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Review Article

Chemical constituents and bioactivity of Formosan lauraceous plants

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ABSTRACT

Taiwan is rich in lauraceous plants. A review of 197 references based on the chemical analysis and bioactivity of indigenous lauraceous plants carried out by native scientists from 1963 to 2014 has been compiled. About 303 new compounds and thousands of known compounds comprising alkaloids and non-alkaloids with diverse structures have been isolated or identified from indigenous plants belonging to the 11 lauraceous genera. The volatile components, however, have been excluded from this review. This review provides an overview of the past efforts of Taiwan scientists working on secondary metabolites and their bioactivity in native lauraceous plants. The potential of lauraceous plants worthy of further study is also noted. The contents will be helpful for the chemotaxonomy of Lauraceae and be of value for the development of native Formosan lauraceous plants.

1. Introduction

The Lauraceae family is composed of about 45 genera and 2250 species widely distributed throughout the tropics, especially in Southeast Asia and Brazil, together with a smaller number in temperate regions. There are 11 genera, 50 species, 10 varieties, and three forms of indigenous plants in Taiwan [1]. Studies on the secondary metabolites, excluding the volatile components, of Formosan lauraceous plants were initiated by the late Prof. Tomita Masao of Kyoto University, Japan, and the late Prof. Sheng-Teh Lu of Kaohsiung Medical College, Taiwan. Their studies, starting from 1963, focused on alkaloids. Non-alkaloidal constituents, along with alkaloidal components, were thereafter studied mainly by Prof. Shoei-Sheng Lee (School of Pharmacy, National Taiwan University), Prof. Yueh-Hsiung Kuo (Department of Chinese Pharmaceutical Sciences and Chinese Medicine Resources, China Medical University), Prof. Yang-Chang Wu (Graduate Institute of Integrated Medicine, China Medical University), Prof. Sheng-Yang Wang (Department of Forestry, National Chung-Hsing University), Prof. Tian-Shung Wu (Department of Chemistry, National Cheng Kung University), Prof. Ih-Sheng Chen (School of Pharmacy, Kaohsiung Medical University), Prof. Wen-

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Hsiung Li (Department of Agricultural Chemistry, National Pingtung University of Science and Technology), and Prof. Chung-Yi Chen (Department of Medical Technology, Fooyin University). Starting from 1988, chemical studies have been accompanied by bioactivity assays [2,3]. To date, four reviews and one collective issue on natural-product researches in Taiwan [4–8], from 1945 to 1996, have been published. However, the bioactivity of the isolates was not included. Another review of bioactivity research, published in 2007, covered only 27 Formosan lauraceous plants with 40 references [9].

To provide comprehensive information concerning the past achievements of Taiwan scientists in studying native Formosan lauraceous plants, we endeavored to compile all related isolation and bioactivity papers, following the genus order, with the exception of those concerning the volatile oils. The structures of new compounds from these plants, including those first occurring in nature, are depicted. As for the known compounds, their occurrence is provided in Tables S1–S11. The scientific names of those indigenous plants are adopted according to the Flora of Taiwan [1] and a review [10].

Approximately 303 new nonvolatile compounds (Fig. 1–8) and thousands of known ones (Tables S1–S11) have been characterized from native lauraceous plants of 11 genera. This review, with 197 references, reveals the attempts in this field by Taiwan's natural-product chemists and pharmacologists.

2. Phytochemical studies of Formosan lauraceous plants

2.1. *Beilschmiedia*

There are 200 species of the *Beilschmiedia* genus distributed in tropical regions, with two species, *B. erythrophloia* Hayata and *B. tsangii* Merr., found in Taiwan [1]. The latter species grows only in Hengchun Peninsula. In 2006, investigation of *B. tsangii* has led to the isolation of five new compounds from the stem, including two tetrahydrofuran-type lignans, beilschmins A and B (**1**, **2**), a dihydrofuran-type lignan, beilschmin C (**3**), and two 1-phenylbutylbenzoates, tsangins A and B (**4**, **5**) [11]; three new epoxyfuranoid lignans from the leaves, i.e., 4α,5α-epoxybeilschmins A and B (**6**, **7**) and beilschmin D (**8**) [12]; and 15 new compounds from the root, including 10 endiandric acid analogues [tsangibeilins A–D (**9**–**12**), endiandramides A and B (**13**, **14**), endiandric acids K–M (**15**–**17**), and tricyclotsangibelin (**18**)], three lignans [beilschminols A and B (**19**, **20**) and tsangin C (**21**)], and two sesquiterpenes [(+)-5-hydroxybarbatenal (**22**) and (4*R*,5*R*)-4,5-dihydroxycaryophyll-8(13)-ene (**23**)] [13,14]. The structure of beilschmin C (**3**) was erroneously elucidated [11] and was revised to **6** [12,15].

Investigation of *B. erythrophloia* root has led to the isolation of 11 new compounds, including nine endiandric acid

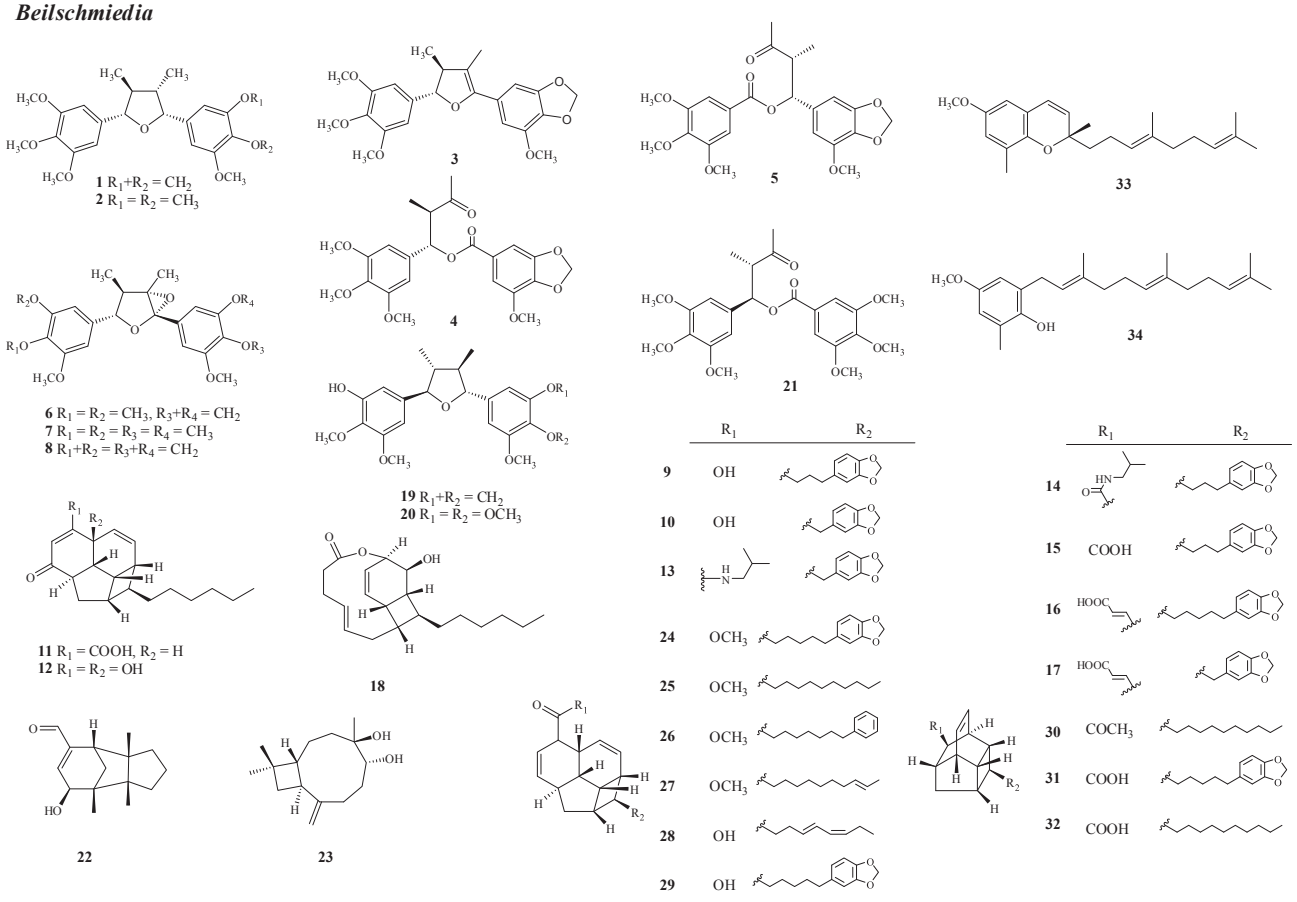

Fig. 1 – Structures of new compounds from *Beilschmiedia* (1–34).

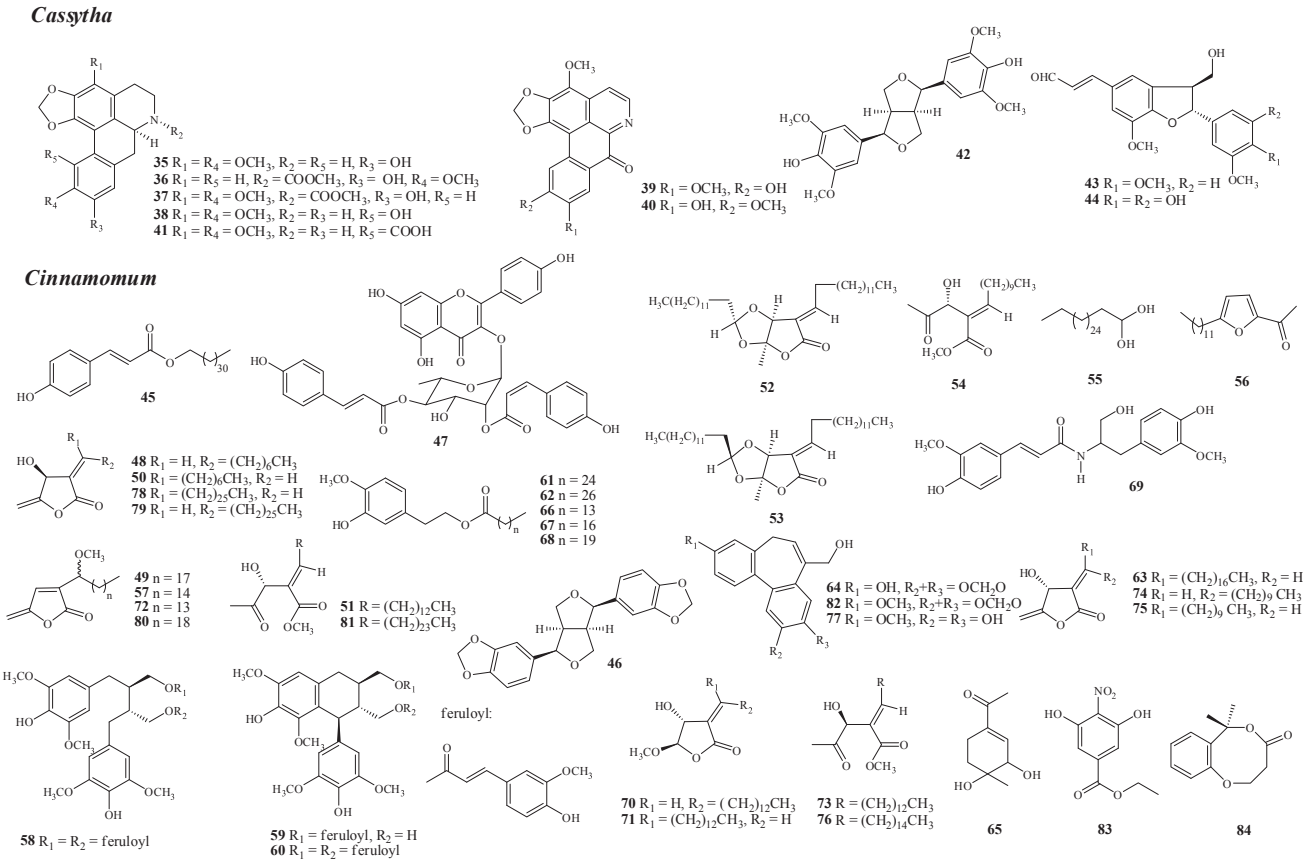

Fig. 2 – Structures of new compounds from *Cassytha* (35–44) and *Cinnamomum* (45–84).

analogues—erythrophloins A–F (**24**–**29**), beilcyclone A (**30**), and endianaric acids I and J (**31**, **32**); one benzopyran, dehydrooligandrol methyl ether (**33**); and one benzenoid, farnesylol (**34**) [16,17].

The occurrence of known isolates in Formosan *Beilschmiedia* is shown in Table S1 [11–14,16,17].

2.2. *Cassytha*

There are about 30 species of *Cassytha* with twining parasitic herbs, mostly distributed in tropical Pacific regions, with one species, *C. filiformis* L., in Taiwan [1]. From the fresh stem of this Formosan species, a new phenolic aporphine alkaloid, (−)-cassyfiline (**35**), was isolated [18]. Later studies on the fresh herb have led to the isolation of nine new compounds, including six aporphines—cathafiline (**36**), cathaformine (**37**) [19], cassyformine (**38**), filiformine (**39**) [20], isofiliformine (**40**), and cassythic acid (**41**) [21]; one lignan, (+)-diasyringaresinol (**42**) [20]; and two neolignans, 4-*O*-methylbalanophonin (**43**) and cassyformin (**44**) [22].

The occurrence of known isolates in Formosan *Cassytha* is shown in Table S2 [19–22].

2.3. *Cinnamomum*

The *Cinnamomum* genus contains about 25 species, distributed over tropical and subtropical eastern Asia, Australia, and the Pacific islands. Eleven indigenous species, one variety, and one form grow in Taiwan [1].

Investigation of Formosan *C. camphora* (L.) J. Presl* has led to the isolation of two new compounds, i.e., dotriaconyl-*trans*-coumarate (**45**) [23] and the lignan, (+)-diasesamin (**46**) [24], from the leaves.

From *C. kotoense* Kanehira & Sasaki, 11 new compounds in total have been isolated, including five from the leaves, i.e., the flavonoid kaempferol 3-*O*-α-L-[2-(*Z*)-*p*-coumaroy-4-(*E*)-*p*-coumaryl]rhamnopyranoside (**47**) [28], three butanolides [kotomolides A and B (**48**, **49**) and isokotomolide A (**50**)], and one secobutanolide, secokotomolide A (**51**) [29]; five from the stem wood, i.e., three butanolides [kotolactones A and B (**52**, **53**) and secokotomolide (**54**)], one long chain alcohol, kotodiol (**55**), and one furan, 2-acetyl-5-dodecylfuran (**56**) [30]; and one from the stem, i.e., the butanolide, kotomolide (**57**) [31].

From *C. osmophloeum* Kanehira, three new lignans, 9,9′-di-*O*-feruloyl-(+)-5,5′-dimethoxy secoisolariciresinol (**58**) (heartwood and root), (7′*S*,8′*R*,8*R*)-lyoniresinol-9-*O*-(*E*)-feruloyl ester (**59**), and (7′*S*,8′*R*,8*R*)-lyoniresinol-9,9′-di-*O*-(*E*)-feruloyl ester (**60**) (heartwood), have been isolated [35].

From *C. reticulatum* Hayata, nine new compounds have been isolated, including four from the leaves, i.e., 2-(4-hydroxy-3-methoxyphenyl)ethyl hexacosanoate (**61**), 2-(4-hydroxy-3-

* The original name of *Cinnamomum camphora* Sieb. was used in reference [23].

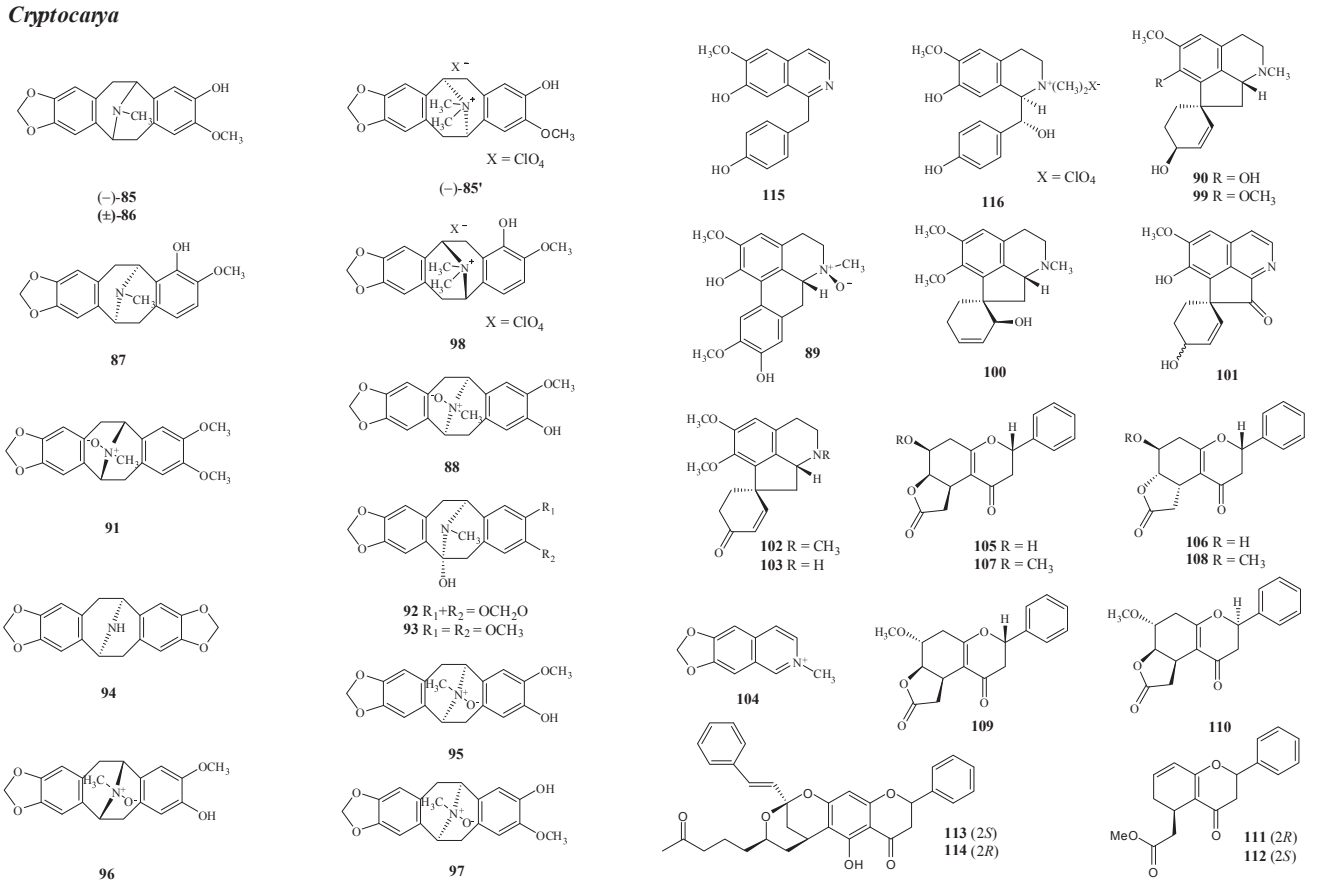

Fig. 3 – Structures of new compounds from *Cryptocarya* (85–116).

methoxyphenyl)ethyl octacosanoate (**62**) [38], isoreticulide (**63**) [39], and reticuol (**64**) [40], and five from the stem, i.e., reticuone (**65**) [41], a mixture of 4-hydroxy-3-methoxyphenethyl pentadecyrate (**66**), 4-hydroxy-3-methoxyphenethyl stearate (**67**), 4-hydroxy-3-methoxyphenethyl heneicosyrate (**68**) [42], and cinnaretamine (**69**) [43].

From *C. subavenium* Miq., eight new compounds have been isolated, including seven butanolides, i.e., subamolides A–C (**70**–**72**), secosubamolide (**73**) [45] (stem), subamolides D and E (**74**, **75**), and secosubamolide A (**76**) [46] (leaves), and one sesquiterpeneoid, subamol (**77**) [47] (root).

From the endemic variety *C. tenuifolium* Sugimoto f. *nervosum* (Meissn.) Hara, seven new compounds have been isolated, including five from the stem, i.e., four butanolides [tenuifolide A (**78**), isotenuifolide A (**79**), tenuifolide B (**80**), and secotenuifolide A (**81**)] and one sesquiterpenoid, tenuifolin (**82**) [51]; and two from the leaves, i.e., ethyl 3,5-dihydroxy-4-nitrobenzoate (**83**) [50] and the benzodioxocinone, 2,3-dihydro-6,6-dimethylbenzo[*b*][1,5]-dioxocin-4(6*H*)-one (**84**) [52].

The occurrence of known isolates in Formosan *Cinnamomum* is shown in Table S3 [23–40,42–51].

2.4. *Cryptocarya*

Approximately 230 species of *Cryptocarya* are distributed throughout tropical and subtropical regions. Three of them, i.e., *C. chinensis* (Hance) Hemsl., *C. concinna* Hance (*C. konishii* Hayata), and *C. elliptica* Merr., grow in Taiwan [1]. The last species is found only on Lanyu Island, and its chemical constituents and biological activity have not yet been investigated. Lu et al found that *C. chinensis* is rich in the pavine bases [53]. A total of 31 new alkaloids have been isolated from this plant, including (−)-caryachine (**85**) and (±)-caryachine (**86**) [53] (leaves, bark, and wood); (−)-caryachine *N*-metho salt (**85′**) [63], neocaryachine (**87**) [54], (−)-isocaryachine-*N*-oxide B (**95**), (+)-isocaryachine-*N*-oxide (**96**), (−)-caryachine-*N*-oxide (**97**), (+)-cryprochine (**99**) [59], and 6,7-methylenedioxy-*N*-methylisoquinoline (**104**) [57] (bark); (+)-eschscholtzidine-*N*-oxide (**91**), (−)-12-hydroxycrychine (**92**), (−)-12-hydroxy-*O*-methylcaryachine (**93**), (−)-*N*-demethylcrychine (**94**), isocryprochine (**100**), prooxocryptochine (**101**), isoamuronine (**102**), and (+)-8,9-dihydrostepharine (**103**) [56] (wood); (−)-isocaryachine-*N*-oxide (**88**), isoboldine-β-*N*-oxide (**89**), 1-hydroxycryprochine (**90**) [55], six new tetrahydroflavanones, [cryptochinones A–F (**105**–**110**)] [60], and four flavanones [cryptoflavanones A–D (**111**–**114**)] [61] (leaves); and neocaryachine *N*-metho perchlorate (**98**) [58] (callus).

Chemical investigation of *C. concinna* has led to the isolation of two new benzylisoquinolines, including the free-base crykonisine (**115**) [65] from the wood and the quaternary (+)-(1*R*,1a*R*)-1a-hydroxymagnocurarine (**116**) [66] from the stem.

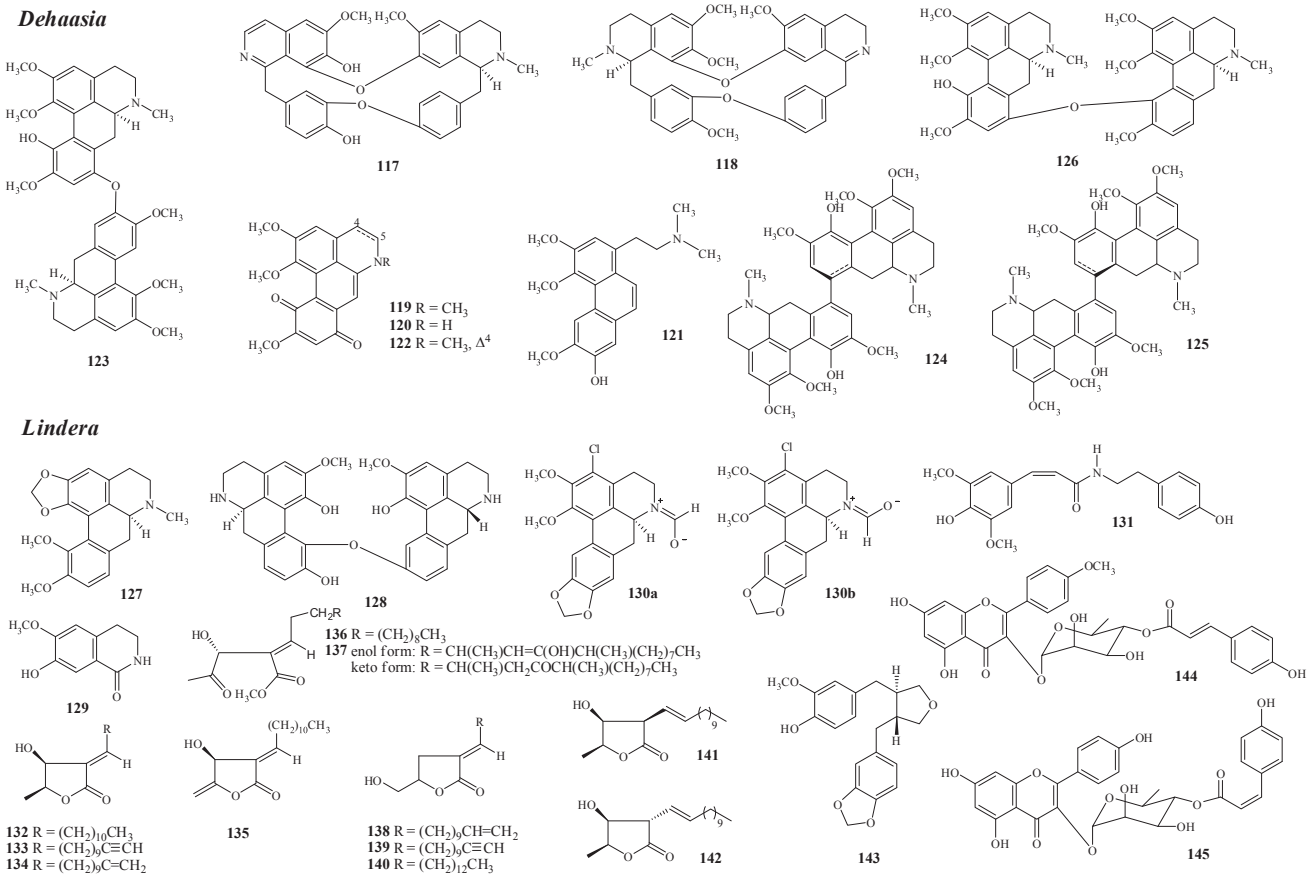

Fig. 4 – Structures of new compounds from *Dehaasia* (117–126) and *Lindera* (127–145).

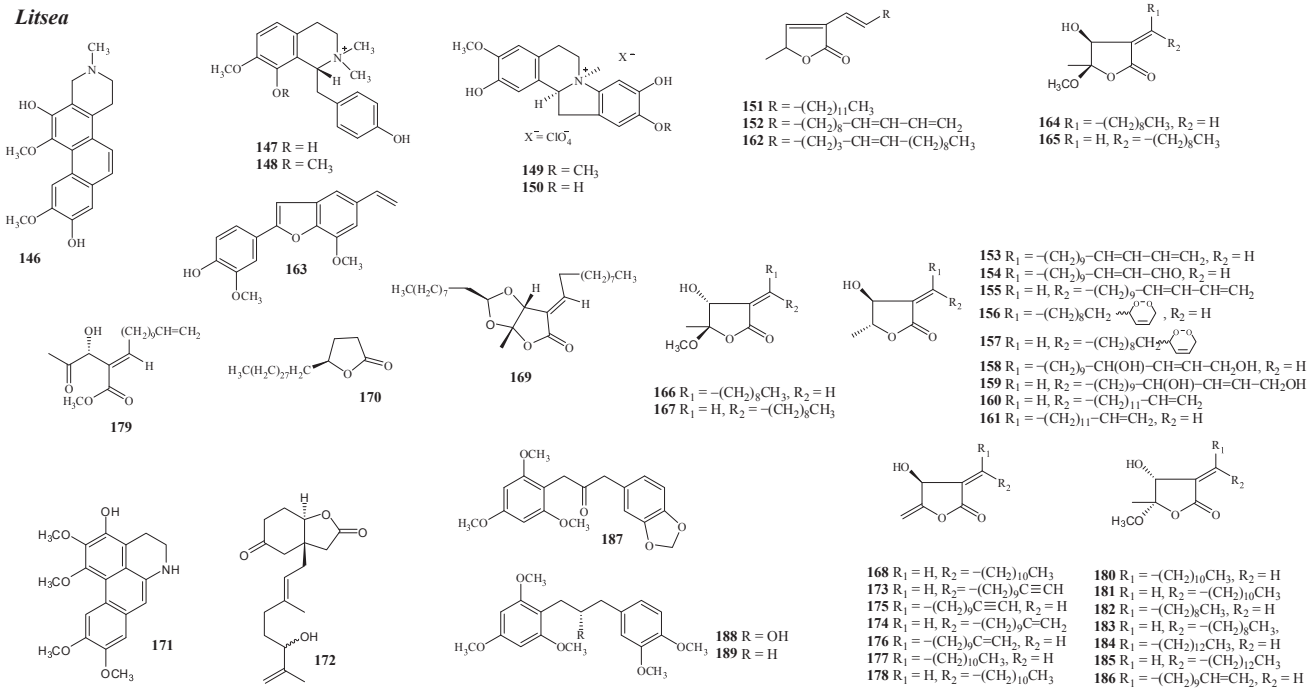

Fig. 5 – Structures of new compounds from *Litsea* (146–189).

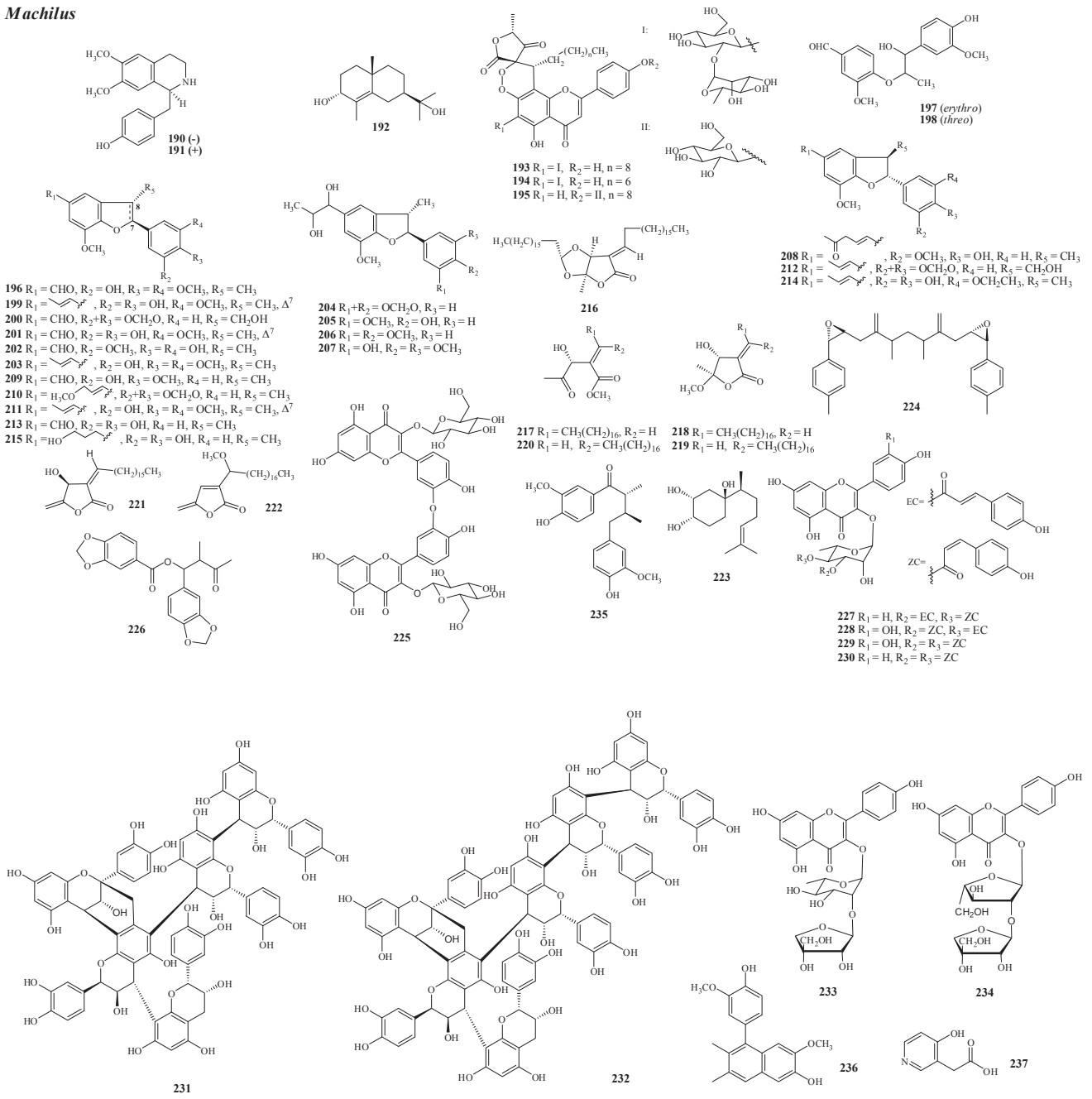

Fig. 6 – Structures of new compounds from *Machilus* (190–237).

C. chinensis contains pavine alkaloids, which have not been detected in *C. concinna*. These two species also contain benzylisoquinoline alkaloids, like those found in *Machilus* plants. These significant differences may provide valuable information regarding chemotaxonomy [53].

The occurrence of known isolates in Formosan *Cryptocarya* is shown in Table S4 [53,55–62,64,65].

2.5. *Dehaasia*

There are about 35 species of *Dehaasia* distributed throughout Indo-Malaysia, but only one species, *D. incrassata* (Jacq.) Kosterm. (*D. triandra* Merr.), grows on Lanyu Island of Taiwan [1]. Ten new alkaloids have been isolated, including two bisbenzylisoquinolines, dehatridine (**117**) (leaves) and dehatrine (**118**) (trunk) [67]; four simple aporphine alkaloids, isocorydione (**119**), norisocorydione (**120**) [68], secoxanthoplanine (**121**), and dehydroisocorydione (**122**) [69]; and four bisaporphines, dehatriphine (**123**) [68], (8,8′-*R*)-bisisocorydine (**124**), (8,8′-*S*)-bisisocorydine (**125**), and 11,8′-*O*-bisisocorydine (**126**) [69] (leaves).

The occurrence of known isolates in Formosan *Dehaasia* is shown in Table S5 [67,68,70–73].

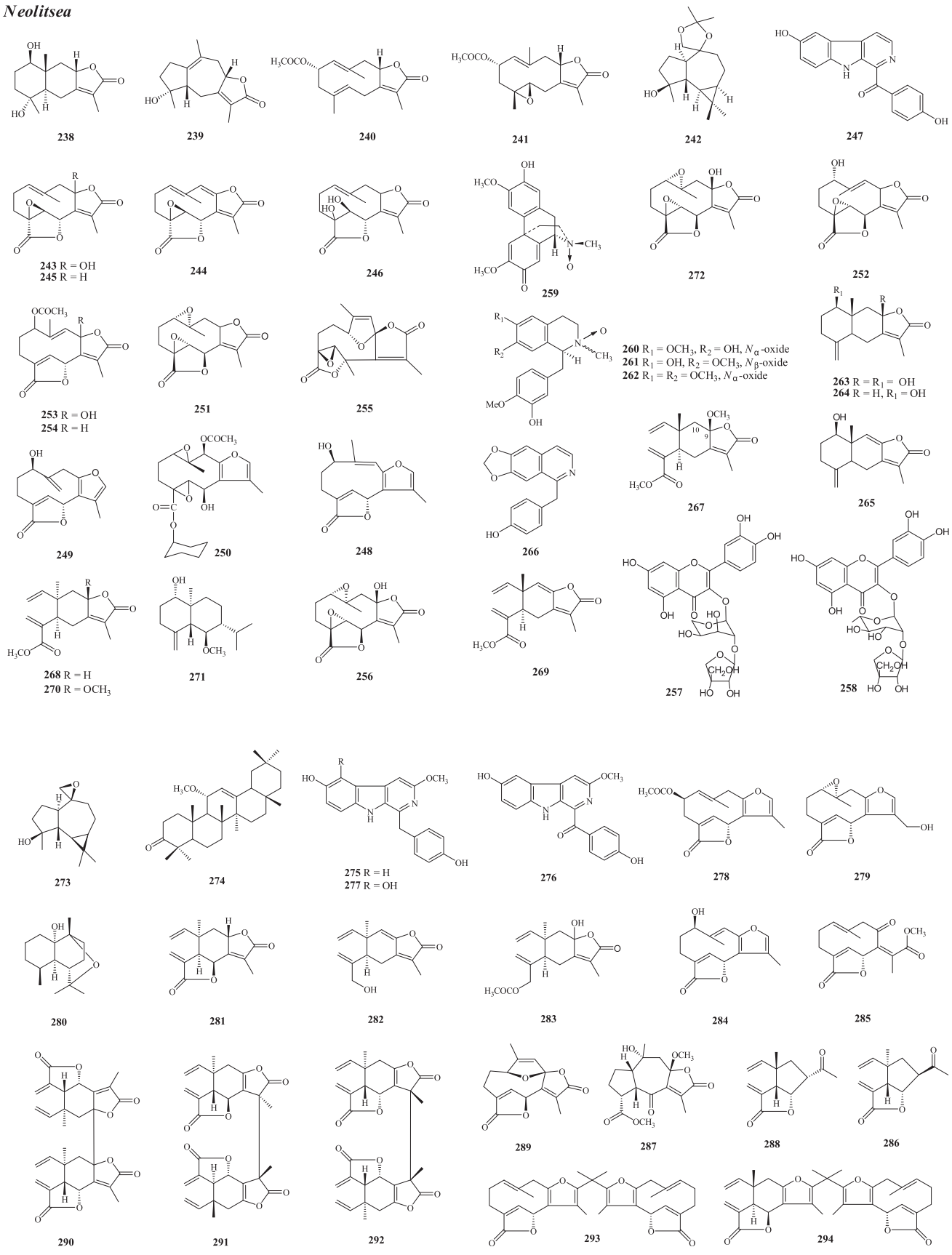

Fig. 7 – Structures of new compounds from *Neolitsea* (238–294).

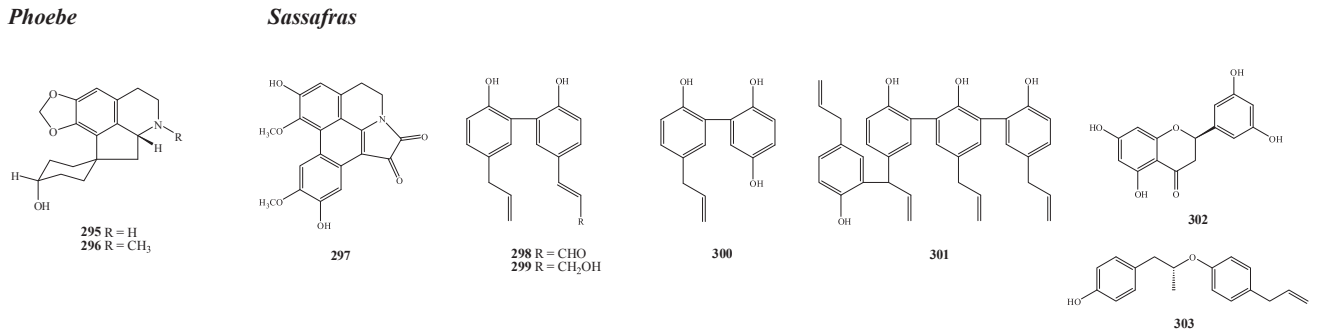

Fig. 8 – Structures of new compounds from *Phoebe* (295–297) and *Sassafras* (298–303).

Among the above new isolates, eight new alkaloids have been isolated from the leaves of *D. incrassata* with the aid of centrifugal partition chromatography [68,69].

2.6. *Lindera*

The *Lindera* genus is made up of about 100 species, widely distributed in the warmer and tropical regions of the northern hemisphere, excluding Africa. Six species grow in Taiwan [1].

The root of *L. aggregata* (Sims) Kosterm. [*L. strychnifolia* (Sieb. & Zucc. ex Miq.) F. Vill.] is traditionally noted for its analgesic activity and its ability to reduce flatulence. Its chemical constituents and bioactivity have been extensively studied. However, the Formosan species has never been examined.

Chemical investigation of Formosan *L. megaphylla* Hemsl. (*L. oldhamii* Hemsl.) has yielded three new alkaloids, including the aporphine *O*-methylbulbocapnine (**127**) [74] from the leaves and trunk, the bisbenzylisoquinoline lindoldhamine (**128**) [75,76], and the isoquinoline northalifoline (**129**) [77] from the pedicels.

From the aerial part of *L. glauca* (Sieb. & Zucc.) Bl., two new alkaloids, the aporphine (+)-3-chloro-*N*-formylnonantenine (**130**) [82] and the amide *N*-*cis*-sinapolyltyramine (**131**) [83], have been isolated.

From the stem bark and wood of *L. communis* Hemsl., six new compounds, including four butanolides [lincomolides A–B (**132**, **133**) [85] (bark) and C–D (**134**, **135**)] and the seco-butanolides secolincomolides A–B (**136**, **137**) [86] in enol and keto tautomers (wood), have been isolated.

The endemic *L. akoensis* has yielded eight new compounds, including five butanolides—majorenolide (**138**), majorynolide (**139**), and majoranolide (**140**) [87], with revised forms via a δ-lactone structure (root), 3β-((*E*)-dodec-l-enyl)-4β-hydroxy-5β-methyldihydrofuran-2-one (**141**) [88] and 3α-((*E*)-dodec-l-enyl)-4β-hydroxy-5β-methyldihydrofuran-2-one (**142**); one lignan, linderinol (**143**); and two flavonoid glycosides, 4′-*O*-methylkaempferol 3-*O*-α-L-(4″-*O*-*E*-*p*-coumaroyl)rhamnoside (**144**) and kaempferol 3-*O*-α-L-(4″-*O*-*Z*-*p*- coumaroyl)rhamnoside (**145**) [89] (aerial part).

The occurrence of known isolates in Formosan *Lindera* is shown in Table S6 [74,77–89].

2.7. *Litsea*

The *Litsea* genus contains approximately 400 *species*, 12 of which are distributed in Taiwan [1].

From *L. cubeba* (Lour.) Pers., five new alkaloids have been isolated. They are the phenanthrene alkaloid litebamine (**146**) [90] (wood), the quaternary benzylisoquinolines (–)-oblongine (**147**) and (–)-8-*O*-methyloblongine (**148**) [66] (stem), and the dibenzopyrrocoline alkaloids (–)-litcubine (**149**) and (–)-litcubinine (**150**) [91] (root).

From the stem bark of endemic *L. akoensis* Hayata, 12 new butanolides have been isolated, i.e., akolactones A and B (**151**, **152**), litseakolides A and B (**153**, **154**) [96], litseakolide C (**155**) [97], litseadioxanins A and B (**156**, **157**), litseatrinolides A and B (**158**, **159**), and litseakolides D_1 and D_2 (**160**, **161**) [98]. A mixture of akolactones A and C (**151**, **162**) [99] has been isolated from the leaves.

Investigation of the leaves of *L. acutivena* Hayata [*Actinodaphne acutivena* (Hay.) Nakai] has led to the isolation of eight new compounds, the norneolignan dehydroxymethylailanthoidol (**163**); the butanolides, litseakolides D–G (**164**–**167**), isolincomolide D (**168**) [102], and acutilactone (**169**); and the lactone, 4-nonacosyl-dihydrofuran-2-one (**170**) [103].

Two new compounds, the aporphine dehydrothalbaicaline (**171**) and the lactonic compound (**172**) [107], have been isolated from the stem of *L. coreana* Levl. [*L. lancifolia* (Roxb. ex Nees) Benth. et Hook. ex F. Vill.].

From the leaves of *L. lii* Chang var. *nunkao-tahangesis* (Liao) Liao, seven new butanolides have been isolated, i.e., litsealiicolides A and B (**173**, **174**), isolitsealiicolides A–C (**175**–**177**) [110], litsealiicolide C (**178**), and secoisolitsealiicolide B (**179**) [111].

From the endemic *L. hypophaea* Hayata (*Actinodaphne pedicellata* Hayata; *L. kostermansii* Chang), 10 new compounds have been isolated, including seven butanolides [litseakolides H–N (**180**–**186**)] and three biarylpropanoids [hypophaone (**187**), hypophaol (**188**), and hypohane (**189**)] [112].

The occurrence of known isolates in Formosan *Litsea* is shown in Table S7 [92–101,103–112].

Of these isolates, laurolitsine is the most abundant and can be used as starting material for preparing bioactive compounds. Among the new isolates, the dibenzpyrrocolines **149** and **150** were isolated with the aid of centrifugal partition chromatography and were semisynthesized [91].

Table 1 – Bioactivity of compounds isolated from Formosan lauraceous plants.

Plant [a]	Part	Compound	Bioactivity	Reference
Beilschmiedia erythrophloia	root	**26** and suberosol B	antituberculosis	[16]
B. tsangii	root	**11**, **12**, and **18**	anti-inflammatory	[13, 14]
	stem	**1**, **2**, **4**–**6**, 2,6,11-trimethyldodeca-2,6,10-triene, α-tocopheryl quinone, and α-tocospiro B	cytotoxicity	[11]
	leaves	**1** and **2**	antituberculosis	[12]
Cassytha filiformis	whole herb	**41**, 1,2-methylenedioxy-3,10,11-trimethoxyaporphine, (–)-*O*-methylflavinatine, (–)-salutaridine, isohamnetin-3-*O*-β-glucoside, isohamnetin-3-*O*-rutinoside, actinodaphnine, and *N*-methylactinodaphnine	vasorelaxing activity	[21, 165]
		actinodaphnine	antiplatelet	[165]
		ocoteine	α_1-adrenoceptor antagonist	[166]
Cinnamomum insularimontanum	root	actinodaphnine	cytotoxicity	[25]
C. kotoense	stem wood	isoobtusilactone A and lincomolide B	antituberculosis	[30]
	leaves	**47** and kaempferol 3-*O*-α-L-[2,4- di-(*E*)-*p*-coumaroy-4-(*E*)-*p*-coumaryl]-rhamnopyranoside	anti-inflammatory	[28]
		48, **49**, and **54**	cytotoxicity	[29, 167–170]
		49	antioxidant	[171]
	leaves	isoobtusilactone A	cytotoxicity	[172–175]
C. osmophloeum	leaves	kaempferitrin, kaempferol 3-*O*-β-D-apiofuranosyl-(1→2)-α-L-arabinofuranosyl-7-*O*-α-L-rhamnopyranoside, and kaempferol 3-*O*-β-D- apiofuranosy-(1→4)-α-L- rhamnopyranosyl-7-*O*-α-L- rhamnopyranoside	anti-inflammatory	[37]
C. subavenium	stem	**71** and linderanolide B	anti-tyrosinase	[176]
		71–**74**	cytotoxicity	[45, 177, 178]
	leaves	**75** and **76**	cytotoxicity	[46, 179]
Cryptocarya chinensis	wood	(–)-antofine and dehydroantofine	cytotoxicity	[64]
	leaves	cryptocaryone and pinocembrin	antituberculosis	[64]
		cryptocaryanone A and infectocaryone	cytotoxicity	[60]
C. concinna	root	cryptocaryone	cytotoxicity	[180]
Lindera akoensis	root	litsenolide B, litsenolide C, litsenolide C_2, and litsenolide A	antituberculosis	[87]
	aerial	(3*Z*,4α,5β)-3-(dodec-11-enylidene)-4-hydroxy-5-methylbutalactone, (3*E*,4α,5β)-3-(dodec-11-enylidene)-4-hydroxy-5-methylbutalactone, 3-epilitsenolide D, and 3-epilitsenolide D_2	anti-inflammatory	[88, 89]
L. communis	stem bark	**132** and **133**	cytotoxicity	[85]
	stem wood	**134** and **135**	cytotoxicity	[86]
L. erythrocarpa	fruits	lucidone	anti-HCV	[181]
			anti-inflammatory	[84,182]
			anti-tyrosinase	[183]
			hepatoprotective	[184]
			nutraceutical	[185]
L. megaphylla	root	dicentrine	α_1-adrenoceptor antagonist	[186–189]
			antiarrhythmic	[190]
			antiplatelet	[81]
			antitumor	[191]
	flower buds and peduncles	**127** and *N*-methylnandigerine	antiplatelet	[80,192]
Litsea acutivena	leaves	**164**–**168**	cytotoxicity	[102]

(*continued on next page*)

Table 1 – (continued)

Plant [a]	Part	Compound	Bioactivity	Reference
L. akoensis	stem bark	**151**, **152**, **153**, **155**, litsenolide B, litsenolide B_2, litsenolide C_1, litsenolide C_2, and hamabiwalactone A	cytotoxicity	[96,98, 99]
	leaves	a mixture of **151** and **162**	cytotoxicity	[97]
L. cubeba	tree bark	laurotetanine N-methyllaurotetanine	vasorelaxing action antiplatelet	[192]
L. hypophaea	root	**184** and *N-trans*-feruloylmethoxytyramine	antituberculosis	[112]
L. lii var. *nunkao-tahangensis*	leaves	**173**, **174**	cytotoxicity	[111]
Machilus obovatifolia	leaves	**196**–**201**, licarin A, machilin C diacetate, obovaten diacetate, obovatifol, obovatifol diacetate, and perseal E diacetate	cytotoxicity	[119–121]
	stem wood	**211**–**215** and linderanolide E	cytotoxicity	[122,125]
M. philippinensis	root	**235**	antiplatelet, vasorelaxing effect, antioxidative, and antiarrhythmic action	[129]
M. zuihoensis	stem wood	**217**, **222**, and β-bisabolol	cytotoxicity	[125, 126]
	leaves	**225**, quercetin, and ethyl caffeate	anti-inflammatory and superoxide anion scavenging effects	[127]
Neolitsea acuminatissima	stem bark	**262**, **263**, and 2,6-dimethoxy-*p*-benzoquinone	cytotoxicity	[149]
N. daibuensis	root	**273**, isolinderalactone, 7-*O*-methylnaringenin, and prunetin	anti-inflammatory	[153]
N. hiiranensis	leaves	**266** and **268**	anti-inflammatory	[151]
N. konishii	bark	thaliporphine	vasoconstriction cardiotonic	[193] [194,195]
N. parvigemma	stem	deacetylzeylanine, deacetylzeylanine acetate, linderalactone, parvigemone, parvigemonol, zeylanicine, zeylanidine, and zeylanidine-B	antiplatelet	[196]
	stem	linderalactone and pseudoneolinderane	anti-inflammatory	[197]
N. villosa	root	isolinderalactone	cytotoxicity	[144]
Sassafras randaiense	root	magnolol	antituberculosis	[163]

HCV = hepatitis C virus.
[a] Synonyms of the plants are shown in the text of this review.

2.8. *Machilus*

The *Machilus* genus has about 100 species, mainly distributed over East Asia. Of these, six species, including two endemic species and two endemic varieties, grow in Taiwan [1].

From the wood of *M. japonica* Sieb. et Zucc. var. *kusanoi* (Hay.) Liao (*M. kusanoi* Hayata), a new benzylisoquinoline, L-(−)-*N*-norarmepavine (**190**) [113], has been isolated.

From *M. japonica* var. *japonica* Sieb. et Zucc. (*M. pseudolongifolia* Hayata; *Persea japonica* Sieb. et Zucc.), five new compounds have been yielded, including a benzylisoquinoline, *dl*-norarmepavine (**191**) [115] (root wood); a sesquiterpene, machikusanol (**192**) [116] (wood); and three flavone-butanolide adducts, apigenosylides A–C (**193**–**195**) [117] (leaves).

From *M. obovatifolia* (Hay.) Kanehira et Sasaki (*Persea obovatifolia* (Hay.) Kostermans), 20 new neolignans have been isolated. They are obovatinal (**196**), perseals A and B (**197**, **198**) [118], obovaten (**199**), and perseals C–E (**200**–**202**) [119, 120] from the leaves; machlusols A–F (**203**–**208**) [121], and perseal F (**209**) [122] from the stem wood; and machifolins A–F (**210**–**215**) [123] from the stem bark.

From *M. zuihoensis* Hay., 10 new compounds have been isolated, including seven butanolides [machilactone (**216**), methyl (2*E*)-2-(1-hydroxy-2-oxopropyl)eicos-2-enoate (**217**), machicolides A and B (**218**, **219**) [125], secomahubanolide (**220**), zuihoenalide (**221**), and 3-(1-methoxyoctadecyl)-5-methylene-5-*H*-furan-2-one (**222**)] [126], the sesquiterpene, 3,4-dihydroxy-β-bisabolol (**223**) [125], and the steryl epoxide, machillene (**224**) [126] from the stem wood and the biflavonol glycoside, 3′,3′-*O*-bisquercetin-3-*O*-β-D-glucopyranoside (**225**) [127] from the leaves.

From the leaves of the endemic variety of *M. zuihoensis* Hay. var. *mushaensis* (Lu) Y. C. Liu, one new compound, machilolin A (**226**) [128], has been isolated.

From *M. philippinensis* Merr. [*M. arisanensis* Hayata; *M. acuminatissima* (Hay.) Kanehira, *Cinnamomum philippinense* (Merr.) Chang], 11 new compounds have been isolated, including four acyl flavonol monorhamnosides [kaempferol-3-*O*-α-L-(3″-*O*-

E,4″-O-Z-di-p-coumaroyl)rhamnopyranoside (**227**), quercetin-3-O-α-L-(3″-O-Z,4″-O-E-di-p-coumaroyl)rhamnopyranoside (**228**), quercetin-3-O-α-L-(3″,4″-di-O-Z-p-coumaroyl)rhamnopyranoside (**229**), and kaempferol-3-O-α-L-(3″,4″-di-O-Z-p-coumaroyl)rhamnopyranoside (**230**)] [130]; two proanthocyanidins, machiphilitannins A (**231**) and B (**232**) [131]; and two flavonoid glycosides, kaempferol-3-O-(2-O-β-D-apiofuranosyl)-α-L-rhamnopyranoside (**233**) and kaempferol-3-O-(2-O-β-D-apiofuranosyl)-α-L-arabinofuranoside (**234**) [132] from the leaves; and a lignan, cinnamophilin (**235**) [129], a naphthalenol, cinnamophilin A (**236**) [133], and a pyridine derivative, 2-(4′-hydroxypyridin-3′-yl)acetic acid (**237**) [134] from the root.

The occurrence of known isolates in Formosan *Machilus* is shown in Table S8 [114–117,119,120,122–132,134–136].

Among the above new isolates, three acylated monorhamnosylflavonoids (**229**–**231**) have been characterized from the leaves of *M. philippinensis* via application of the high-performance liquid chromatography–solid-phase extraction–nuclear magnetic resonance (HPLC–SPE–NMR) hyphenated technique [130].

2.9. *Neolitsea*

There are about 85 species of *Neolitsea* distributed over the Asiatic mainland and Malaysia, with nine species, two varieties, and one form growing in Taiwan [1].

From *N. buisanensis* Yamamoto & Kamikoti f. *buisanensis* (Hay.) Hatus, nine new sesquiterpenoids, i.e., neobuisanolides A–E (**238**–**242**) (leaves) [137] and linderanines A–D (**243**–**246**) (root) [138], and one β-carboline, neolitcarboline A (**247**) (leaves) [137], have been isolated.

From *N. parvigemma* (Hay.) Kaneh. & Sasaki, three new furanosesquiterpenoid lactones have been isolated. They are deacetylzeylanidine (**248**) [140] from the root and parvigemone (**249**) and neolitrane (**250**) [141] from the stem.

From the leaves of *N. acutotrinervia* (Hay.) Kaneh. & Sasaki, four new germacranediolides have been isolated. They are acutotrine (**251**), acutotrinone (**252**), autotrinol (**253**), and zeylaninone (**254**) [143].

From the stem wood of *N. villosa* (Bl.) Merr., two new sesquiteripenoids have been isolated, i.e., pseudoneoliacine (**255**) and villosine (**256**) [144].

From the leaves of *N. konishii* (Hay.) Kaneh. & Sasaki, two new flavonol diosides, quercetin 3-O-(2-O-β-D-apiofuranosyl)-α-arabinopyranoside (**257**) and quercetin 3-O-(2-O-β-D-apiofuranosyl)-α-L-rhamnopyranoside (**258**) [104], have been isolated.

From the leaves of *N. sericea* (Bl.) Koidz. var. *aurata* (Hay.) Hatus. [*N. aurata* (Hay.) Koidz.], four new isoquinolines—9*S*,17*S*-pallidine N_{α}-oxide (**259**), 1*S*,2*S*-reticuline N_{α}-oxide (**260**), 6*R*,6a*S*-boldine N_{β}-oxide (**261**), and 6*S*,6a*S*-*N*-methyllaurotetanine N_{α}-oxide (**262**) [147]—have been characterized via the application of HPLC–SPE–NMR.

From the stem bark of *N. acuminatissima* (Hay.) Kaneh. & Sasaki, four new compounds, including three eudeomanolide sesquiterpenoids, neolitacumones A–C (**263**–**265**), and the benzylisoquinoline neolitacumonine (**266**) [149], have been isolated.

Chemical investigation of the leaves of *N. hiiranensis* Liu & Liao has led to the isolation of eight new compounds, including seven sesquiterpenoids [hiiranlactones A–D (**267**–**270**), (−)-*ent*-6α-methoxyeudesm-4(15)-en-1β-ol (**271**), (+)-villosine (**272**), and hiiranepoxide (**273**)] and one triterpenoid, hiiranterpenone (**274**) [151].

From various parts of *N. daibuensis* Kamik., 20 new compounds have been isolated, including three β-carboline alkaloids [daibucarbolines A–C (**275**–**277**)] and three sesquiterpenoids [daibulactones A (**278**) and B (**279**) and daibuoxide (**280**)] [153] (root) and elemanodaibulactones A–C (**281**–**283**), daibulactones C–G (**284**–**288**), daibuguaianin (**289**), and five dimeric sesquiterpenoids [daibudilactones A–E (**290**–**294**)] [154] (stem).

The occurrence of known isolates in Formosan *Neolitsea* is shown in Table S9. [137–155]

2.10. *Phoebe*

There are about 94 species of the *Phoebe* genus in Indo-Malaysia, Central America, China, and Taiwan. The latter has only one species, *P. formosana* (Hay.) Hay. [1]. Chemical investigation has yielded three new alkaloids, including two hexahydroproaporphines, lauformine (**295**) and *N*-methyllauformine (**296**) [156], from its bark and a neutral aporphine alkaloid, laurodionine (**297**) [157], from its wood.

The occurrence of known isolates in Formosan *Phoebe* is shown in Table S10 [158–160].

2.11. *Sassafras*

There are three species of the *Sassafras* genus, distributed in eastern North America, eastern China, and Taiwan [1]. Chemical investigation of various parts of the endemic *Sassafras randaiense* (Hay.) Rehder has yielded six new compounds, including the biphenyls randainal (**298**), randaiol (**299**) [161] (heartwood), and randainol (**300**) [162] (root); the dimeric neolignan (+)-sassarandailin (**301**); the flavonoid *R*-(+)-5-7-3′5′-tetrahydroxyflavanone (**302**) [163] (root); and the lignan sassarandainol (**303**) (stem).

The occurrence of known isolates in Formosan *Sassafras* is shown in Table S11 [161–163].

3. Bioactivity of Formosan lauraceous plants

The bioactivity of isolates from Formosan lauraceous plants is shown in Table 1.

4. Conclusion

Several aspects are observed and described as follows.

1. Chemical investigations of 48 species and 7 varieties belonging to 11 genera of indigenous lauraceous plants are summarized in this review.
2. Of the Formosan *Machilus*, *M. japonica* [113,114], *M. obovatifolia* [124], *M. thunbergii* [124], and *M. zuihoensis* [124] have been found to contain L-(−)-*N*-norarmepavine and *dl*-*N*-

norarmepavine. *M. philippinensis* [1], formerly named as *M. acuminatissima* [65] and *M. arisanensis* [124], also contains these benzylisoquinolines. Furthermore, *Nothaphoebe konishii* [136] contains L-(−)-*N*-norarmepavine. Due to this chemical evidence, Lu [124] indicated in 1965 that the occurrence of these benzylisoquinolines reveals a close relationship among Formosan *Machilus* plants. *N. konishii* was renamed as *M. konishii* in 1996 due to its morphological character [1,10,164].

3. The occurrence of β-carboline alkaloids is unique in Formosan *N. buisanensis* [137] and *N. daibusensis* [153].
4. The existence of endiandric acid analogues from the root was first found in Formosan *Beilschmiedia* plants [16,17].
5. The leaves, wood, and bark of Formosan *C. chinensis* are rich in pavine alkaloids, which are not found in *C. concinna* or other lauraceous plants.
6. The existence of a new phenanthrene alkaloid, litebamine [90], and two new dibenzopyrrocoline alkaloids, (−)-litcubine and (−)-litcubinine [91], in Formosan *L. cubeba* is also striking in *Litsea* species.
7. *D. incrassata* is rich in bisbenzylisoquinolines and bisaporphines, exhibiting a different status in Lauraceae chemistry.
8. Apigenosylides A–C with novel flavone-butanolide adduct skeletons have been found in *M. japonica* var. *kusanoi*.
9. Twenty-eight taxa of Formosan lauraceous plants have been identified by their bioactivity. One species may show one or several kinds of bioactivity. Past studies have revealed cytotoxicity, anti-inflammatory, cardiovascular, and antituberculosis activity as the main interests. Not every part of each Formosan lauraceous plant has been screened exhaustively in different assay platforms. According to our recent investigation on the bioactivity of Formosan lauraceous plants, the constituents exhibiting inhibitory activity against inflammation, oxidation, and hyperglycemia and anti-eβG-glucuronidase activity are worthy of further examination. The discovery of new secondary metabolites and new bioactivity is expected to make great progress in the near future.

Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.jfda.2015.10.008.

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