⁶⁷ Xylococcins X₁ (**110**), X₂ (**111**),⁶⁸ 3-deacetyl-xylococcin M (**112**), and 3-deacetyl-xylococcin N (**113**),⁶⁹ were obtained from the fruit of the Chinese *X. granatum*. Interestingly, xylococcins X (**114**) and Y (**115**) were identified as a mixture from the fruit of the Indian *X. moluccensis*.⁷⁰ Xylogranatins A–E, identified by our group from the fruit of the Chinese *X. granatum*,^{71,72} and named after Wu-xylogranatins A–E (**116–120**) in this paper. They were mexicanolides with different

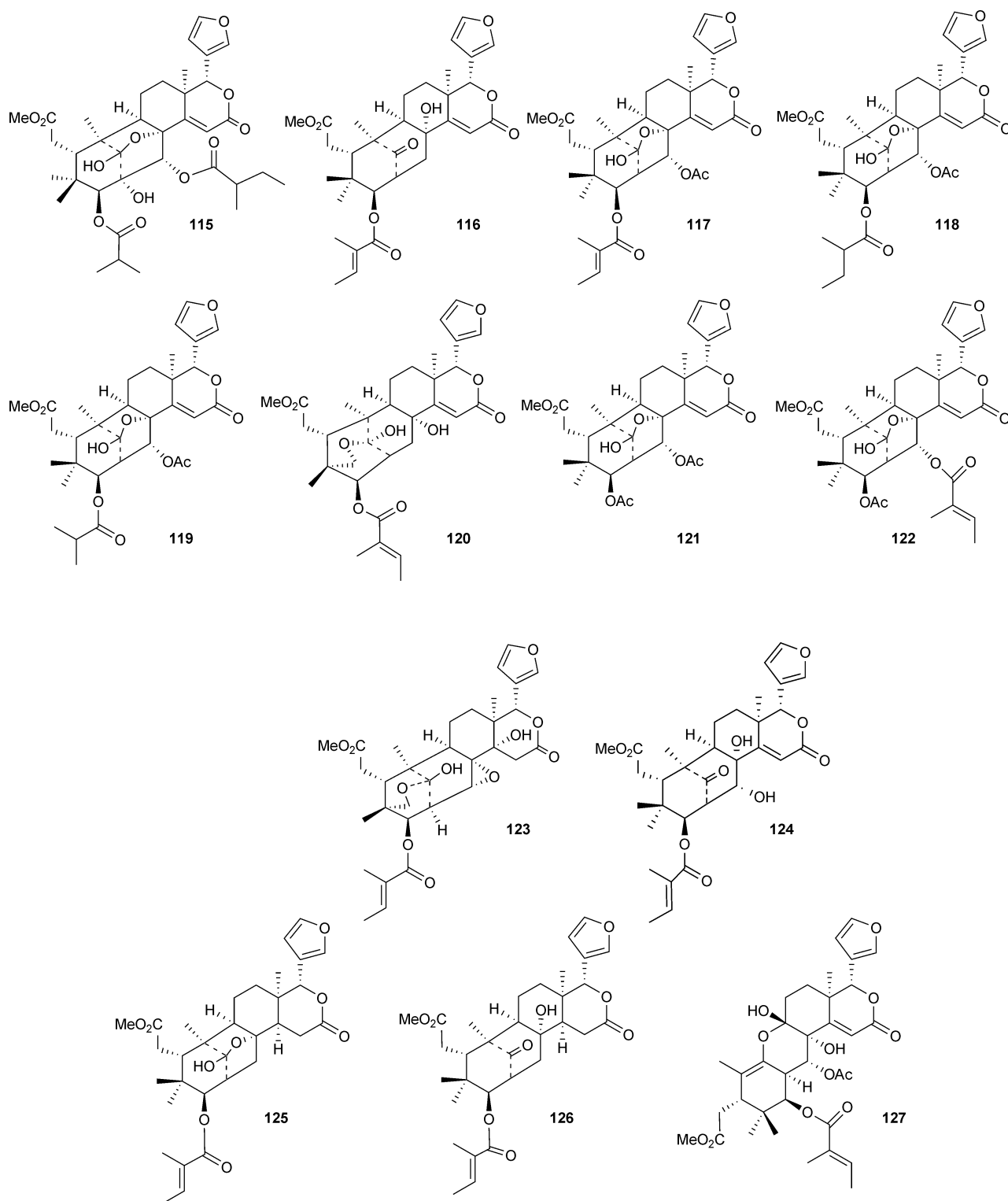




structures from those of the same names, obtained by Yue and his coworkers from the seeds of the Chinese *X. granatum*.⁷³ Lin-xylocarpins F–G (**121–122**),⁷⁴ granaxylocarpin C (**123**),⁷⁵ 30 α -hydroxyl-xylogranatin A (**124**),⁷⁶ Wu-xylocarpins A–B (**125–126**),⁷⁷ were identified from the fruits or seeds of the Chinese *X. granatum*. Among the above limonoids, Wu-xylogranatin E (**120**) and granaxylocarpin C (**123**) are two mexicanolides with an oxygen bridge between C₁ and C₂₉. Wu-xylocarpins A and B (**125–126**), however, were identified as a mixture. Yue-xylogranatins A–D (**127–130**)⁷³ and granaxylocarpin A–B (**131–132**)⁷⁵ are six unusual 9,10-*seco* mexicanolides isolated from the seeds of the Chinese *X. granatum*. The structure of granaxylocarpin B (**132**) is the same as that of Lin-xylocarpin H (**132**).⁷⁴

4.1.1.4 Obacunols. 7 α -Acetoxydihydronomilin (**133**) was isolated by Fallis and his coworkers from the methanol extracts of the seeds of *X. granatum* and the structure was elucidated by X-ray analysis.^{65,78}

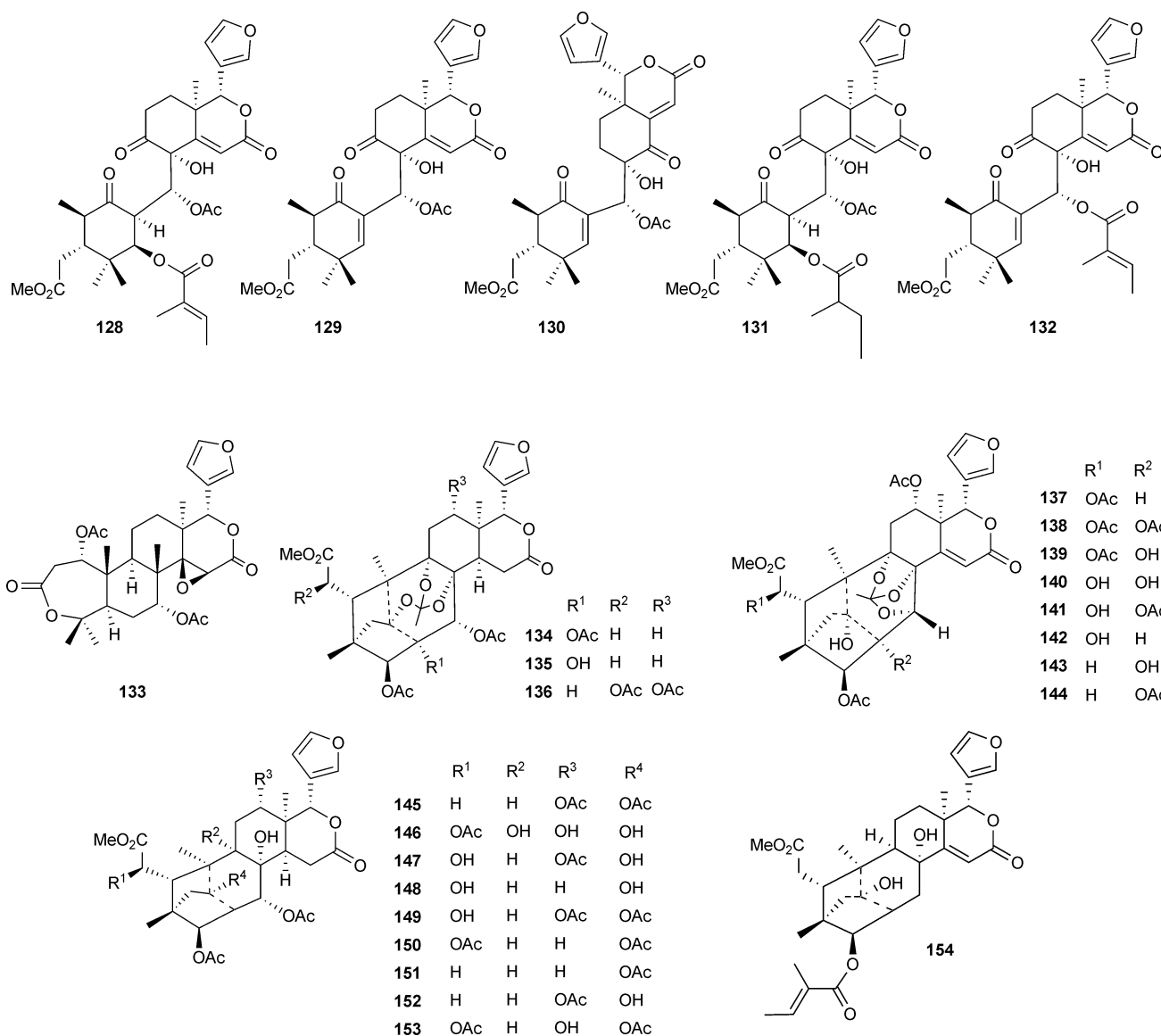
4.1.1.5 Phragmalins. Twenty three phragmalins, including three 1,8,9-phragmalin orthoesters, eight 8,9,30-phragmalin orthoesters and twelve polyhydroxylated phragmalins, were isolated from the timber, seeds and fruits of *X. moluccensis* and *X. granatum*. Xylocensin E (**134**), the first 1,8,9-phragmalin orthoester, was identified from the timber of the African *X. moluccensis*.⁴⁶ It was obtained again by Taylor and his coworkers from the timber of the Australian *X. moluccensis*, together with 3 β ,30 α -diacetyl-phragmalin (**135**).⁴⁸ Lin-xylocarpin I (**136**), the third 1,8,9-phragmalin orthoester, was isolated from the fruits of the Chinese *X. granatum*.⁷⁴ Xylocensins O–V (**137–144**),^{15,79–81} eight 8,9,30-phragmalin orthoesters, were identified from the stem barks of the Chinese *X. granatum*. Lin-xylocensin U (revised as **145**),^{75,80} xylocensins Y (**146**), Z₁ (**147**), Z₂ (**148**),⁸² granaxylocarpins D–E (**149–150**),⁷⁵ Lin-xylocarpins A–E (**149–153**),⁷⁴ xylogranatin E₂ (**154**),⁷⁶ are twelve polyhydroxylated phragmalins identified from the stem bark, fruits and seeds of the Chinese *X. granatum*. The structure of Lin-xylocensin U



(revised as **145**), initially identified by Lin and his coworkers as 1,3,8,30-tetraacetates,⁸⁰ was revised as 1,3,12,30-tetraacetates (**145**) by comparison of its NMR data with those of granaxylcarpin D (**149**).⁷⁵

4.1.1.6 Aromatic B-ring and B,C-seco limonoids. Xylogranatins F–R (**155–167**), thirteen limonoids with a new carbon

skeleton, were isolated from the seeds of the Chinese *X. granatum*.¹⁹ Xylogranatins F–Q (**155–165**, **167**) are the first aromatic B-ring limonoids found in nature. They belong to two substructural classes, of which one subclass (**155–157**) was determined to comprise a pyridine ring and the other (**158–165**, **167**) contain a central furan core. Xylogranatin R (**166**), a B,C-seco limonoid, was considered as a key biosynthetic intermediate.



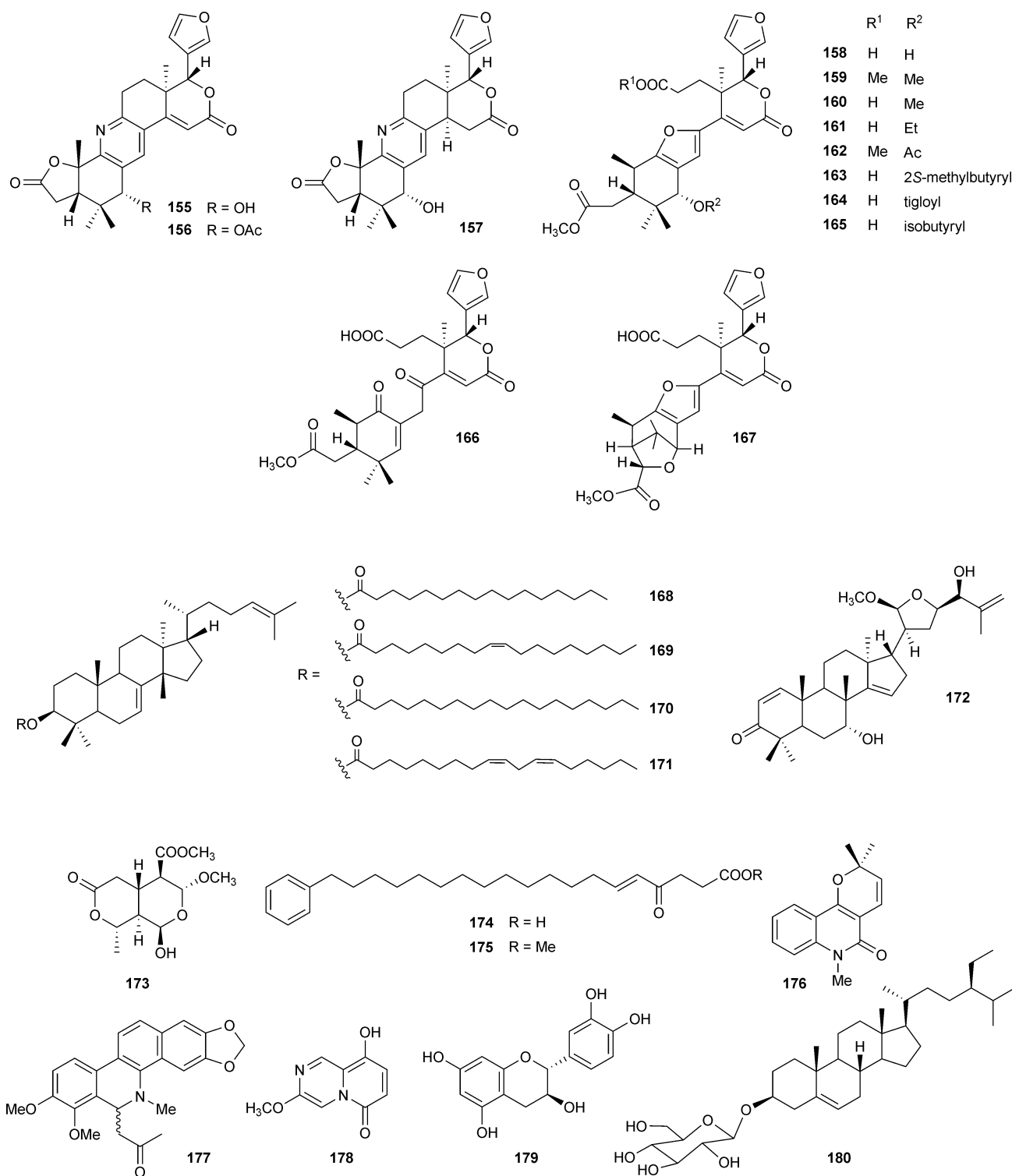
The structures of these compounds suggest a new biogenetic pathway to tetranortriterpenoids. Xylogranatins F (**155**), G (**156**) and R (**166**) were found to exhibit marked antifeedant activity against the third instar larvae of *Mythimna separata* (Walker), a pest to wheat in the north of China, at a concentration of 1 mg mL⁻¹. The most potent compound tested was xylogranatin G (**156**). Its AFC₅₀ (concentration for 50% antifeedant activity) values at the exposure time of 24 and 48 hours were 0.31 and 0.30 mg mL⁻¹, respectively.¹⁹

4.1.2 Protolimonoids. Five protolimonoids, including four butyrospermol fatty acid esters (**168–171**)⁸³ and protoxylogranatin A (**172**),⁸⁴ were identified from the fruits and seeds of the Chinese *X. granatum*. The absolute stereochemistry of protoxylogranatin A (**172**) was determined by the modified Mosher MTPA ester method.

4.1.3 Miscellaneous. Xylomollin (**173**), a monoterpene isolated as the bitter principle from the young fruits of the east

African *X. moluccensis*, showed antifeedant activity against the African army worm *Spodoptera exempta*.⁸⁵ It also strongly inhibits the respiratory reaction of mitochondria from rat liver.⁸⁵ The absolute configuration of xylomollin (**173**) was determined by chemical transformation and total synthesis.^{86–88} Two phenolic acid, (5*E*)-4-oxo-19-phenylnonadec-5-enoic acid (**174**) and (5*E*)-4-oxo-19-phenylnonadec-5-enoic acid, methyl ester (**175**), were identified from the wood of the Fijian *X. moluccensis*.⁸⁹ Two alkaloids, *N*-methylflindersine (**176**), acetonyldihydrochelerythrine (**177**), were isolated as insect antifeedants from the east African *X. granatum*.⁹⁰ Recently, xylogranatinin (**178**), a new pyrido[1,2-*a*]pyrazine alkaloid, has been identified by our group from the fruit of the Chinese mangrove *Xylocarpus granatum*,⁹¹ together with (+)-catechin (**179**) and daucosterol (**180**).

Three aqueous extracts, from the dried husks, seeds and leaves of the Malaysian *X. granatum*, were tested *in vitro* against adult worms of subperiodic *Brugia malayi*. The relative movability value of the adult worms over the 24 h observation period was used as a measure of the antifilarial activity of the aqueous



extracts. The dried seed extract of *X. granatum* was demonstrated to be the strongest one.⁹² When tested for antibacterial effect, the methanol extract of the bark of the Sundarban *X. moluccensis* displayed moderate inhibitory activity against *Escherichia coli*, *Vibrio cholerae*, *Staphylococcus aureus*, *Staphylococcus epidermis*, *Shigella dysenteriae*, *Staphylococcus pyogenes*, *Salmonella typhi*, *Pseudomonas aeruginosa* and *Enterobacter aerogenes*. While the chloroform fraction inhibited the growth of

Escherichia coli, *Vibrio cholerae*, *Shigella dysenteriae*, *Shigella sonnei*, *Staphylococcus epidermis*, *Staphylococcus pyogenes* and *Pseudomonas aeruginosa*, the ethyl acetate fraction was active against all test organisms except *Vibrio cholera* and *Staphylococcus epidermis*. The residual methanol fraction inhibited the growth of all the test organisms with moderate zone of inhibition.⁹³ The methanol extract of the bark of the Sundarban *X. granatum* was studied for its antidiarrhoeal properties in

experimental diarrhoea induced by castor oil and magnesium sulfate in mice. At the doses of 250 and 500 mg kg⁻¹ per oral, the methanol extract showed significant and dose-dependent anti-diarrhoeal activity in both models. The extracts also significantly reduced the intestinal transit in charcoal meal test when compared to atropine sulfate (5 mg kg⁻¹ i.m.). The results showed that the extracts of *X. granatum* bark had a significant anti-diarrhoeal activity and supported its traditional uses in herbal medicine.^{93,94} The methanol extracts of the bark and pneumatophore of the Sundarban *X. granatum* also exhibited CNS depressant activity. The activity of the pneumatophore extract was more potent than that of the bark extract.⁹⁵

5 Myrsinaceae

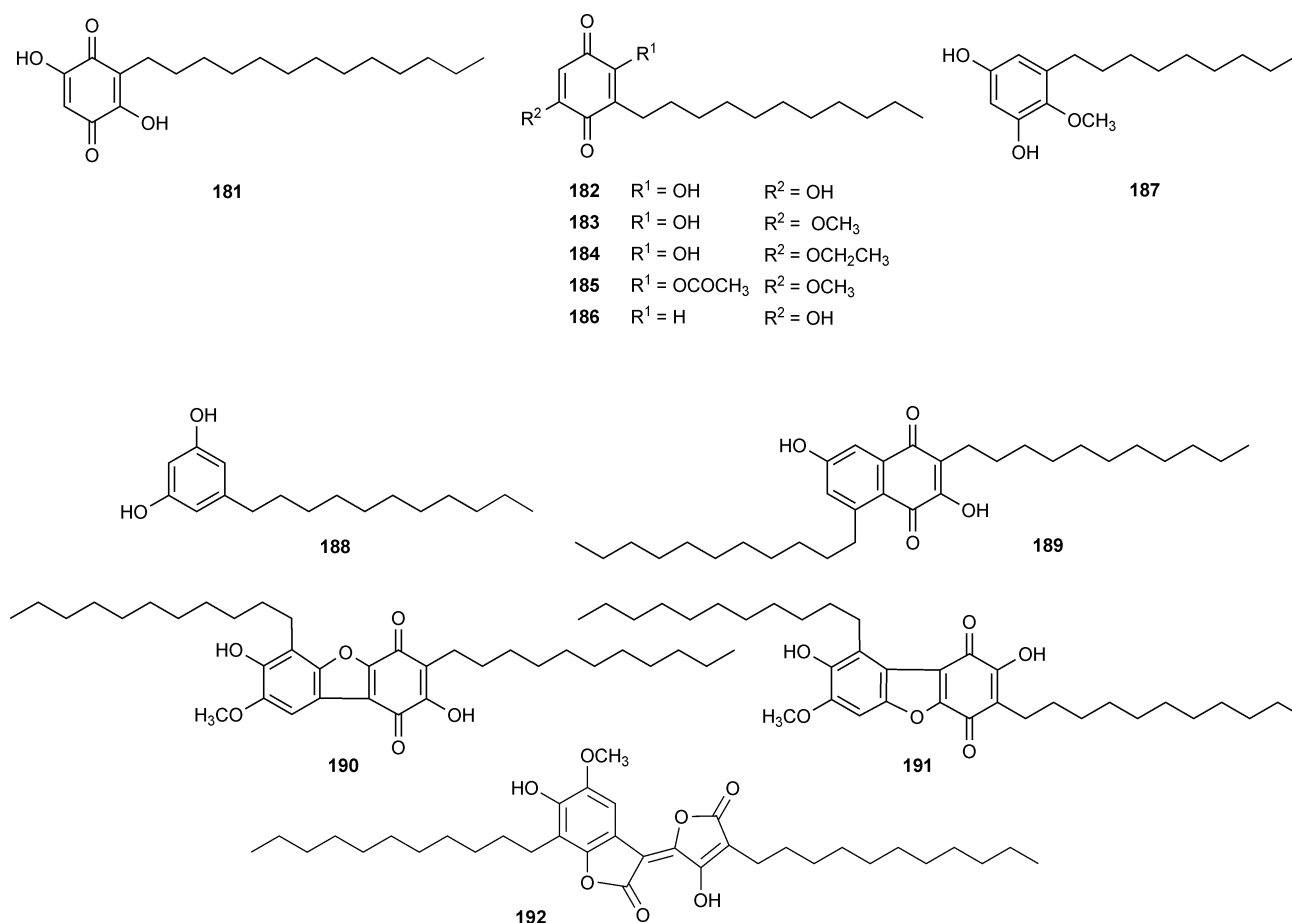
5.1 *Aegiceras*

The genus of mangrove *Aegiceras* has two species, *A. corniculatum*, and *A. floridum*. Two flavones, four phenolic acids, ten triterpenes, and twelve hydroquinone derivatives, have been reported from the stems, twigs, and barks of *A. corniculatum*. Obviously, hydroquinone derivatives and triterpenes are the main secondary metabolites of this genus.

5.1.1 Hydroquinone derivatives. Examination of an orange pigment from the Australian *A. corniculatum* by Hensens and Lewis yielded two hydroquinones, rapanone (**181**) (2,5-

dihydroxy-3-tridecyl-1,4-benzoquinone) and embelin (**182**) (2,5-dihydroxy-3-undecyl-1,4-benzoquinone).⁹⁶ Extracts of the twigs and stems of the Philippines *A. corniculatum* were toxic to the fish *Tilapia nilotica*. 5-*O*-Methylembelin (**183**), identified from these extracts, was demonstrated to be toxic to the fish at a concentration of 1 ppm.⁹⁷ Ten hydroquinone derivatives, 5-*O*-methylembelin (**183**), 5-*O*-ethylembelin (**184**), 2-*O*-acetyl-5-*O*-methylembelin (**185**), 2-dehydroxy-5-*O*-methylembelin (**186**), 2-methoxy-3-nonylresorcinol (**187**), 3-undecylresorcinol (**188**), 3,7-dihydroxy-2,5-diundecylnaphthoquinone (**189**), 2,7-dihydroxy-8-methoxy-3,6-diundecyldibenzofuran-1,4-dione (**190**), 2,8-dihydroxy-7-methoxy-3,9-diundecyldibenzofuran-1,4-dione (**191**), and 10-hydroxy-4-*O*-methyl-2,11-diundecylgompholactone (**192**), were isolated from the stems and twigs of the Chinese Xiamen *A. corniculatum*.⁹⁸

1,4-Benzoquinone derivatives, 5-*O*-methylembelin (**183**) and 5-*O*-ethylembelin (**184**), showed antiproliferative activity against a panel of human tumor cell lines upon comparison to normal marsupial kidney cells (PtK2).⁹⁹ They arrested HL-60 cells in the G₀/G₁ phase of the cell cycle in a dose- and time-dependent manner. In HeLa cells, exposure to 100 μM of **183** or **184** for 6 hours induced a complete disassembly of the microtubule network and an increased number of cells blocked in mitotic stages. Treatment with 10 μM of **182** and **183** for 24 hours induced apoptosis in HL-60 cells. The evidences above suggested that both **182** and **183** were promising novel antimitotic and anticancer molecules targeting microtubular proteins.⁹⁹



5.1.2 Triterpenoids. Genin-A (**193**) was isolated from the bark of the Indian *A. majus* (Syn. *A. corniculatum*).⁸ The C₂₉-triterpene alcohol, aegiceradiol (**194**), was obtained from *A. majus* Gaertn (Syn. *A. corniculatum*) and identified as 3 β ,28-dihydroxy-olean-12,15-diene. Its partial synthesis from genin-A (**193**) was also achieved.¹⁰⁰ 28-Norolean-12,17-dien-3 β -ol (**195**) (nor-echinocystadienol), named aegiceradienol,¹⁰¹ was identified as the C₂₉ triterpene alcohol by direct comparison with an authentic specimen from the bark of the Indian *A. majus* (Syn. *A. corniculatum*).¹⁰² Aegicerin (**196**), a triterpene from the Indian *A. majus* Gaertn (Syn. *A. corniculatum*), was characterized as 3 β -hydroxy-13 β :28-epoxy-16-oxo-18 β -oleanane.¹⁰³ Six triterpenes, 16 α -hydroxy-13,28-epoxy-oleanan-3-one (**197**), protoprimumagenin (**198**), aegicerin (**199**), embelinone (**200**), schimpefinone (**201**), and primulagenin A (**193**) were identified from the stem bark of the Chinese *A. corniculatum*.^{104,105}

5.1.3 Miscellaneous. Isorhamnetin (**202**) (quercetin 3'-methyl ether) was isolated from the bark of the Indian *A. majus* (Syn. *A. corniculatum*).⁸ Isorhamnetin (**202**), isorhamnetin 3-O- α -L-rhamnofuranosyl-(1 \rightarrow 6)- β -D-glucopyranoside (**203**), syringic acid (**204**), and gallic acid (**205**), were isolated from the stem bark of the Chinese *A. corniculatum*.¹⁰⁴ From the same source of plant, β -sitosterol (**62**), daucosterol (**180**), protocathechuic acid (**206**), vanillic acid (**207**), were obtained.¹⁰⁵

6 Rhizophoraceae

6.1 *Bruguiera*

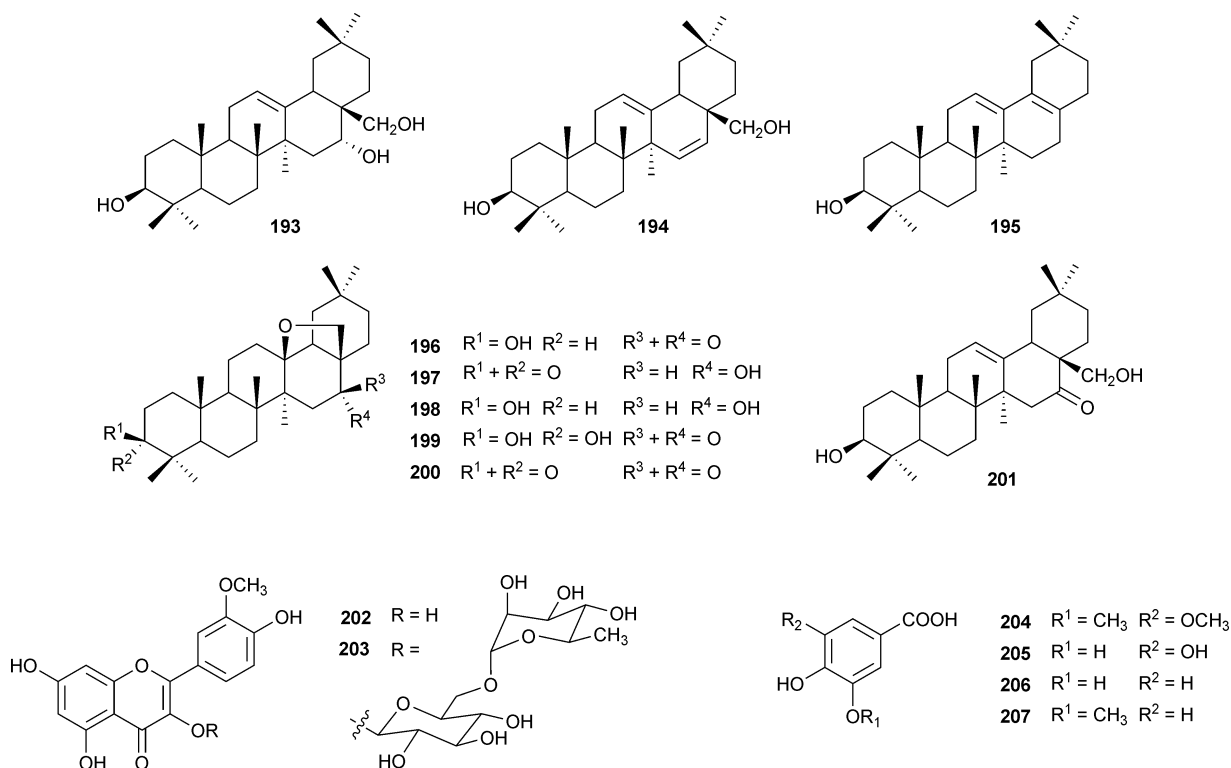
The genus of *Bruguiera* has six species and one variety which derives from *B. sexangula*, including *B. cylindrica*, *B. exaristata*,

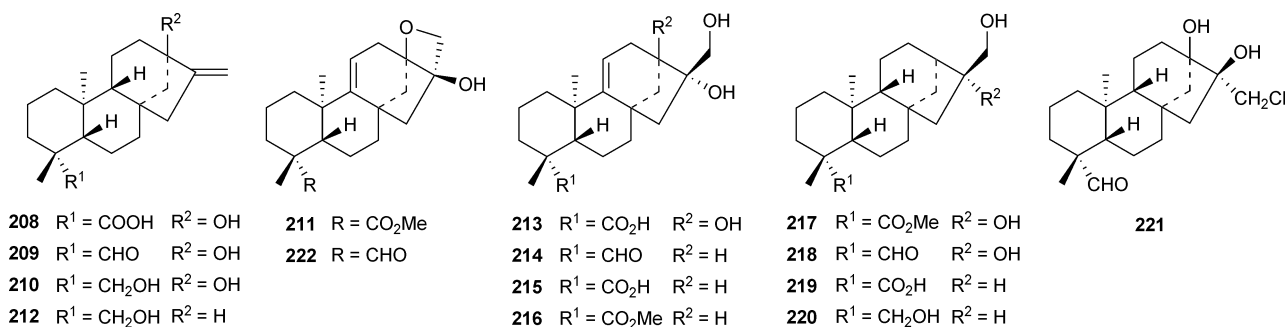
B. gymnorrhiza, *B. hainessi*, *B. parviflora*, *B. sexangula* and *B. sexangula* var. *rhynchopetala*. The initial chemical investigation on it can be traced back to 1978, when Sarkar and Ganguly identified gymnorrhizol (**236**), viz. 3-epi- δ -amyrin, from the leaves of the Indian *Bruguiera gymnorrhiza*.¹⁰⁶ Until now, one catechin derivative, three lignan, five disulfides, eleven aromatic compounds, twenty two triterpenes and twenty seven diterpenes, have been isolated from the bark, flowers, fruits, leaves, roots, and stems of *B. cylindrica*, *B. gymnorrhiza*, *B. parviflora*, and *B. sexangula* var. *rhynchopetala*.

6.1.1 Diterpenoids

6.1.1.1 Kauranes. Four *ent*-kauranes, steviol (**208**), *ent*-kaur-16-en-13-hydroxy-19-al (**209**), *ent*-kaur-16-en-13,19-diol (**210**), methyl-*ent*-kaur-9(11)-en-13,17-epoxy-16-hydroxy-19-oate (**211**), were identified from the outer layer of the root bark of *B. gymnorrhiza* collected from the Andaman and Nicobar Islands.¹⁰⁷ Among those compounds, the crystal structure of *ent*-kaur-16-ene-13,19-diol (**210**), isolated from the roots of *B. cylindrica*, was further established by single-crystal X-ray study.¹⁰⁸

Twelve *ent*-kauranes, *ent*-kaur-16-en-13-hydroxy-19-al (**209**), 16-*ent*-kaurene-13,19-diol (**210**), 16-*ent*-kauren-19-ol (**212**), 13,16 α ,17-trihydroxy-*ent*-9(11)-kaurene-19-oic acid (**213**), 16 α ,17-dihydroxy-*ent*-9(11)-kaurene-19-al (**214**), 16 α ,17-dihydroxy-*ent*-9(11)-kauren-19-oic acid (**215**), methyl-16 α ,17-dihydroxy-*ent*-9(11)-kauren-19-oate (**216**), methyl-16 α ,17-dihydroxy-*ent*-kauran-19-oate (**217**), 16 α ,17-dihydroxy-*ent*-kauran-19-al (**218**), 16 α H-17-hydroxy-*ent*-kauran-19-oic acid (**219**), 16 α H-17,19-*ent*-kauranediol (**220**), and 17-chloro-13,16 β -dihydroxy-*ent*-kauran-19-al (**221**), were identified from the stems of the Chinese *B. gymnorrhiza*.¹⁰⁹ 16-*ent*-Kauren-19-ol (**212**) exhibited cytotoxicity to the K562 (human chronic myeloid leukemia) cell line with an





IC₅₀ value of 6.8 µg mL⁻¹.¹⁰⁹ Moreover, six *ent*-kauranes, methyl-*ent*-kaur-9(11)-en-13,17-epoxy-16-hydroxy-19-oate (**211**), 16 α ,17-dihydroxy-*ent*-9(11)-kaurene-19-al (**214**), methyl-16 α ,17-dihydroxy-*ent*-9(11)-kauren-19-oate (**216**), (16*R*)-13,17-epoxy-16-hydroxy-*ent*-kaur-9(11)-en-19-al (**222**), ceriopsin F (**223**), 16,17-dihydroxy-19-nor-*ent*-kaur-9(11)-en-3-one (**224**), were obtained from the stems of the Chinese *B. sexangula* var. *rhynchopetala*.¹¹⁰

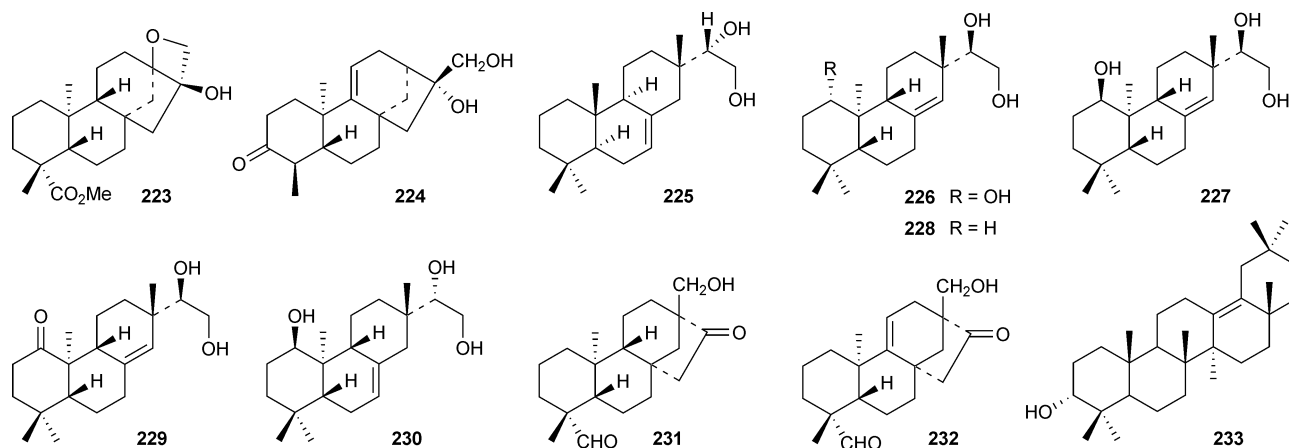
6.1.1.2 Pimaranes. An isopimarane, 15(*S*)-isopimar-7-en-15,16-diol (**225**), and an *ent*-pimarane, *ent*-8(14)-pimarene-1 α ,15*R*,16-triol (**226**), were identified from the outer layer of the root bark of *B. gymnorrhiza* collected from the Andaman and Nicobar Islands.¹⁰⁷ (1 α H,15*R*)-*ent*-pimar-8(14)-ene-1,15,16-triol (**227**) was another *ent*-pimarane characterized from the stems of the Chinese *B. sexangula* var. *rhynchopetala*.¹¹⁰ Five pimaranes, 15(*S*)-isopimar-7-en-15,16-diol (**225**), *ent*-8(14)-pimarene-1 α ,15*R*,16-triol (**226**), *ent*-8(14)-pimarene-15*R*,16-diol (**228**), *ent*-8(14)-pimarene-1-oxo-15*R*,16-diol (**229**), and isopimar-7-ene-1 β ,15*R*,16-triol (**230**), were obtained from the stems of the Chinese *B. gymnorrhiza*.¹¹¹

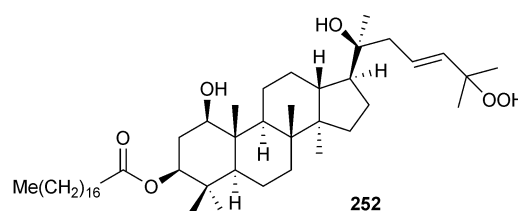
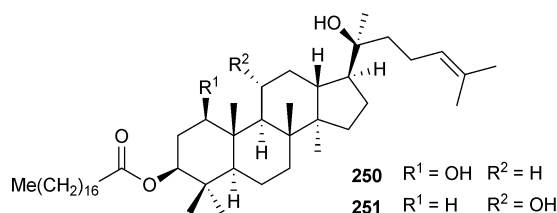
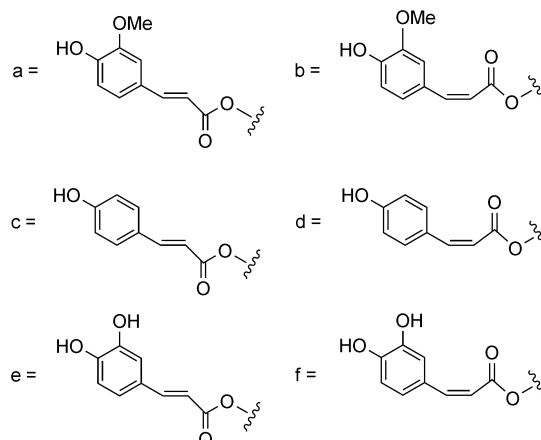
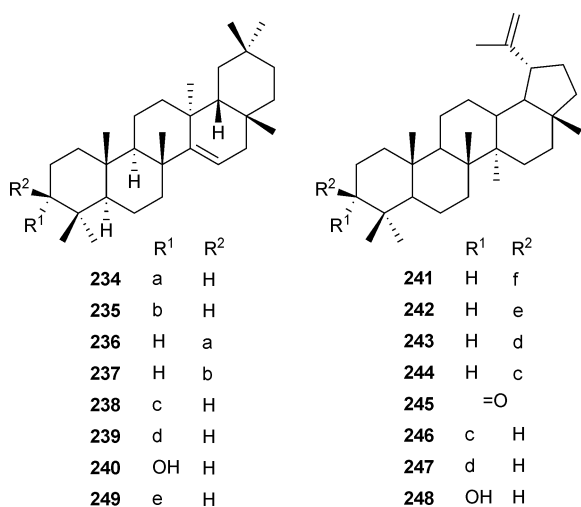
6.1.1.3 ent-Beyeranes. One *ent*-beyerane, (4*R*,5*S*,8*R*,9*R*,10*S*,13*S*)-*ent*-17-hydroxy-16-oxobeyeran-19-al (**231**), was identified from the stems of the Chinese *Bruguiera gymnorrhiza*.¹⁰⁹ and *B. sexangula* var. *rhynchopetala*.¹¹⁰ And another one, *ent*-17-hydroxy-16-oxobeyer-9(11)-en-19-al (**232**), was characterized from the stems of the Chinese *B. sexangula* var. *rhynchopetala*.¹¹⁰

6.1.2 Triterpenoids. Gymnorrhizol (**233**), viz. 3-epi- δ -amyrin, was isolated from the leaves of the Indian *B. gymnorrhiza*.¹⁰⁶ Six

pentacyclic triterpenoid esters, 3 α -*E*-feruloyltaraxerol (**234**), 3 α -*Z*-feruloyltaraxerol (**235**), 3 β -*E*-feruloyltaraxerol (**236**), 3 β -*Z*-feruloyltaraxerol (**237**), 3 α -*E*-coumaroyltaraxerol (**238**), and 3 α -*Z*-coumaroyltaraxerol (**239**), were identified from the fruits of the Thailand *B. cylindrica*, together with 3 α -taraxerol (**240**) and 3 β -taraxerol (**51**).¹¹² The absolute configuration of 3 α -*Z*-feruloyltaraxerol (**235**) dichloromethane solvate was established by single-crystal X-ray study.¹¹³ Six lupane derivatives, lupeol (**56**), 3 β -*Z*-caffeoyllupeol (**241**), 3 β -*E*-caffeoyllupeol (**242**), 3 β -*Z*-coumaroyllupeol (**243**), dioslupecin A (**244**), and lupenone (**245**), were characterized from the fruits of the Thailand *B. parviflora*.¹¹⁴ 3 β -*Z*-Caffeoyllupeol (**241**) showed antimalarial activity with an EC₅₀ value of 8.6 µg mL⁻¹.¹¹⁴ Nine lupane-type triterpenes, viz. lupeol (**56**), 3 β -*E*-caffeoyllupeol (**242**), 3 β -*Z*-coumaroyllupeol (**243**), 3 β -*E*-coumaroyllupeol (**244**), lupenone (**245**), 3 α -*E*-coumaroyllupeol (**246**), 3 α -*Z*-coumaroyllupeol (**247**), 3 α -lupenol (**248**), and 3 α -*E*-caffeoyltaraxerol (**249**), were identified from the Thailand *B. cylindrica* by spectroscopic methods.¹¹⁵ Three dammarane triterpenes, bruguierins A–C (**250–252**), were isolated from a petroleum ether extract of the flowers of *B. gymnorrhiza*, collected from Samutsongkram province of Thailand.¹¹⁶ Bruguierin A (**250**), the dammarane triterpene stearic acid ester, inhibited phorbol ester-induced NF- κ B (nuclear factor- κ B) luciferase activity with an IC₅₀ value of 1.4 µM and selectively inhibited cyclooxygenase-2 (COX-2) activity with an IC₅₀ value of 0.37 µM.¹¹⁶

6.1.3 Disulfides. Gymnorrhizol (**253**), an unusual novel macrocyclic polydisulfide possessing an unprecedented carbon skeleton, characterized by a 15-membered macrocycle that was

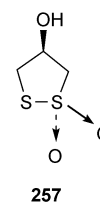
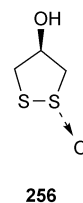
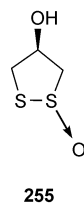
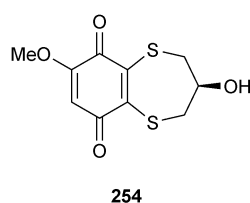
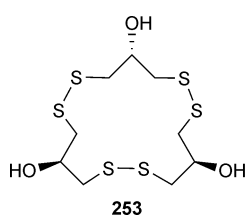


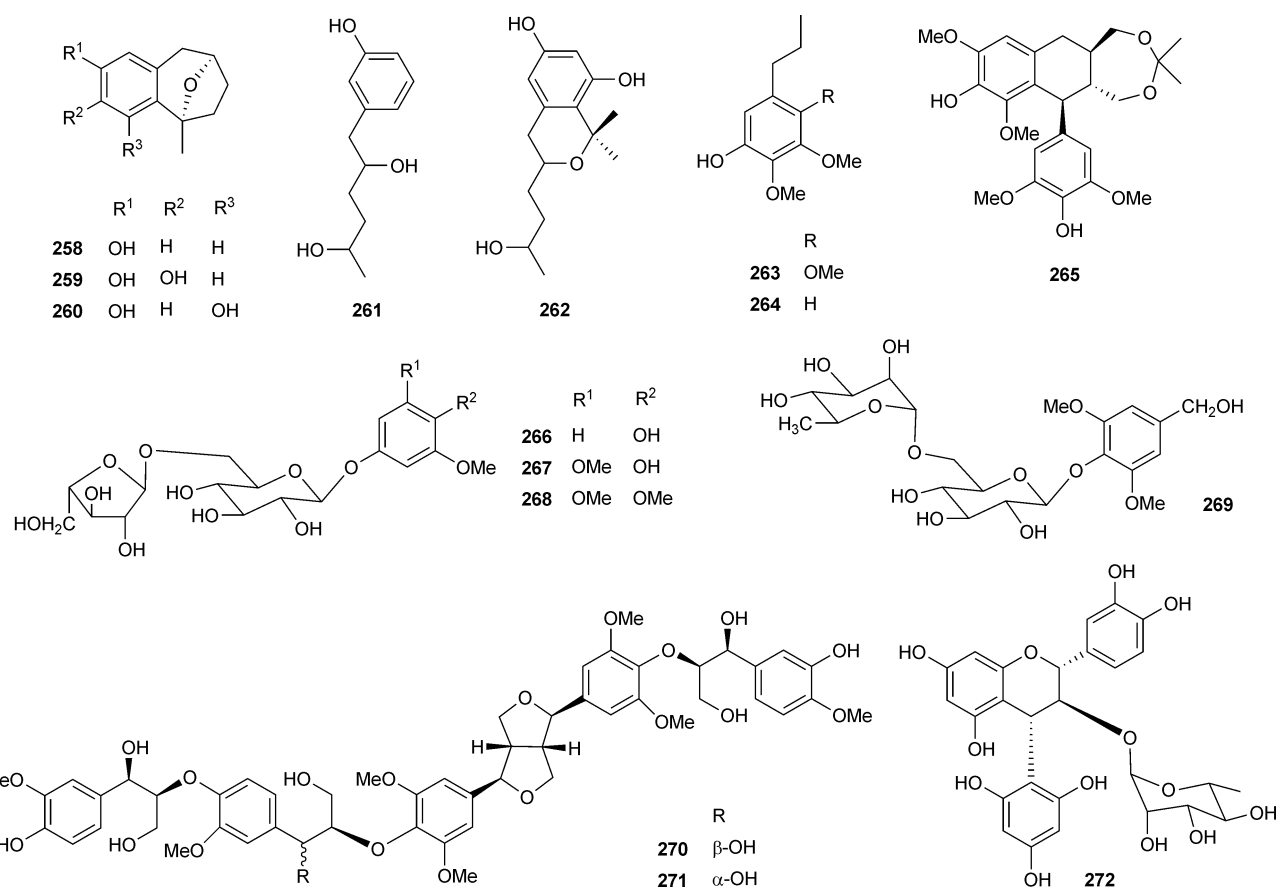


composed of three repeated 1,3-dimercaptopropan-2-ol units, was identified from the stems and leaves of the Chinese *B. gymnorrhiza*.¹⁶ Its structure was further confirmed by X-ray crystallographic analysis.¹⁷ The total synthesis of gymnorrhizol (253), a potent protein tyrosine phosphatase 1B inhibitor with an IC₅₀ value of 14.9 μM, was prepared in three steps, starting from (*R*)-1-bromo-3-chloroisopropanol and 1,3-dichloropropan-2-ol.¹⁸ (–)-3,4-Dihydro-3-hydroxy-7-methoxy-2*H*-1,5-benzodithiopyne-6,9-dione (254), brugierol (255), and isobrugierol (256), were characterized from the stems of the Chinese *B. sexangula* var. *rhynchopetala*.¹¹⁰ Brugierol (255), isobrugierol (256), and bruguiesulfurol (257), were identified from the flowers of the Thailand *B. gymnorrhiza*. The structure of bruguiesulfurol (257) was confirmed by X-ray crystallographic analysis.¹¹⁷ Brugierol (255), isobrugierol (256), and bruguiesulfurol (257), were found to activate antioxidant response element (ARE) luciferase activity with EC₅₀ values of 56.3, 3.7 and 1.8 μM, respectively. Brugierol (255) and isobrugierol (256) also inhibited phorbol ester-induced NF-κB luciferase activity with IC₅₀ values of 85.0 and 14.5 μM, respectively. Moreover, brugierol (255) inhibited COX-2 activity with an IC₅₀ value of 6.1 μM.¹¹⁷

6.1.4 Miscellaneous. Five aromatic compounds, bruguierols A–C (258–260), 1-(3-hydroxyphenyl)-hexane-2,5-diol (261), and 3-(3-hydroxybutyl)-1,1-dimethylisochroman-6,8-diol (262), were identified from the stems of the Chinese Xiamen *B. gymnorrhiza*.¹¹⁸ Bruguierol C (260) showed moderate inhibitory activity against *Staphylococcus aureus* SG 511, *Micrococcus luteus* ATCC 10240, *Enterococcus faecalis* 1528 (vanA), *Escherichia coli* SG 458 and *Mycobacterium vaccae* IMET 10670 with MIC values of 12.5 μg mL^{–1}.¹¹⁸

Two aromatic compounds, bruguierol D (263) and 2,3-dimethoxy-5-propylphenol (264), were isolated from the branches of the Chinese Xiamen *Bruguiera gymnorrhiza*, together with a lignan named brugunin A (265). The structures of bruguierol D (263) and brugunin A (265) were identified as 2,3,4-trimethoxy-5-propylphenol and 7'*S*,8'*R*,8*R*-4,4'-dihydroxy-3,3',5,5'-tetramethoxy-2,7'-cyclo lignin-9,9'-acetone, respectively.¹¹⁹ Four phenolic glycosides rhyncosides A–D (266–269), and two new lignan derivatives, namely rhyncosides E–F (270–271), were identified from the stems of the Chinese *Bruguiera sexangula* var. *rhynchopetala*.¹²⁰ The fatty acids in the fresh leaves of the Australian *B. sexangula* and *B. gymnorrhiza* were mainly





palmitic acid, linoleic acid, and linolenic acid.¹²¹ The triterpenes, *viz.* β-amyrin (**53**), betulin (**54**), α-amyrin (**55**), lupeol (**56**), oleanolic acid (**57**), and ursolic acid (**58**), and sterols, *viz.* cholesterol (**59**), campesterol (**60**), stigmasterol (**61**), sitosterol (**62**), and stigmasterol-7-en-3β-ol (**63**), were characterized from the fresh leaves of the Indian *B. gymnorrhiza* by analytic methods.³⁹ The total lipids and other lipid components of leaves of the Indian *B. gymnorrhiza* were analyzed by TLC and GC.⁴¹ 3-*O*-α-L-Rhamnopyranosyl-(+)-catechin-(4α→2)-phloroglucinol (**272**) was identified from the bark of the Indonesian *B. gymnorrhiza* in the presence of phloroglucinol as a nucleophile capture.¹²²

6.2 Ceriops

The genus of *Ceriops* has two species and two varieties, namely *C. tagal* (Perr.), *C. decandra*, *C. tagal* var. *australasica* and *C. tagal* var. *typical*. So far, twenty three diterpenes and twenty nine triterpenes have been reported from the stems, twigs, roots, leaves, hypocotyls and fruits of *C. tagal* (Perr.) and *C. decandra*. The diterpenes that have been obtained can be categorized as four types, *viz.* dolabrane, kaurane, beyerane, and pimarane, while triterpenes were classified into three types, *viz.* lupane, dammarane, and oleanane. Obviously, diterpenoids and triterpenoids are the main secondary metabolites of this genus.

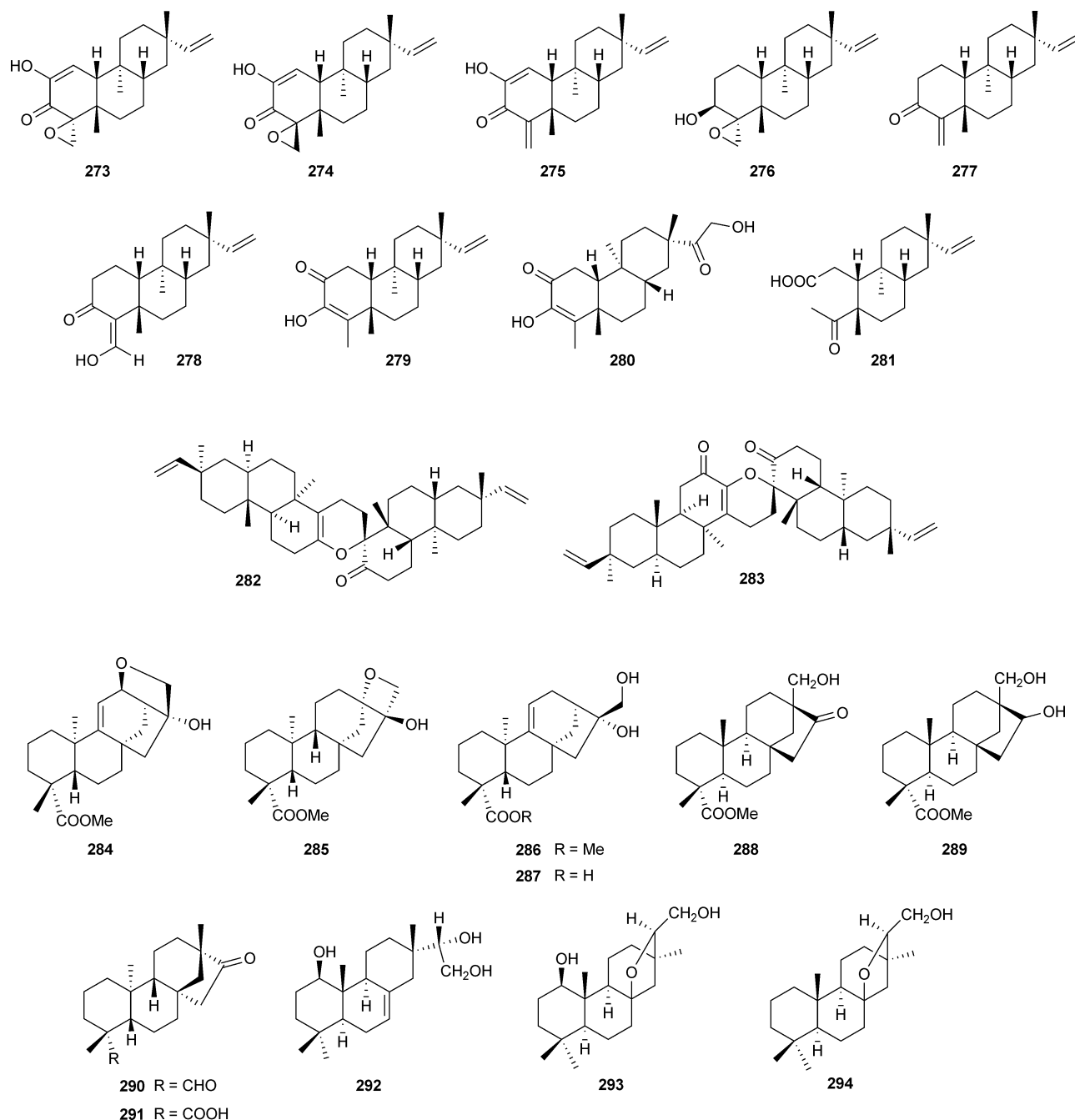
6.2.1 Diterpenoids

6.2.1.1 Dolabranes. Chemical investigation of the stems and twigs of *Ceriops tagal* (Perr.), collected from Hainan Island of

China, led to the isolation of seven dolabranes, tagalsin A–G (**273–279**).¹²³ From the roots of the same species collected from Nakhon Si Thammarat province in the southern part of Thailand, tagalsin F (**278**) and 7-glycoloyl-2-hydroxy-1,4b,7,10a-tetramethyl-4a,4b,5,6,7,8,8a,9,10,10a-decahydrophenanthren-3(4*H*)-one (**280**), were obtained. Their relative stereochemistry was established by single-crystal X-ray analysis.^{124,125} Tagalsin H (**281**), a ring A-*seco* dolabrane-type norditerpene, was characterized from the stems and twigs of the Chinese Hainan Island *C. tagal*.¹²³ Two novel bisdolabranes, tagalsins I and J (**282–283**), were obtained from the stems and twigs of the Chinese Hainan Island *C. tagal*. The stereochemistry of tagalsins I (**282**) was determined by single-crystal X-ray diffraction.¹²⁶

6.2.1.2 Kauranes. From the roots of *Ceriops decandra* collected from the Indian Kauvery estuary (Parangipettai coast), an epoxy *ent*-kaurane named ceriopsin E (**284**) was identified and its structure was confirmed by single-crystal X-ray analysis.¹²⁷ Chemical reinvestigation on the roots of the same plant materials identified four kauranes, *viz.* ceriopsin F (**285**), steviol (**208**), methyl *ent*-16β,17-dihydroxy-9(11)-kauran-19-oate (**286**), and *ent*-16β,17-dihydroxy-9(11)-kauran-19-oic acid (**287**).¹²⁸

6.2.1.3 Beyeranes. Two beyeranes, ceriopsins A and B (**288–289**), were obtained from the roots of the Indian Kauvery estuary *C. decandra*.¹²⁹ Chemical reinvestigation on the roots of the same plant materials led to the discovery of another two beyeranes, ceriopsin G and isosteviol (**290–291**).¹²⁸



6.2.1.4 Pimaranes. Two pimaranes, ceriopsins C and D (**292–293**), were identified from the roots of the Indian Kauvery estuary *C. decandra*.¹²⁹ 8,15*R*-epoxypimarane-16-ol (**294**), previously reported pimarane, which was synthesized from *ent*-8,15*R*-epoxypimarane-3 β ,12 α ,16-triol isolated from *Liatris laevigata*,¹³⁰ was characterized from the roots of the Indian Kauvery estuary *C. decandra* for the first time.¹²⁸

6.2.2 Triterpenoids

6.2.2.1 Lupanes. Sixteen lupanes, viz. betulinic acid (**50**), betulin (**54**), lupeol (**56**), 3 β -*Z*-coumaroyllupeol (**246**), 3 β -*E*-coumaroyllupeol (**247**), lupenone (**248**), 3 β -*E*-feruloyllupeol (**295**), 3 β -*Z*-feruloyllupeol (**296**), 3 β -*E*-caffeoyllupeol (**297**), 3 β -*E*-

feruloylbetulin (**298**), 3 α -betulinic acid (**299**), betulinaldehyde (**300**), 3 β -hydroxylupan-29-oic acid (**301**), 30-nor-lup-3 β -ol-20-one (**302**), lup-20(29)-en-3 β ,30-diol (**303**), and 3 β ,20-dihydroxylupane (**304**), were identified from the leaves of the Thailand *C. decandra*.¹³¹ The relative stereochemistry of 3 β -*E*-feruloyllupeol (**295**) and 3 β -hydroxylupan-29-oic acid (**301**) was established by single-crystal X-ray analysis.^{132,133} Lupanes **50**, **54**, **56**, **245**, **295–296**, **298–299**, and 3 β -*E*-caffeoylbetulin (**305**), 3 β -*E*-feruloylbetulinic acid (**306**), 3 β -*E*-caffeoylbetulinic acid (**307**), 3 β -acetylbetulinic acid (**308**) and betulonic acid (**309**), were obtained from the hypocotyls and fruits of *C. tagal* collected at the Mangrove Research Station in Nakhon Si Thammarat Province, Thailand.¹³⁴ 3 β -*E*-feruloylbetulinic acid (**306**) exhibited potent

cytotoxic activity against KB, BC, and NIC-H187 cell lines, with IC_{50} values of 3.8, 3.0, and 1.8 $\mu\text{g mL}^{-1}$, respectively.¹³⁴ 3 β -*E*-feruloyllupeol (**295**) was identified again from the embryo of the Chinese Hainan *C. tagal*.¹³⁵ The ethanol extract of the leaves and pneumatophores of the Bangladeshi Sundarban *Ceriops decandra* (Syn. *Ceriops candolleana*), at the oral doses of 250 and 500 mg kg^{-1} , showed a dose-dependent and significant inhibition of acetic acid-induced writhing in mice. On the contrary, the bark extract was devoid of any significant activity.¹³⁶

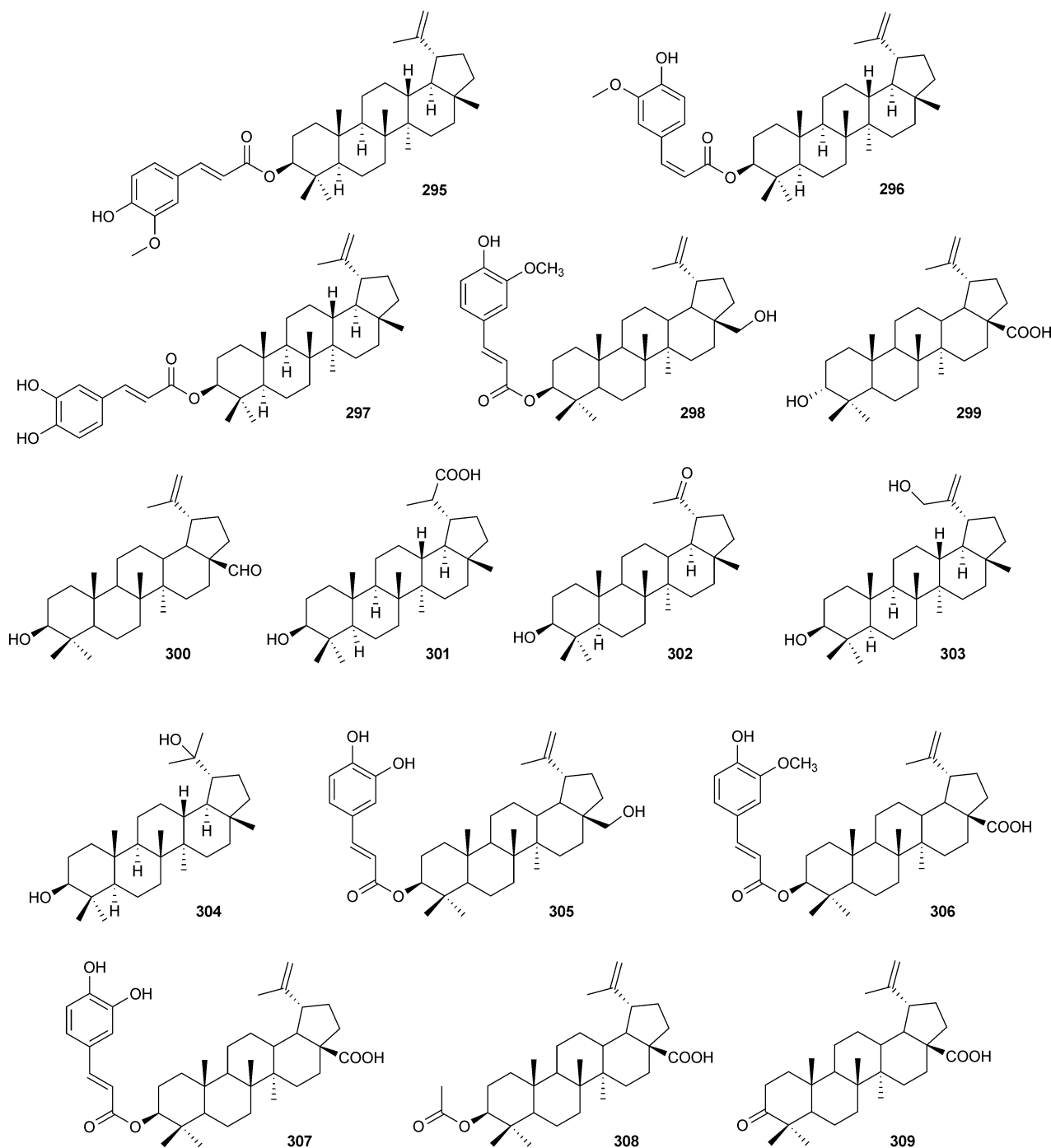
6.2.2.2 Dammaranes. Seven dammaranes, cereotagaloperoxide (**310**), cereotagalol A (**311**), and cereotagalol B (**312**),

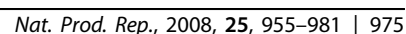
isofouquierol (**313**), fouquierol (**314**), dammarenediol II (**315**) and ocotillol II (**316**), were identified from the hypocotyls and fruits of the Thailand *C. tagal*.¹³⁴

6.2.2.3 Oleanane. Oleanolic acid (**57**) was characterized from the hypocotyls and fruits of the Thailand *C. tagal*.¹³⁴

6.3 Rhizophora

The mangrove plants of the genus *Rhizophora* have nine species, viz. *R. apiculata*, *R. harrisonii*, *R. lamarckii*, *R. mangle*, *R. mucronata*, *R. racemosa*, *R. samoensis*, *R. selala*, and *R. stylosa*. To





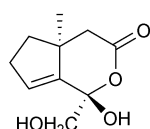
and ursolic acid (**58**) were originally characterized from the fresh mangrove leaves of the Indian *R. mucronata*, together with α -amyrin and β -amyrin.³⁹

6.3.3 Miscellaneous. A sesquiterpene, mucronatone (**326**), was identified as 3-hydroxy-3,7,11-trimethyl-9-oxododeca-1,10-diene from the fruits of the Thailand *R. mucronata*.¹⁴⁰ β -sitosterol (**62**), daucosterol (**180**), lichixanthone (**327**), atranorin (**328**) and palmitone (**329**), were obtained from outer layer of the root bark of *R. mucronata* collected from the Indian Andaman and Nicobar islands.¹⁴¹ 1-D-*O*-Methyl-muco-inositol (**330**) was isolated from the roots of the Australian *R. mucronata*.¹⁴²

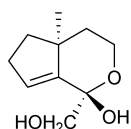
7 Rubiaceae

7.1 *Scyphiphora hydrophyllacea*

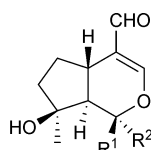
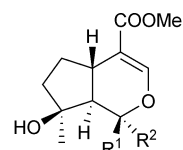
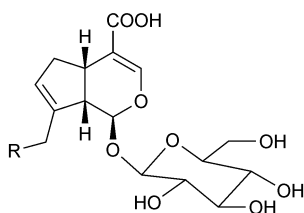
The Rubiaceae family of the mangrove plants only has one species, viz. *Scyphiphora hydrophyllacea* Gaertn. F. Six iridoids, hydrophylins A (**331**), B (**332**),¹⁴³ scyphiphins A₁ (**333**), A₂ (**334**), B₁ (**335**), and B₂ (**336**),¹⁴⁴ were identified from the aerial parts of *S. hydrophyllacea* collected from Wenchang of Hainan Island, China. Three other iridoids, scyphiphorins A (**337**), B (**338**), and geniposidic acid (**339**), were characterized from the stem bark of the same source of plant, together with betulinic acid (**50**), betulin (**54**), oleanolic acid (**57**), cholesterol (**59**), 4-(4'-



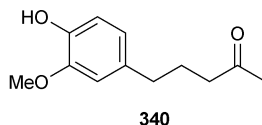
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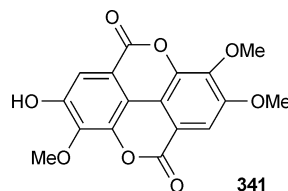
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333 R¹ = H R² = OH334 R¹ = OH R² = H335 R¹ = H R² = OH336 R¹ = OH R² = H337 R = $\text{Ph}-\text{C}(=\text{O})-\text{O}-\text{Z}$ 338 R = $\text{HO}-\text{CH}_2-\text{CH}(\text{Me})-\text{CH}_2-\text{CH}(\text{Me})-\text{C}(=\text{O})-\text{O}-\text{Z}$

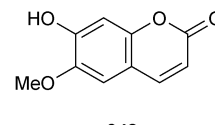
339 R = OH



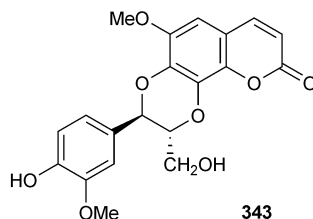
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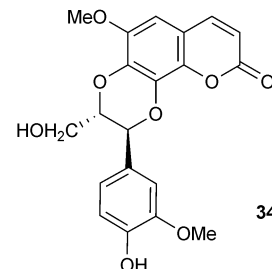
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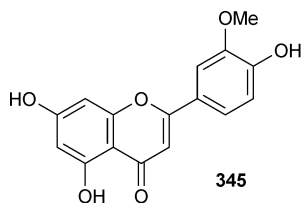
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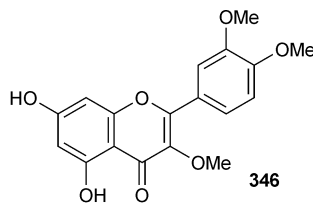
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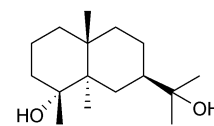
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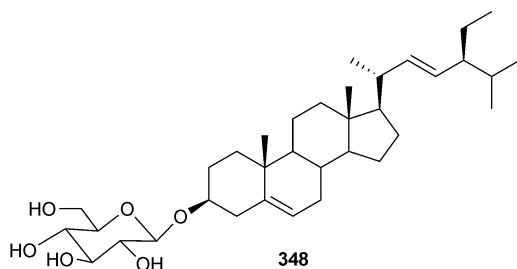
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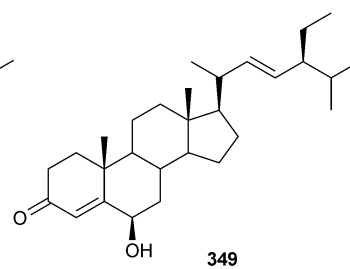
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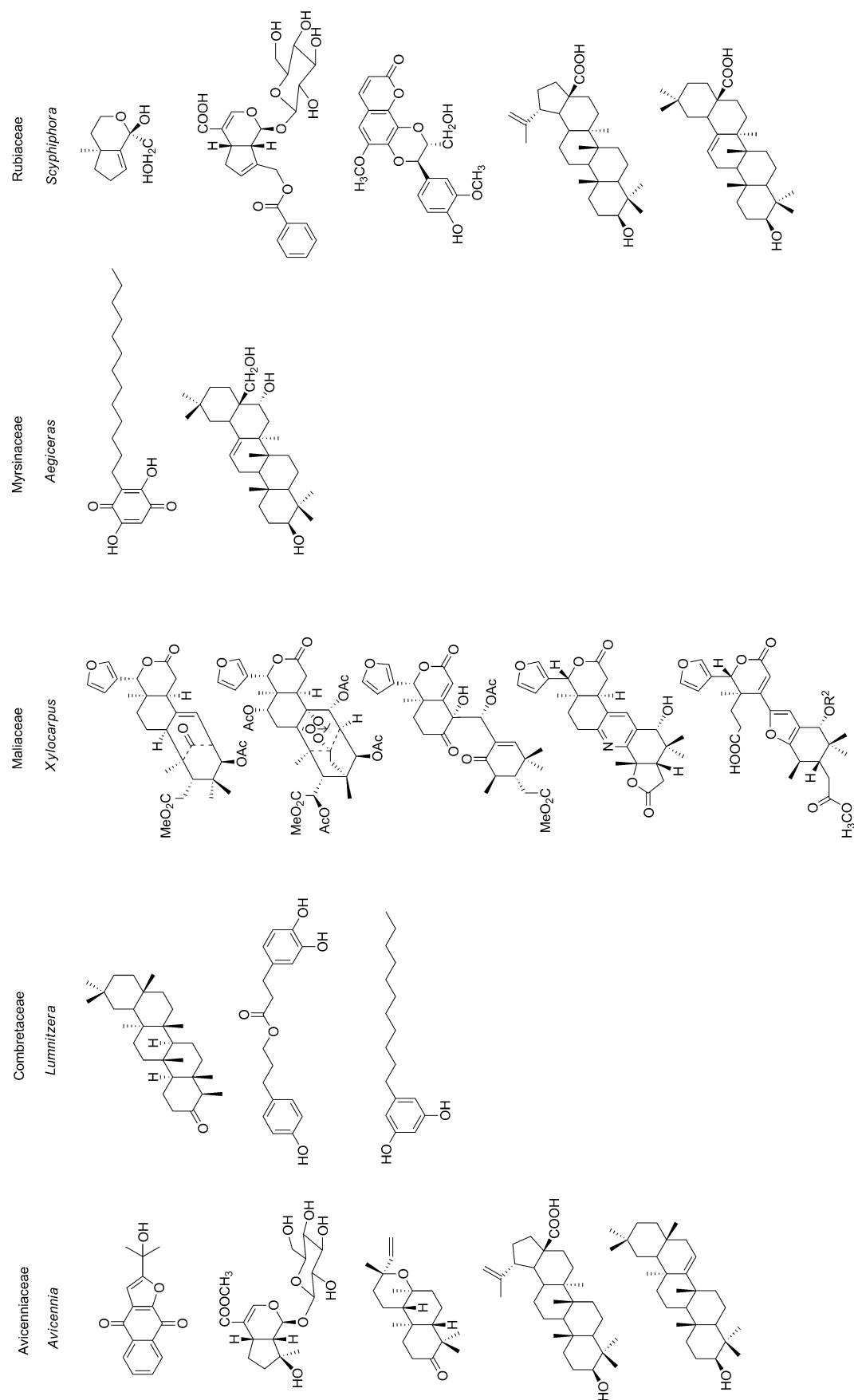


Fig. 1 Representative structures indicating chemotaxonomic markers for the genera *Avicennia*, *Lumnitzera*, *Xylocarpus*, *Aegiceras*, and *Scyphiphora*.

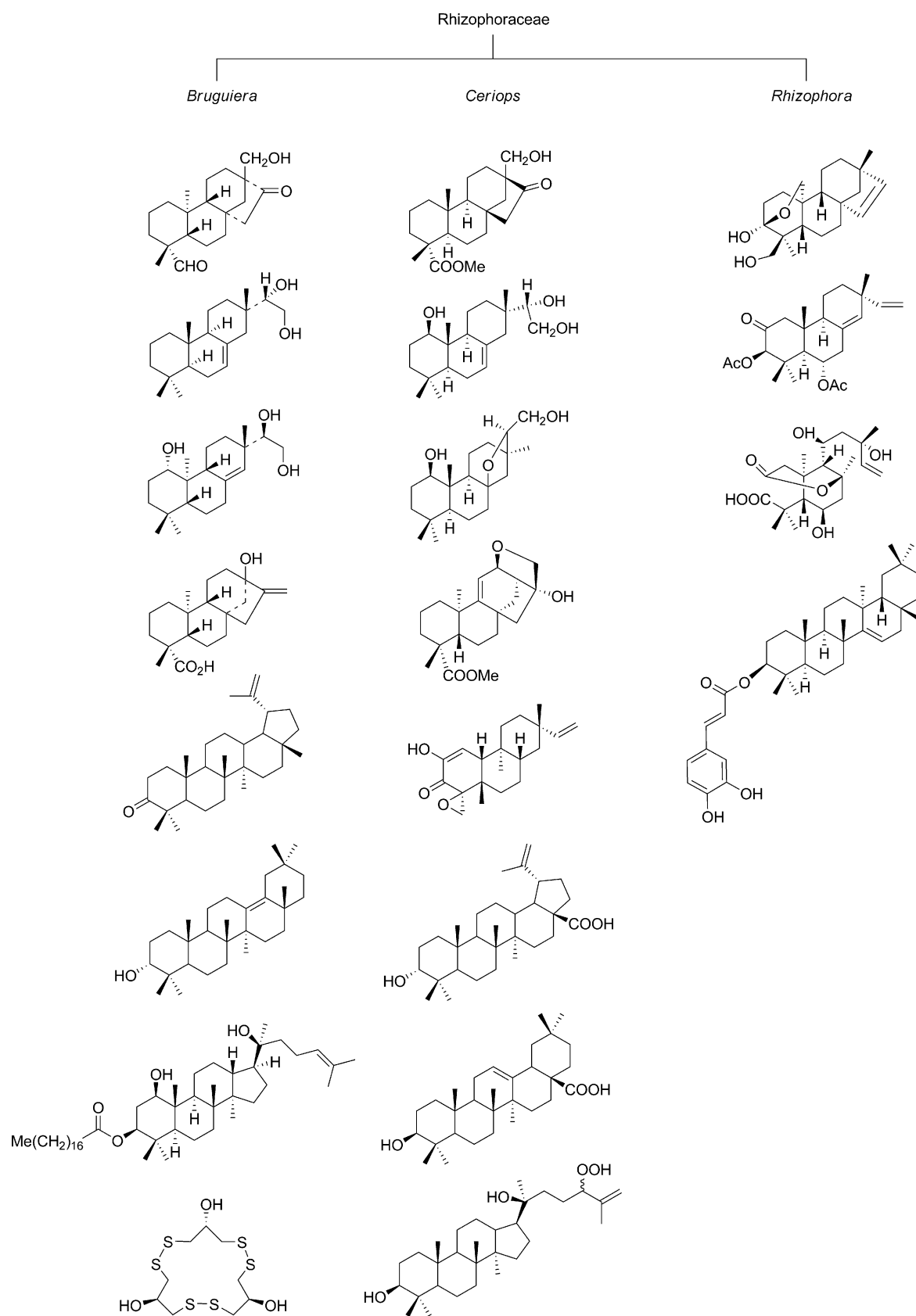


Fig. 2 Representative structures indicating chemotaxonomic trends within the Rhizophoraceae.

hydroxyl-3'-methoxybenzyl)butan-2-one (340), 3,3',4'-trimethoxy-ellagic acid (341), scopoletin (342), cleomiscosin A (343), cleomiscosin B (344), and 5,7,4'-trihydroxy-3'-methoxy flavone (345).^{145,146} Ursolic acid (58), daucosterol (180), 5,7-dihydroxy-3,3,4'-trimethoxy-flavone (346), cryptomeridiol (347), stigmasterol- β -D-glucoside (348), and stigmast-4-en-6 β -ol-3-one (349), were obtained from the stems of the same plant.¹⁴⁷

8 Molecular phylogeny, chemotaxonomy and concluding remarks

The molecular phylogeny of mangroves was investigated. The chloroplast gene *matK* and the internal transcribed spacer (ITS) regions of nuclear ribosomal DNA were sequenced from seventeen samples of thirteen species representing six genera of the angiosperm family Rhizophoraceae from China.¹⁴⁸ Phylogenetic analyses were initially conducted based on sequences of the *matK* gene and the ITS regions, respectively, using *Byrsonima crassifolia* and *Bunchosia armeniaca* (Malpighiaceae) as outgroups. The combined phylogeny shows that each genus formed a monophyletic group and the monophyletic relationships of the mangrove genera and of the inland genera were strongly supported. A dendrogram, constructed after pooling both RAPD and RFLP data, using a similarity index was analyzed for genome relationships among eleven true major mangrove, three true minor mangrove, two mangrove associate, two mangrove parasite, three terrestrial and one cultivated species from Indian.¹⁴⁹ The dendrogram showed clustering of all the major mangroves, except for *Nypa fruticans* (Arecaceae), into one group. All species under the tribe Rhizophorae formed a subcluster, to which *Xylocarpus granatum* was found to be the most closely related species. The clustering pattern implied that *Excoecaria agallocha* and *Acanthus ilicifolius* should be considered as true minor mangroves. The present study also provided molecular data favouring the separation of *Avicennia* spp. from the Verbenaceae to create a monotypic family the Avicenniaceae. Moreover, the molecular markers showed a rather distant relationship between true mangroves and mangrove associates, considered as terrestrial plants.

Naphthoquinones, iridoid glucosides, labdanes, lupanes and oleananes are the main natural products of the genus *Avicennia*. Friedelin, lignans such as 3-(4-hydroxyphenyl)-propyl-3'-(3,4-dihydroxyphenyl)-propionate, and 1,3-dihydroxy-5-undecylbenzene are the representative structures of the genus *Lumnitzera* (Fig. 1). Mexicanolides and phragmalins are the main natural products of the genus *Xylocarpus*. The 8,9,30-phragmalin orthoester is a type of phragmalin found for the first time in the stem bark of *X. granatum* and its content is relatively high in comparison with the other types of limonoids in the bark of this plant. Recently, 8,9,30-phragmalin orthoester, propionate, isobutylate and 2-methylbutanoate have been found in the leaves of *Swietenia mahagoni*.¹⁵⁰ It was indicated that this type of phragmalin could be used as a chemotaxonomic marker of the genera *Xylocarpus* and *Swietenia*. Lately, 9,10-*seco*-mexicanolides and aromatic B-ring limonoids have been first reported from the genus *Xylocarpus*. These novel limonoids can be seen as the significant chemotaxonomic markers of this genus. Hydroquinone derivatives and oleananes are the main natural products of the genus *Aegiceras*. Clearly, iridoid glucosides, coumarins,

lupanes and oleananes are the representative structures of the genus *Scyphiphora* (Fig. 1).

Three true mangrove genera, *Bruguiera*, *Ceriops* and *Rhizophora*, belong to the family Rhizophoraceae. Two types of diterpenoids, beyerane and pimarane, and three types of triterpenoids, lupane, oleanane and dammarane, are common natural products in this family. *ent*-Pimarane coexists with isopimarane in the genus *Bruguiera*. Kaurane exists in the genera *Bruguiera* and *Ceriops*, but not in the genus *Rhizophora*. Dolabrane only exists in the genus *Ceriops* and labdane only in the genus *Rhizophora*. The former can be seen as the significant chemotaxonomic marker of the genus *Ceriops* and the latter of the genus *Rhizophora*. Disulfides and polydisulfides, only found in the genus *Bruguiera*, are significant chemotaxonomic markers of this genus (Fig. 2).

In this review, we have systematically summarized the source, chemistry and bioactivities of natural products from true mangrove plants since 1913, concentrating on work that has appeared in the literature during the recent half century. It includes 349 metabolites. Out of these, about 200 are reported exclusively from true mangroves. To date, the chemical constituents of true mangrove species belonging to four families, *viz.* Combretaceae, Myrtaceae, Pellicieraceae, and Sonneratiaceae, have not been effectively investigated. Gymnorrhizol, a potent proteintyrosinephosphatase 1B inhibitor, was identified from the stems and leaves of *Bruguiera gymnorrhiza*. Xylogranatins F, G and R, limonoids identified from the seeds of *Xylocarpus granatum*, exhibited marked antifeedant activity against the third instar larvae of *Mythimna separata* (Walker), a pest to wheat in the north of China. The above findings demonstrate that true mangrove plants are a promising and rewarding source for the production of bioactive substances with novel carbon frameworks.

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10 References

- 1 K. Kathiresan and B. L. Bingham, *Adv. Mar. Biol.*, 2001, **40**, 81.
- 2 B.-S. Wang, S.-C. Liang, W.-Y. Zhang and Q.-J. Zan, *Acta Bot. Sin.*, 2003, **45**, 644.
- 3 L. D. Lacerda, *Mangrove Ecosystems: Function and Management*, Springer, Berlin, 2002, ch. 1.2.
- 4 I. Valiela, J. L. Bowen and J. K. York, *BioScience*, 2001, **51**, 807.
- 5 E. C. Ashton and D. J. Macintosh, *For. Ecol. Manage.*, 2002, **166**, 111.
- 6 P. Lin and Q. Fu, *Environmental Ecology and Economic Utilization of Mangroves in China*, China Higher Education Press/Springer, Beijing/Berlin, 2000, ch. 1.
- 7 K. Bournot, *Arch. Pharm.*, 1913, **251**, 351.
- 8 K. V. Rao and P. K. Bose, *J. Indian Chem. Soc.*, 1959, **36**, 358.
- 9 D. A. H. Taylor, *J. Chem. Soc.*, 1965, 3495.

- 10 A. Akisanya, C. W. L. Bevan, T. G. Halsall, J. W. Powell and D. A. H. Taylor, *J. Chem. Soc.*, 1961, 3705.
- 11 A. Akisanya, C. W. L. Bevan, J. Hirst, T. G. Halsall and D. A. H. Taylor, *J. Chem. Soc.*, 1960, 3827.
- 12 R. A. Toscano, R. Mata, J. Calderon and R. Segura, *J. Chem. Crystallogr.*, 1996, **26**, 707.
- 13 T. Konishi, M. Takasaki, H. Tokuda, S. Kiyosawa and T. Konoshima, *Biol. Pharm. Bull.*, 1998, **21**, 993.
- 14 T. Konoshima, T. Konishi, M. Takasaki, K. Yamazoe and H. Tokuda, *Biol. Pharm. Bull.*, 2001, **24**, 1440.
- 15 J. Wu, Q. Xiao, J.-S. Huang, Z.-H. Xiao, S.-H. Qi, Q.-X. Li and S. Zhang, *Org. Lett.*, 2004, **6**, 1841.
- 16 Y.-Q. Sun and Y.-W. Guo, *Tetrahedron Lett.*, 2004, **45**, 5533.
- 17 Y.-Q. Sun, G. Zhan and Y.-W. Guo, *Z. Kristallogr. - New Cryst. Struct.*, 2004, **219**, 121.
- 18 J.-X. Gong, X. Shen, L.-G. Yao, H.-L. Jiang, K. Krohn and Y.-W. Guo, *Org. Lett.*, 2007, **9**, 1715.
- 19 J. Wu, S. Zhang, T. Bruhn, Q. Xiao, H.-X. Ding and G. Bringmann, *Chem.-Eur. J.*, 2008, **14**, 1129.
- 20 L. Han, X. Huang, H.-M. Dahse, U. Moellmann, H. Fu, S. Grabley, I. Sattler and W. Lin, *J. Nat. Prod.*, 2007, **70**, 923.
- 21 C. Ito, S. Katsuno, Y. Kondo, H. T.-W. Tan and H. Furukawa, *Chem. Pharm. Bull.*, 2000, **48**, 339.
- 22 A. S. R. Anjaneyulu, Y. L. N. Murthy, V. L. Rao and K. Sreedhar, *Indian J. Chem., Sect. B*, 2003, **42**, 3117.
- 23 G. König, H. Rimpler and D. Hunkler, *Phytochemistry*, 1987, **26**, 423.
- 24 H. Demuth, H. R. Jensen and B. J. Nielsen, *Phytochemistry*, 1989, **28**, 3361.
- 25 R. Nass and H. Rimpler, *Phytochemistry*, 1996, **41**, 489.
- 26 M. S. N. Pandey and H. S. Garg, *Indian J. Chem., Sect. B*, 1996, **35**, 459.
- 27 G. König and H. Rimpler, *Phytochemistry*, 1985, **24**, 1245.
- 28 M. T. Fauvel, A. B. Melou, C. Moulis, J. Gleye and S. R. Jensen, *Phytochemistry*, 1995, **38**, 893.
- 29 M. T. Fauvel, C. Moulis, M. Bon and I. Fouraste, *Nat. Prod. Lett.*, 1997, **10**, 139.
- 30 A. Bousquet-Mélou and M. T. Fauvel, *Biochem. Syst. Ecol.*, 1998, **26**, 935.
- 31 M. T. Fauvel, M. Bon, F. Crasnier, C. Moulis and I. Fouraste, *Nat. Prod. Lett.*, 1999, **14**, 99.
- 32 C. Subrahmanyam, S. R. Kumar and G. D. Reddy, *Indian J. Chem., Sect. B*, 2006, **45**, 2556.
- 33 S. G. Majumdar, P. Ghosh and S. Thakur, *Indian J. Chem., Sect. B*, 1981, **20**, 632.
- 34 H. Sharp, D. Thomas, F. Currie, C. Bright, Z. Latif, S. D. Sarker and R. J. Nash, *Biochem. Syst. Ecol.*, 2001, **29**, 325.
- 35 M. T. Fauvel, K. Taoubi, J. Gleye and I. Fouraste, *Planta Med.*, 1993, **59**, 387.
- 36 K. H. Bell and H. Duewell, *Aust. J. Chem.*, 1961, **14**, 662.
- 37 M. Adrian-Romero, S. J. Wilson, G. Blunden, M. H. Yang, A. Carabot-Cuervo and A. K. Bashir, *Biochem. Syst. Ecol.*, 1998, **26**, 535.
- 38 S. G. Majumdar and G. Patra, *J. Indian Chem. Soc.*, 1979, **56**, 111.
- 39 A. Ghosh, S. Misra, A. K. Dutta and A. Choudhury, *Phytochemistry*, 1985, **24**, 1725.
- 40 G. P. Wannigama, J. K. Volkman, F. T. Gillan, P. D. Nichols and R. B. Johns, *Phytochemistry*, 1981, **20**, 659.
- 41 S. Misra, A. Choudhury, P. K. Pal and A. Ghosh, *Phytochemistry*, 1986, **25**, 1083.
- 42 S. G. Majumdar and G. Patra, *J. Indian Chem. Soc.*, 1980, **57**, 568.
- 43 A. S. R. Anjaneyulu, Y. L. N. Murthy, V. L. Rao and K. Sreedhar, *Arkivoc*, 2003, (iii), 25.
- 44 T. C. Lin, F. L. Hsu and J. T. Cheng, *J. Nat. Prod.*, 1993, **56**, 629.
- 45 J.-D. Wang, M.-L. Dong, W. Zhang, X. Shen and Y.-W. Guo, *Chin. J. Nat. Med.*, 2006, **4**, 187.
- 46 J. D. Connolly, M. Maclellan, D. A. Okorie and D. A. H. Taylor, *J. Chem. Soc., Perkin Trans. I*, 1976, 1993.
- 47 D. A. H. Taylor, *Phytochemistry*, 1983, **22**, 1297.
- 48 D. A. Mulholland and D. A. H. Taylor, *Phytochemistry*, 1992, **31**, 4163.
- 49 W. Waratchareeyakul, S. Chantrapromma, H.-K. Fun, I. A. Razak, C. Karalai and C. Ponglimanont, *Acta Crystallogr., Sect. E*, 2004, **60**, o1964.
- 50 S. J. Uddin, L. Nahar, J. A. Shilpi, M. Shoeb, T. Borkowski, S. Gibbons, M. Middleton, M. Byres and S. D. Sarker, *Phytother. Res.*, 2007, **21**, 757.
- 51 C. L. Céspedes, J. R. Salazar, M. Martínez and E. Aranda, *Phytochemistry*, 2005, **66**, 2481.
- 52 O. Koul, J. S. Multani, G. Singh, W. M. Daniewski and S. Berlozecki, *J. Agric. Food Chem.*, 2003, **51**, 2937.
- 53 J. S. Calderó, C. L. Céspedes, R. Rosas, F. Gómez-Garibay, J. R. Salazar, L. Lina, E. Aranda and I. Kubo, *Z. Naturforsch., Teil C*, 2001, **56**, 382.
- 54 S. S. Nathan, K. Kalaivani and K. Murugan, *Acta Trop.*, 2005, **96**, 47.
- 55 S. Omar, K. Godard, A. Ingham, H. Hussain, V. Wongpanich, J. Pezzuto, T. Durst, C. Eklü, M. Gbeassor, P. Sanchez-Vindas, L. Poveda, B. J. R. Philogene and J. T. Arnason, *Ann. Appl. Biol.*, 2003, **143**, 135.
- 56 S. Omar, J. Zhang, S. MacKinnon, D. Leaman, T. Durst, B. J. R. Philogene, J. T. Arnason, P. E. Sanchez-Vindas, L. Poveda, P. A. Tamez and J. M. Pezzuto, *Curr. Top. Med. Chem.*, 2003, **3**, 133.
- 57 J. Bickii, N. Njifutie, J. A. Foyere, L. K. Basco and P. Ringwald, *J. Ethnopharmacol.*, 2000, **69**, 27.
- 58 S. MacKinnon, T. Durst, J. T. Arnason, C. Angerhofer, J. Pezzuto, P. E. Sanchez-Vindas, L. J. Poveda and M. Gbeassor, *J. Nat. Prod.*, 1997, **60**, 336.
- 59 B. Sundarasivarao, A. Nazma and J. Madhusudhanarao, *Curr. Sci.*, 1977, **46**, 714.
- 60 C. Penido, K. A. Costa, M. F. D. S. Costa, J. D. F. G. Pereira, A. C. Siani and M. D. G. M. Henriques, *Int. Immunopharmacol.*, 2006, **6**, 109.
- 61 D. A. Okorie and D. A. H. Taylor, *J. Chem. Soc. C*, 1970, 211.
- 62 K. A. Alvi, P. Crews, B. Aalbersberg and R. Prasad, *Tetrahedron*, 1991, **47**, 8943.
- 63 U. Kokpol, W. Chavasiri, S. Tip-Pyang, G. Veerachato, F. Zhao, J. Simpson and R. T. Weavers, *Phytochemistry*, 1996, **41**, 903.
- 64 J. Wu, Z.-H. Xiao, Y. Song, S. Zhang, Q. Xiao, C. Ma, H.-X. Ding and Q.-X. Li, *Magn. Reson. Chem.*, 2006, **44**, 87.
- 65 A. S. Ng and A. G. Fallis, *Can. J. Chem.*, 1979, **57**, 3088.
- 66 J. Wu, S. Zhang, Q. Xiao, Q.-X. Li, J.-S. Huang, L.-J. Long and L.-M. Huang, *Tetrahedron Lett.*, 2004, **45**, 591.
- 67 J. Wu, S. Zhang, Q. Xiao, Q.-X. Li, J.-S. Huang, Z.-H. Xiao and L.-J. Long, *Z. Naturforsch., Teil B*, 2003, **58**, 1216.
- 68 F. Cheng, Y. Zhou, J. Wu and K. Zou, *Z. Naturforsch., Teil B*, 2006, **61**, 626.
- 69 J. Wu, S. Zhang, Y. Song, Z.-H. Xiao, Q. Xiao and Q.-X. Li, *Z. Naturforsch., Teil B*, 2005, **60**, 1291.
- 70 A. D. Roy, R. Kumar, P. Gupta, T. Khaliq, T. Narender, V. Aggarwal and R. Roy, *Magn. Reson. Chem.*, 2006, **44**, 1054.
- 71 J. Wu, Y. Zhou, S. Zhang, Q. Xiao, M.-Y. Li and Z.-H. Xiao, *Chem. Pharm. Bull.*, 2006, **54**, 1582.
- 72 J. Wu, H.-X. Ding, M.-Y. Li and S. Zhang, *Z. Naturforsch., Teil B*, 2007, **62**, 569.
- 73 S. Yin, C.-Q. Fan, X.-N. Wang, L.-P. Lin, J. Ding and J.-M. Yue, *Org. Lett.*, 2006, **8**, 4935.
- 74 J.-X. Cui, J. Wu, Z.-W. Deng, P. Proksch and W.-H. Lin, *J. Nat. Prod.*, 2007, **70**, 772.
- 75 S. Yin, X.-N. Wang, C.-Q. Fan, L.-P. Lin, J. Ding and J.-M. Yue, *J. Nat. Prod.*, 2007, **70**, 682.
- 76 J. Wu, M.-Y. Li, S. Zhang, Q. Xiao and Q.-X. Li, *Z. Naturforsch., Teil B*, 2007, **62**, 859.
- 77 M.-Y. Li, J. Wu, S. Zhang, Q. Xiao and Q.-X. Li, *Magn. Reson. Chem.*, 2007, **45**, 705.
- 78 F. R. Ahmed, A. S. Ng and A. G. Fallis, *Can. J. Chem.*, 1978, **56**, 1020.
- 79 J. Wu, Q. Xiao, S. Zhang, Q.-X. Li, Z.-H. Xiao, H.-X. Ding and Q.-X. Li, *Tetrahedron*, 2005, **61**, 8382.
- 80 J.-X. Cui, Z.-W. Deng, J. Li, H.-Z. Fu, P. Proksch and W.-H. Lin, *Phytochemistry*, 2005, **66**, 2334.
- 81 J. Wu, Q. Xiao and Q.-X. Li, *Biochem. Syst. Ecol.*, 2006, **34**, 838.
- 82 Y. Zhou, F. Cheng, J. Wu and K. Zou, *J. Nat. Prod.*, 2006, **69**, 1083.
- 83 J. Wu, M.-Y. Li, Z.-H. Xiao and Y. Zhou, *Z. Naturforsch., Teil B*, 2006, **61**, 1447.
- 84 M.-Y. Li, J. Wu, S. Zhang, Q. Xiao and Q.-X. Li, *J. Asian Nat. Prod. Res.*, 2008, **10**, 503.

- 85 I. Kubo, I. Miura and K. Nakanishi, *J. Am. Chem. Soc.*, 1976, **98**, 6704.
- 86 M. Nakane, C. R. Hutchinson, D. Vanengen and J. Clardy, *J. Am. Chem. Soc.*, 1978, **100**, 7079.
- 87 J. K. Whitesell, P. K. S. Wang and D. A. Aguilar, *J. Org. Chem.*, 1983, **48**, 2511.
- 88 J. K. Whitesell and M. A. Minton, *J. Am. Chem. Soc.*, 1986, **108**, 6802.
- 89 M. G. Bercich, R. C. Cambie, A. R. Lal and D. Sidwell, *Aust. J. Chem.*, 1998, **51**, 795.
- 90 F. Y. Chou, K. Hostettmann, I. Kubo, K. Nakanishi and M. Taniguchi, *Heterocycles*, 1977, **7**, 969.
- 91 Y. Zhou, J. Wu and K. Zou, *Chem. Nat. Compd. (Engl. Transl.)*, 2007, **43**, 426.
- 92 M. Z. Zaridah, S. Z. Idid, A. W. Omar and S. Khozirah, *J. Ethnopharmacol.*, 2001, **78**, 79.
- 93 S. J. Uddin, J. A. Shilpi, S. M. S. Alam, M. Alamgir, M. T. Rahman and S. D. Sarker, *J. Ethnopharmacol.*, 2005, **101**, 139.
- 94 R. Rouf, S. J. Uddin, J. A. Shilpi and M. Alamgir, *J. Ethnopharmacol.*, 2007, **109**, 539.
- 95 S. D. Sarker, S. J. Uddin, J. A. Shilpi, R. Rouf, M.-E.-M. Ferdous and L. Nahar, *Fitoterapia*, 2007, **78**, 107.
- 96 O. D. Hensens and K. G. Lewis, *Aust. J. Chem.*, 1966, **19**, 169.
- 97 E. Gomez and O. D. L. Cruz-Giron, *J. Nat. Prod.*, 1989, **52**, 649.
- 98 M.-J. Xu, Z.-W. Deng, M. Li, J. Li, H.-Z. Fu, P. Proksch and W.-H. Lin, *J. Nat. Prod.*, 2004, **67**, 762.
- 99 M.-J. Xu, J.-R. Cui, H.-Z. Fu, P. Proksch and W.-H. Lin, *Planta Med.*, 2005, **71**, 944.
- 100 K. V. Rao and P. K. Bose, *Tetrahedron*, 1962, **18**, 461.
- 101 K. V. Rao and P. K. Bose, *Sci. Cult.*, 1959, **24**, 489.
- 102 K. V. Rao and P. K. Bose, *J. Org. Chem.*, 1962, **27**, 1470.
- 103 K. V. Rao, *Tetrahedron*, 1964, **20**, 973.
- 104 D.-J. Zhang, J. Wu, S. Zhang and J.-S. Huang, *Fitoterapia*, 2005, **76**, 131.
- 105 D.-J. Zhang, J. Wu, S. Zhang, Z.-H. Xiao and J.-S. Huang, *Chin. Tradit. Patent Med.*, 2005, **27**, 1308.
- 106 A. Sarkar and S. N. Ganguly, *Indian J. Chem., Sect. B*, 1978, **16**, 742.
- 107 C. Subrahmanyam, B. V. Rao, R. S. Ward, M. B. Hursthouse and D. E. Hibbs, *Phytochemistry*, 1999, **51**, 83.
- 108 A. W. Salae, S. Chantrapromma, H.-K. Fun and C. Ponglimanont, *Acta Crystallogr., Sect. E*, 2007, **63**, o1899.
- 109 L. Han, X.-S. Huang, I. Sattler, H.-M. Dahse, H.-Z. Fu, W.-H. Lin and S. Grabley, *J. Nat. Prod.*, 2004, **67**, 1620.
- 110 S.-Y. Bao, Z.-W. Deng, H.-Z. Fu, P. Proksch and W.-H. Lin, *Helv. Chim. Acta*, 2005, **88**, 2757.
- 111 L. Han, X.-S. Huang, I. Sattler, H.-M. Dahse, H.-Z. Fu, S. Grabley and W.-H. Lin, *Pharmazie*, 2005, **60**, 705.
- 112 S. Laphookhieo, C. Karalai, C. Ponglimanont and K. Chantrapromma, *J. Nat. Prod.*, 2004, **67**, 886.
- 113 S. Chantrapromma, H.-K. Fun, I. A. Razak, S. Laphookhieo and C. Karalaia, *Acta Crystallogr., Sect. E*, 2003, **59**, o1864.
- 114 P. Chumkaew, S. Kato and K. Chantrapromma, *Chem. Pharm. Bull.*, 2005, **53**, 95.
- 115 C. Karalai and S. Laphookhieo, *Aust. J. Chem.*, 2005, **58**, 556.
- 116 S. Homhual, N. Bunyaphatsara, T. Kondratyuk, A. Herunsalee, W. Chaikul, J. M. Pezzuto, H. H. S. Fong and H.-J. Zhang, *J. Nat. Prod.*, 2006, **69**, 421.
- 117 S. Homhual, H.-J. Zhang, N. Bunyaphatsara, T. P. Kondratyuk, B. D. Santarsiero, A. D. Mesecar, A. Herunsalee, W. Chaikul, J. M. Pezzuto and H. H. S. Fong, *Planta Med.*, 2006, **72**, 255.
- 118 L. Han, X.-S. Huang, I. Sattler, U. Moellmann, H.-Z. Fu, W.-H. Lin and S. Crabley, *Planta Med.*, 2005, **71**, 160.
- 119 L. Han, X.-S. Huang, I. Sattler, H.-Z. Fu, S. Grabley and W.-H. Lin, *J. Asian Nat. Prod. Res.*, 2007, **9**, 327.
- 120 S.-Y. Bao, Y. Ding, Z.-W. Deng, P. Proksch and W.-H. Lin, *Chem. Pharm. Bull.*, 2007, **55**, 1175.
- 121 R. W. Hogg and F. T. Gillan, *Phytochemistry*, 1984, **23**, 93.
- 122 S. Achmadi, G. Syahbirin, E. T. Choong and R. W. Hemingway, *Phytochemistry*, 1994, **35**, 217.
- 123 Y. Zhang, Z.-W. Deng, T.-X. Gao, P. Proksch and W.-H. Lin, *Phytochemistry*, 2005, **66**, 1465.
- 124 H.-K. Fun, C. Pakhathirathien, S. Chantrapromma, C. Karalai and K. Chantrapromma, *Acta Crystallogr., Sect. E*, 2006, **62**, o5539.
- 125 S. Chantrapromma, H.-K. Fun, C. Pakhathirathien, C. Karalai and K. Chantrapromma, *Acta Crystallogr., Sect. E*, 2007, **63**, o459.
- 126 Y. Zhang, Y. Lu, L. Mao, P. Proksch and W.-H. Lin, *Org. Lett.*, 2005, **7**, 3037.
- 127 A. S. R. Anjaneyulu, V. L. Rao, E. Lobkovsky and J. Clardy, *J. Nat. Prod.*, 2002, **65**, 592.
- 128 A. S. R. Anjaneyulu and V. L. Rao, *Phytochemistry*, 2003, **62**, 1207.
- 129 A. S. R. Anjaneyulu and V. L. Rao, *Phytochemistry*, 2002, **60**, 777.
- 130 W. Herz and P. Kulanthaivel, *Phytochemistry*, 1983, **22**, 715.
- 131 C. Ponglimanont and P. Thongdeeying, *Aust. J. Chem.*, 2005, **58**, 615.
- 132 C. Pakhathirathien, S. Chantrapromma, H.-K. Fun, S. Anjum, A. U. Rahman and C. Karala, *Acta Crystallogr., Sect. E*, 2005, **61**, o2942.
- 133 P. Thongdeeying, S. Chantrapromma, H.-K. Fun, S. Anjum, S. Ali and C. Ponglimanont, *Acta Crystallogr., Sect. E*, 2005, **61**, o1861.
- 134 C. Pakhathirathien, C. Karalai, C. Ponglimanont, S. Subhadhirasakul and K. Chantrapromma, *J. Nat. Prod.*, 2005, **68**, 1787.
- 135 L. He, Y.-S. Wang, Q.-J. Wang and Z.-P. Lou, *Pharmazie*, 2005, **60**, 716.
- 136 S. J. Uddin, J. A. Shilpi, J. Barua and R. Rouf, *Fitoterapia*, 2005, **76**, 261.
- 137 A. S. R. Anjaneyulu and V. L. Rao, *Nat. Prod. Lett.*, 2001, **15**, 13.
- 138 A. S. R. Anjaneyulu, V. Anjaneyulu and V. L. Rao, *Indian J. Chem., Sect. B*, 2000, **39**, 803.
- 139 A. S. R. Anjaneyulu, V. Anjaneyulu and V. L. Rao, *J. Asian Nat. Prod. Res.*, 2002, **4**, 53.
- 140 S. Laphookhieo, C. Karalai and C. Ponglimanont, *Chem. Pharm. Bull.*, 2004, **52**, 883.
- 141 B. V. Rao, C. V. Rao, C. Subrahmanyam and M. A. Jairaj, *J. Indian Chem. Soc.*, 2005, **82**, 155.
- 142 A. Richter, B. Thonke and M. Popp, *Phytochemistry*, 1990, **29**, 1785.
- 143 Y.-B. Zeng, W.-L. Mei, Y.-X. Zhao and H.-F. Dai, *Z. Naturforsch., Teil B*, 2008, **63**, 108.
- 144 Y.-B. Zeng, W.-L. Mei, Y.-X. Zhao, L. Zhuang, K. Hong and H.-F. Dai, *Chin. Chem. Lett.*, 2007, **18**, 1509.
- 145 S.-H. Tao, J. Wu, S. Zhang, M.-Y. Li and Q.-X. Li, *Helv. Chim. Acta*, 2007, **90**, 1718.
- 146 S.-H. Tao, J.-Y. Pan, S.-H. Qi, Q.-X. Li and S. Zhang, *Chinese Tradit. Herb. Drugs*, 2007, **38**, 348.
- 147 H.-F. Dai, W.-L. Mei, J. Wu, X. M. Li and B.-G. Wang, *Chin. Pharm. J. (Beijing, China)*, 2006, **41**, 1452.
- 148 M. Parani, M. Lakshmi, P. Senthilkumar, N. Ram and A. Parida, *Theor. Appl. Genet.*, 1998, **97**, 617.
- 149 S. Shi, Y. Zhong, Y.-L. Huang, Y.-Q. Du, X.-Z. Qiu and H.-T. Chang, *Biochem. Syst. Ecol.*, 2002, **30**, 309.
- 150 S. A. M. Abdelgaleil, M. Doe, Y. Morimoto and M. Nakatani, *Phytochemistry*, 2006, **67**, 452.