Review Article

Chemical constituents and bioactivity of Formosan lauraceous plants

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\textbf{A B S T R A C T}

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.

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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 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-
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, 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., 4a,5a-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 tricyclotsangibeilin (18)], three lignans [beilschminols A and B (19, 20) and tsangin C (21)], and two sesquiterpenes [(+)-5-hydroxybarbatenal (22) and (4R,5R,8)-4,5-dihydroxyxyrylcarphyl-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...
analogs—erythrophaols A–F (24–29), beilcyclone A (30), and endianaric acids I and J (31, 32); one benzopyran, dehydrogoladrol methyl ether (33); and one benzenoid, farney- 
lol (34) [16,17].

The occurrence of known isolates in Formosan Beilschmie-
dia 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—cathafileine (36), cathaforemine (37) [19], cassymorine (38), filiformine (39) [20], isofiliformine (40), and cassymytic acid (41) [21]; one lignan, (−)-diaseamin (42) [20]; and two neolignans, 4-O-methylbalanophonin (43) and cassymyforn (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., dotriacyl-trans-
coumarate (45) [23] and the lignan, (−)-diaseamin (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]hamnopyranoside (47) [28], three butanolides [kotolactones A and B (48, 49) and isokotolactone A (50)], and one secobutanolide, secoisolariciresinol A (51) [29]; five from the stem wood, i.e., three butanolides [kotolactones A and B (52, 53) and secoisolariciresinol (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) (heart- 
wood and root), (7′S,8′R,8R)-lyoniresinol-9-O-(E)-feruloyl ester (59), and (7′S,8′R,8R)-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-
ketophenyl)ethyl hexacosanoate (61), 2-(4-hydroxy-3-
Cryptocarya

Three of them, i.e., C. chinesis (Hance) Hemsl., C. concinna Hance (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. chinesis 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), (−)-cyprochine (99) [59], and 6,7-methylenedioxy-N-methylisoquinoline (104) [57] (bark); (+)-eschscholtzidine-N-oxide (91), (−)-12-hydroxyxycrine (92), (−)-12-hydroxy-O-methylxycrine (93), (−)-N-demethylxycrine (94), isocryptochrome (100), prooxycryptochrome (101), isoamuronine (102), and (+)-8,9-dihydrostepharine (103) [56] (wood); (−)-isocaryachine-N-oxide (88), isoboldin-β-N-oxide (89), 1-hydroxyxycrone (90) [55], six new tetrahydroflavanones, [cryptochinones A–F (105–110)] [60], and four flavanones [cryptoflavonanes A–D (111–114)] [61] (leaves); and neo-caryachine 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 (−)-(1R,1aR)-1a-hydroxymagnocurarine (116) [66] from the stem.

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

methylxophenyl)ethyl octacosanoate (62) [38], isoreticulide (63) [39], and reticulol (64) [40], and five from the stem, i.e., reticucone (65) [41], a mixture of 4-hydroxy-3-methoxyphenethyl penta-decyrate (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], subamolides D and E (74, 75), and secosubamolide A (76) [46] (leaves), and one sesquiterpenoid, subamol (77) [47] (root).

From the endemic variety C. tenufolium Sugimoto f. nervosum (Meissn.) Hara, seven new compounds have been isolated, including five from the stem, i.e., four butanolides (tenufolide A (78), isotenufolide A (79), tenufolide B (80), and sectenufolide A (81)) and one sesquiterpenoid, tenufolin (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(6H)-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,
Fig. 4 – Structures of new compounds from Dehaasia (117–126) and Lindera (127–145).

Fig. 5 – Structures of new compounds from Litsea (146–189).
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 bis-benzylisoquinolines, dehatridine (117) (leaves) and dehatrine (118) (trunk) [67]; four simple aporphine alkaloids, iso-corydione (119), norisocorydione (120) [68], secocanthoplanine (121), and dehydroisocorydione (122) [69]; and four bisaporphines, dehatriline (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).
Among the above new isolates, eight new alkaloids have been isolated from the leaves of *D. incisa* 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 isoinoline 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-sinapolyltryramine (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 secobutanolides secoisolincomolides A–B (136, 137) [86] in enol and keto tautomers (wood), have been isolated.

The endemic *L. koensis* 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-1-enyl)-4β-hydroxy-8β-methylidihydrofuran-2-one (141) [88] and 3α-((E)-dodec-1-enyl)-4β-hydroxy-8β-methylidihydrofuran-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 56 [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-methylbiongine (148) [66] (stem), and the dibenzopyrrocoline alkaloids (–)-lucubine (149) and (–)-lucubine (150) [91] (root).

From the stem bark of endemic *L. akouensis* Hayata, 12 new butanolides have been isolated, i.e., akolactones A and B (151, 152), litseakolides A and B (153, 154) [96], litseakolid C (155) [97], litseadioxaninas A and B (156, 157), litseatinolides A and B (158, 159), and litseakolides D1 and D2 (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 acutivnea* (Hay.) Nakai] has led to the isolation of eight new compounds, the normeolinigan dehydroxy-plantarlanthoid (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 spirophene dehydrothalaactaline (171) and the lactonic compound (172) [107], have been isolated from the stem of *L. coreana* Levl. [ *L. lancifolia* (Roxb. ex Nees) Benth. ex Hook. ex F. Vill.].

From the leaves of *L. lii* Chang var. *nunkao-tahangesis* (Liao Liao), seven new butanolides have been isolated, i.e., litsealilicolides A and B (173, 174), isolitsealicolides A–C (175–177) [110], litsealicolide C (178), and secosiolitsealicolide 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 [hypophaene (187), hypophaenol (188), and hypohane (189)] [112].

The occurrence of known isolates in Formosan *Litsea* is shown in Table 57 [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 dibenzopyrrocolines 149 and 150 were isolated with the aid of centrifugal partition chromatography and were semisynthesized [91].
| 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-trimethyldec-2,6,10-triene, α-tocopheryl quinone, and α-tocospiro B | cytotoxicity | [11] |
| Cassytha filiformis | leaves | 1 and 2 | antituberculosis | [12] |
|          | 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] |
| Cinnamomum insularimontanum | root | actinodaphnine | antiplatelet | [165] |
| C. kotoense | stem wood | isoobutulisactone 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] |
|          | leaves | 48, 49, and 54 | cytotoxicity | [29, 167–170] |
|          | leaves | 49 | antioxidant | [171] |
| C. osmophloeum | leaves | isoobutulisactone A | cytotoxicity | [172–175] |
|          | leaves | kaempferitin, kaempferol 3-O-β-D-apiofuranosyl-(1→2)-α-L-arabinofuranosyl-7-O-α-L-rhamnopyranoside, and kaempferol 3-O-β-D-apiofuranosyl-(1→4)-α-L-rhamnopyranosyl-7-O-α-L-rhamnopyranoside | anti-inflammatory | [37] |
| C. subavenium | stem | 71 and linderanolide B | anti-tyrosinase | [176] |
|          | leaves | 71–74 | cytotoxicity | [45, 177, 178] |
| Cryptocarya chinensis | wood | 75 and 76 | cytotoxicity | [46, 179] |
|          | leaves | (−)-antofine and dehydroantofine | cytotoxicity | [64] |
|          | | cryptocaryone and pinocembrin | antituberculosis | [64] |
| C. concinna | root | cryptocaryone | cytotoxicity | [60] |
| Linder akoensis | root | lithsenide B, lithsenide C, lithsenide C2, and lithsenide A | cytotoxicity | [180] |
|          | aerial | (3Z,4α,5β)-3-(dodec-11-enylidene)-4-hydroxy-5-methylbutalactone, (3E,4α,5β)-3-(dodec-11-enylidene)-4-hydroxy-5-methylbutalactone, 3-epilithsenide D, and 3-epilithsenide D2 | anti-inflammatory | [88, 89] |
| L. communis | stem bark | 132 and 133 | cytotoxicity | [85] |
|          | stem wood | 134 and 135 | cytotoxicity | [86] |
| L. erythracarpa | fruits | lucidone | anti-HCV | [181] |
|          | | | anti-inflammatory | [84, 182] |
|          | | | anti-tyrosinase | [183] |
|          | | | hepatoprotective | [184] |
|          | | | nutraceutical | [185] |
|           | | | α1-adrenoceptor antagonist | [186–189] |
|           | | | antiarrhythmic | [190] |
|           | | | antiplatelet | [81] |
|           | | | antitumor | [191] |
|           | | | antiplatelet | [80, 192] |
| L. megaphylla | flower buds | 127 and N-methylmandigerine | cytotoxicity | [102] |
|          | and peduncles | | | |
| Litsea acutivena | leaves | 164–168 | cytotoxicity | [102] |

(continued on next page)
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 Machilus japonica Sieb. et Zucc. var. kusanoi (Hay.) Liao (M. kusanoi Hayata), a new benzylisoquinoline, L-β-N-norarmepavine (190) [113], has been isolated.

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

From Machilus 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; machilusols 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 Machilus pseudolongiphilus Hay., 10 new compounds have been isolated, including seven butanolides [machilactone (216), methyl (2E)-2-(1-hydroxy-2-oxopropyl)leucose-2-enol (217), machilolides A and B (218, 219) [125], secomahubanolide (220), zuihoenalide (221), and 3-(1-methoxyoctadecyl)-5-methylene-5H-furan-2-one (222) [126], the sesquiterpene, 3,4-dihydroxy-β-bisabolol (223) [125], and the steryl epoxide, machilline (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 Machilus zuihoensis Hay. var. mushaensis (Lu) Y. C. Liu, one new compound, machilolin (226) [128], has been isolated.

From Machilus philippinensis Merr. (M. arisanensis Hayata; Cinnamomum philippinense Merr.) Chang), 11 new compounds have been isolated, including four acyl flavonol monohamnmosides [kaempferol-3-O-α-L-(3′-O-
E4-O-Z-di-p-coumaroyl)hamnopyranoside (227), quercetin-3-O-α-L-(3’O-Z,4’-O-E-di-p-coumaroyl)hamnopyranoside (228), quercetin-3-O-α-L-(3’O,4’-O-Z-p-coumaroyl)hamnopyranoside (229), and kaempferol-3-O-α-L-(3’O,4’-O-Z-p-coumaroyl)hamnopyranoside (230) [130]; two proanthocyanidins, machiphilinins 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 A (235) [129], a naphthalenol, cinnamophilin A (236) [133], and a pyridine derivative, 2-(4’-hydroxypryidine-3’y)lactic 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 mono-rhamnopyranosylflavonoids (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. buisnensis* Yamamoto & Kamikoti f. *buisnensis* (Hay.) Hatus, nine new sesquiterpenoids, i.e., neobuisanolides A–E (238–242) (leaves) [137] and linderaines A–D (243–246) (root) [138], and one β-carboline, neolitcarboline A (247) (leaves) [137], have been isolated.

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

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

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, lauromine (295) and N-methyl-lauromine (296) [156], from its bark and a neutral aporphine alkaloid, laurodione (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 randaiinal (298), randaiol (299) [161] (heartwood), and randainol (300) [162] (root); the dimeric noxigeninan (++)-sasserandainol (301); the flavonoid R-5-7-3'-tetrahydroxylavanone (302) [163] (root); and the lignan sasserandainol (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. obvatfolia* [124], *M. thunbergii* [124], and *M. zuhoensis* [124] have been found to contain L-(++)-N-norarmpavine and dl-N-
noramnpavine. *M. philippensis* [1], formerly named as *M. acuminatissima* [65] and *M. arisanensis* [124], also contains these benzylisoquinolines. Furthermore, *Nothaphoebe konishii* [136] contains L-(-)-N-noramnpavine. Due to this chemical evidence, Lu [124] indicated in 1965 that the occurrence of these benzylisoquinolines reveals a close relationship among Formosan *Mathilus* 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 papavine alkaloids, which are not found in *C. concinna* or other laurateous plants.

6. The existence of a new phenanthrene alkaloid, litelamine [3], and two new dibenzopyrrole alkaloids, (–)-litcinamide and (–)-litcinamidine [91], in Formosan *L. cuba* is also striking in *Litsea* species.

7. D. incassata 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 laureaceous 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 laureaceous plant has been screened exhaustively in different assay platforms. According to our recent investigation on the bioactivity of Formosan laureaceous plants, the constituents exhibiting inhibitory activity against inflammation, oxidation, and hyperglycemia and anti-eG-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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