Published in final edited form as:
Curr Bioact Compd. 2008 June 1; 4(1): 15–32. doi:10.2174/157340708784533393.

BIOLOGICALLY ACTIVE NATURAL PRODUCTS OF THE GENUS *CALLICARPA*⊥

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Abstract

About 20 species from *Callicarpa* have reported ethnobotanical and ethnomedical uses, and several members of this genus are well known in the traditional medical systems of China and South Asia. Ethnomedical reports indicate their use in the treatment of hepatitis, rheumatism, fever, headache, indigestion, and other ailments. Several species of *Callicarpa* have been reported to be used against cancer (e.g., *Callicarpa americana* root to treat skin cancer and *Callicarpa rubella* bark to treat tumors of the large intestine). Extracts from about 14 species in this genus have been evaluated for biological activity, including antibacterial, antifungal, anti-insect growth, cytotoxic, and phytotoxic activities. In addition to amino acids, benzenoids, simple carbohydrates, and lipids, numerous diterpenes, flavonoids, phenylpropanoids, phytosterols, sesquiterpenes, and triterpenes have been detected in or isolated from the genus *Callicarpa.* The essential oils of *Callicarpa americana* have recently been reported to have antialgal and phytotoxic activities, and several isolates from this species (and *C. japonica*) were identified as contributing to the mosquito bite-deterrent activity that was first indicated by folkloric usage. Recent bioassay-guided investigations of *C. americana* extracts have resulted in the isolation of several active compounds, mainly of the clerodane diterpene structural type.

Keywords

bioassay; cytotoxicity; *Callicarpa*; diterpenoid; natural products; pharmacognosy

INTRODUCTION

The genus *Callicarpa* is comprised of 40 or more species, many of which have been used by humans in ways suggesting that the genus is a rich source of biologically active natural products. Traditional usage of various parts of members of *Callicarpa* includes preparations used as fish poisons, insect deterrents, and medicinally. Phytochemical and biological studies of extracts from *Callicarpa* lend support to these previous uses, and suggest that this genus may offer a rich supply of bioactive secondary metabolites. The fruits are a striking feature of the genus; hence the genus name "*Callicarpa*", meaning "handsome fruit", and the common

⊥The material presented here is adapted from the Ph.D. dissertation of one of the authors (W.J.) entitled "A Pharmacognostic Investigation of *Callicarpa americana* for Potential Anticancer Agents", completed at the University of Illinois at Chicago, Chicago, IL, 2006.

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name “beautyberry”. The fruits of at least one species (*C. americana* L.) are commonly consumed by birds and small mammals and white-tailed deer [54], and occasionally by humans (see below).

TAXONOMY OF *CALLICARPA*

Traditionally, *Callicarpa* has been included in the family Verbenaceae, but some current botanical authorities have concluded that it is more appropriately included among the Lamiaceae, with both of these families being grouped in the order Lamiales [10,91]. The plant family Lamiaceae (classically called the Labiatae) is the source of numerous natural products and traditional medicines [27]. The predominant phytochemical characteristic of the family is the presence in many of its species of biologically active terpenoid principles, including monoterpenoids and diterpenoids. The genus *Callicarpa* was described by Harley and coworkers [27] as being comprised primarily of small trees and shrubs with fruits typified as drupaceous with a fleshy exocarp and a hard endocarp, and containing four stony pyrenes.

Two representatives of *Callicarpa* are native or naturalized to the southeastern United States, namely, *C. americana* L. and *C. dichotoma* (Lour.) K. Koch (= *C. purpurea* Juss., an ornamental escapee). Radford and colleagues [63] described these members of the genus as shrubs, 1–2.5 m tall, with pubescent twigs, simple, more or less opposite, leaves, and flowers forming cymes. The fruit is a two-lobed and four-seeded drupe, purple (or rarely white). The genus *Callicarpa* and the species *C. americana* were first described by Carl Linnaeus in 1741, but not published validly until some years later, in 1753 [5]. Thus, these two specimens are the type specimens (isolectotypes) of the species *C. americana* L. and the genus *Callicarpa*.

ETHNOBOTANICAL AND ETHNOMEDICAL USES OF *CALLICARPA* SPECIES

The genus *Callicarpa* has a rich history of ethnobotanical usage, mainly in Asia (Table 1). Several species of the genus *Callicarpa* have documented ethnobotanical uses as traditional and ethnomedicines and as fish poisons. For example, *C. arborea* Roxb. has been used in India to treat skin diseases [68], and *C. candicans* (Burm. f.) Hochr. leaves are reported to be used in Palau and the Philippines to stupefy fish [38,39]. *C. formosana* Rolfe is used in Taiwanese folk medicine to treat rheumatism and disorders of the digestive tract (oral infections and unspecified stomach disorders and intestinal complaints) [15]. The bark of *C. lanata* L. has been used in the East Indies as a betel leaf substitute [30]. *C. macrophylla* Vahl is used extensively in Indian and Chinese systems of traditional medicine. In India, the seeds of *C. macrophylla* are used to treat oral infections and “intestinal complaints” [1], the leaf extract is used to treat rheumatism [79], the juice of the fruit is used to treat fever [51], and an aromatic oil from the roots is used to treat “disordered stomach” [79]. In Traditional Chinese Medicine, *C. macrophylla* and two other species (*C. pedunculata* R.Br. and *C. cathayana* Chang) have been used to stop internal and external bleeding and to treat burns [6]. *C. macrophylla* is used also in combination with other herbs in a preparation to treat diarrhea, dysentery, intestinal worms, and skin disorders and to “purify the blood” and eliminate toxins [41].

Several *Callicarpa* species have been used to regulate fertility. The peoples of the Torres Straits (located between Papua New Guinea and Australia) were reported to consume the juice of the chewed leaves of a *Callicarpa* species (local name, “argerarger”; probably *C. thozetii* A. A. Munir) mixed with the leaves of several other shrubs and trees to induce permanent sterility [26]. Members of the Marma tribe in Bangladesh reportedly have used the root juice of *C. lanata* L. [cited as *C. tomentosa* (L.) Murr.] in combination with the root juice of *Streblus asper* Laur. (Moraceae) to “treat irregular menstruation” and to promote delayed menstruation [2], and the leaves are known to be chewed with salt as an anthelmintic [8].

Callicarpa americana L. has a number of documented ethnobotanical uses in North America and the berries have been used occasionally as a food. In the early nineteenth century Rafinesque noted that *C. americana* leaves were used to treat dropsy (apparently by people of European heritage), and the fruits were considered edible, although somewhat acidic and astringent (hence "sourberry", a colloquial name at the time) [64]. On the other hand, M. A. Curtis [18] wrote that "These berries are juicy, slightly aromatic and sweetish, and are sometimes eaten, but are probably not very wholesome." More recently, Fernald and Kinsey stated, "The familiar beauty-berry…has the defoliated branches covered in late autumn and early winter with masses of small currant-like pinkish-purple berries…Their best use is as a table-ornament for which they are almost unequaled [22]." The fruits were also known as a source of purple dye for wool [64].

In a traditional practice of the Alabama Indian tribe in North America, a decoction was prepared from the roots and branches of *C. americana* L. for external use in sweat baths as an antirheumatic, diaphoretic, and febrifuge (against malaria specifically), and the Choctaw tribe used decoctions of various *C. americana* plant parts (including roots and berries) to treat colic [58]. For dysentery, *C. americana* roots mixed with roots of *Rubus* sp. were taken in a decoction [81], and the roots were used to treat dizziness [81]. A root decoction was used by the Koasati tribe to treat stomachache [81]. In North Carolina, *C. americana* bark was used to treat fevers, according to an herbalist informant [17]. Dr. Jonathan L. Hartwell cited one report from the central files of the United States National Cancer Institute of a "cure" of skin cancer achieved with the use of a decoction of the root of *C. americana* in Mississippi (circa 1966), but it is not clear whether this use was based on an ethnomedical tradition, or whether it was a case of "ethnoexperimentation" [28].

PHYTOCHEMICAL STUDIES OF C*ALLICARPA*

Phytochemical screening of several members of the genus *Callicarpa* has been reported, and the presence of flavonoids, essential oils, and terpenoids has been substantiated by detection or isolation of members of these compound classes. An extract of the leaf and stem of *C. angustifolia* King & Gamble tested positive for alkaloids using Mayer's reagent (i.e., formation of precipitate from an aqueous solution of mercuric chloride and potassium iodide), but, to date, the occurrence of alkaloids in any species of the genus has not been confirmed by phytochemical isolation work. Numerous phytochemicals have been isolated from (or detected in) species in *Callicarpa*, including representatives from the following structural classes: clerodane and phyllocladane diterpenes, fatty acids, flavones, lignans, monoterpenes, phenylpropanoids, phytosterols, sesquiterpenes, and triterpenes. A summary of the phytochemical screening results and specific phytochemicals isolated from members of the genus are provided in Tables 2 and 3, respectively.

Several recent phytochemical studies of members of the genus *Callicarpa* have resulted in the isolation of notable diterpenoid constituents. One such study resulted in the isolation of abieta-8,11,13,15-tetraen-18-oic acid (**1**), calliphyllin (**4**), calliterpenone (**6**), 6α-hydroxynidorellol (**17**), and isopimaric acid (**19**), and the authors observed that several of these same compounds have been reported from members of the Lamiaceae, supporting an alliance with the latter plant family [33]. Xu and coworkers [90] reported the isolation of four new clerodane diterpenes [pentandralactone and pentandranoic acids A–C (**24** and **25**–**27**, respectively)]. No biological activities were reported for the compounds described in either of these phytochemical reports [33,90].

BIOLOGICAL EVALUATION OF *CALLICARPA* EXTRACTS AND PURE COMPOUND ISOLATES

Various extracts and other preparations of *Callicarpa americana* L. have been evaluated for biological activity in a number of assay systems, including antiviral potential of the freeze-dried leaf [85], oviposition inhibition activity of an aqueous leaf extract [83], antialgal activity of the leaf essential oil [82], mosquito bite-deterrent activity of volatile constituents from the leaves [11], and cytotoxicity of a chloroform extract of the combined fruits, leaves and twigs [36]. Ethanolic extracts of *C. arborea* Roxb. var. *oblongifolia*, *C. lanata* L., *C. macrophylla* Roxb., and *C. pilosissima* Maxim. were found to lack cytotoxic activity against KB cells [7, 21,77]. *C. pilosissima* Maxim. extracts were evaluated in mice against colon carcinoma 38, B16 melanoma, and P388 murine leukemia, for which activity was observed only against P388 with a 60% increase in life span in the treated mice relative to control at relatively high doses (stated range of 150 to 600 mg/kg/injection) [77]. Other members of the genus have been evaluated for various biological activities (Table 4). 5,6,7-Trimethoxyflavone (**58**), a constituent of *C. japonica*, displayed activity against Herpes simplex virus and other viral pathogens [29].

The demonstration of a plant-growth suppression effect of extracts from *C. acuminata* H.B.K. was the impetus for a bioassay-guided investigation that resulted in the isolation of akhdarenol (**2**), isopimaric acid (**19**), sandaracopimaradien-19-ol (**32**), 5-hydroxy-6,7,4′-trimethoxyflavone (**50**), and α-amyrin (**81**) [3]. These isolates lacked activity when tested singly in assays for alleleochemical potential, but further testing in other assays indicated that several of these compounds possess cytotoxic activity against insect and hamster cells, with the strongest cytotoxic activity in mammalian cells being associated with **2** and **19** [3].

Observation of the use of fresh *C. americana* leaves as a “folk remedy”, used to protect horses and people from mosquito bites, prompted an investigation of the volatile constituents of *C. americana* and *C. japonica* leaves, using biological activity against *Aedes aegypti* and *Anopheles stephensi* to guide chromatographic fractionation, which resulted in the identification of several mosquito bite-deterrent terpenoid components [11]. Of several compounds isolated from *C. americana* essential oil, callicarpenal (**5**), humulene epoxide II, intermediol, and spathulenol were tested against *A. aegypti* and *A. stephensi*, with callicarpenal (**5**) displaying the strongest overall activity (mosquito-deterrence effect and knock-down toxicity) [11]. No structure-activity relationship studies were reported with regard to mosquito bite-deterrent activity in this study, but it seems likely that its aldehyde functionality confers potency to this tetranorclerodane diterpene [11].

An investigation of *Callicarpa americana* L. as a potential source of anticancer natural products was carried out using bioassay-guided isolation methodology [36]. The configuration of the isolates, including the absolute configuration of the secondary hydroxy groups was determined using a modified Mosher ester methodology [75,78]. Using this technique, the C-12 hydroxy group in the side chain of the clerodane-type diterpenes isolated was determined as having an *S* absolute configuration [36]. In all, six new compounds and eight known compounds were isolated from the chloroform extract of the combined fruits, leaves, and twigs of *C. americana* L. [36]. The structures of the new compounds were elucidated as 3β,12(*S*)-dihydroxycleroda-4(18),13-dien-15,16-olide (**8**), 12(*S*),16ξ-dihydroxycleroda-3,13-dien-15,16-olide (**10**), 12(*S*)-hydroxycleroda-3,13-dien-15,16-olide (**12**), 12(*S*)-hydroxycleroda-3,13-dien-16,15-olide (**13**), 12(*S*)-hydroxy-16ξ-methoxycleroda-3,13-dien-15,16-olide (**14**), and 16ξ-hydroxycleroda-3,11(*E*),13-trien-15,16-olide (**16**) using a range of spectroscopic techniques, including 1D and 2D NMR and accurate mass measurement [36]. Of several known compounds isolated in this study, three were previously reported to occur in the genus *Callicarpa* [calliterpenone (**6**), euscaphic acid (**88**), and 5-hydroxy-6,7,4′-

trimethoxyflavone (**50**)] (see Table 3). Five other known compounds obtained in this same investigation [i.e., 3β,16ξ-dihydroxycleroda-4(18),13-dien-15,16-olide (**9**), 2-formyl-16ξ-hydroxy-3-A-norcleroda-2,13-dien-15,16-olide (**11**), genkwanin (**41**), 16ξ-hydroxycleroda-3,13-dien-15,16-olide (**15**), and 5-hydroxy-7,4′-dimethoxyflavone (**45**)] were not previously known to occur in *Callicarpa* [36].

The isolates obtained from the chloroform-soluble extract of the combined fruits, leaves and twigs of *C. americana* [36] were tested for cytotoxicity against a panel of human cancer cell lines (Table 5). 12(*S*),16ξ-Dihydroxycleroda-3,13-dien-15,16-olide (**10**), 2-formyl-16ξ-hydroxy-3-A-norcleroda-2,13-dien-15,16-olide (**11**), genkwanin (**41**), 12(*S*)-hydroxycleroda-3,13-dien-16,15-olide (**13**), 16ξ-hydroxycleroda-3,13-dien-15,16-olide (**15**), and 16ξ-hydroxycleroda-3,11(*E*),13-trien-15,16-olide (**16**) all showed cytotoxic activity with at least one cell line showing activity below 5 μg/mL. By comparison of the relative cytotoxicities of these isolates, a structure-activity relationship trend was suggested [36]. Compounds of the clerodane structure class with a γ-lactone ring in the side chain, and which lacked a free hydroxy group at the 16-position, displayed a slightly less potent cytotoxicity than compounds with a γ-hydroxy group on the α,β-unsaturated γ-lactone ring [36]. One of the new active compounds [12(*S*),16ξ-dihydroxycleroda-3,13-dien-15,16-olide (**10**)] isolated and purified from *C. americana* was tested in an in vivo model of antitumor activity against several cell lines using the hollow fiber assay, in which the human cells are enclosed in selectively permeable polyvinylpyrrolidone fibers and implanted in nude mice [12,57]. The cell lines used in the hollow fiber assay were hormone-dependent prostate cancer (LNCaP), human lung cancer (Lu1), and breast cancer (MCF-7) [36]. Compound **10** was tested in this model at 6.25, 12.5, 25, and 50 mg/kg, administered to the mice via intraperitoneal injection [36].

No cytotoxic activity was observed at either of two physiological sites, even at the highest dose tested (50 mg/kg), and two of the three mice died at each the two highest doses (25 mg/kg and 50 mg/kg) [36]. Despite these negative results, there may be value in continued investigation of members of this genus for anticancer agents, in light of the folkloric evidence for the use of *Callicarpa* species for treatment of cancer, and the promising in vitro results noted in several instances for extracts or isolates.

CONCLUSIONS

The genus *Callicarpa* has a relatively wide geographic distribution, there is considerable ethnobotanical evidence that members of the genus contain pharmacologically active components, and numerous extracts have shown positive results in a range of bioassays relevant to human health. However, to date, relatively few bioassay-guided isolation studies have been carried out to identify active components for drug or agrochemical discovery. A few promising chemical constituents have been obtained with mosquito-deterrent activity [11], cytotoxicity [36], antimicrobial activity [29], among others, but it seems clear that this is just scratching the surface into the elucidation of the potential bioactive natural products from *Callicarpa*, and much more phytochemical prospecting is warranted on this promising genus in the future. In addition, in light of the ongoing debate about the taxonomic position of *Callicarpa*, a thorough evaluation of the chemotaxonomy of this genus as compared to members of Lamiaceae and Verbenaceae would help clarify the relationships among these taxa.

Acknowledgments

Some of the research described here was part of the Ph.D. dissertation project of one of the authors (W.P.J), and was funded by grant U19-CA52956 from the National Cancer Institute, NIH, Bethesda, MD, USA, awarded to A.D.K.

References

1. Ahmad SA, Siddiqui SA, Zaman A. Chemical examination of *Callicarpa macrophylla*, *Lagerstromea lanceolata*, *Ficus palmata*, and *Taxodium mucronatum*. J Indian Chem Soc 1976;53:1165–1166.
2. Alam MK. Medical ethnobotany of the Marma tribe of Bangladesh. Econ Bot 1992;46:330–335.
3. Anaya AL, Mata R, Sims JJ, González-Coloma A, Cruz-Ortega R, Guadaño A, Hernández-Bautista BE, Midland SL, Ríos G, Gómez-Pompa A. Allelochemical potential of *Callicarpa acuminata*. J Chem Ecol 2003;29:2761–2776. [PubMed: 14969362]
4. Atal CK, Srivastava JB, Wali BK, Chakravarty RB, Dhawan BN, Rastogi RP. Screening of Indian plants for biological activity. Part VIII. Indian J Exp Biol 1978;16:330–349. [PubMed: 680833]
5. Atkins S. *Callicarpa japonica*: Labiatae. Curtis's Bot Mag 1999;16:79–83.
6. Bensky, D.; Gamble, A.; Kaptchuk, T. Chinese Herbal Medicine: Material Medica. Seattle: Eastland Press; 1986.
7. Bhakuni DS, Dhar ML, Dhar MM, Dhawan BN, Gupta B, Srimal RC. Screening of Indian plants for biological activity. Part III. Indian J Exp Biol 1971;9:91–102. [PubMed: 5089325]
8. Bhandary MJ, Chandrashedar KR, Kaveriappa KM. Medical ethnobotany of the Siddis of Uttara Kannada district, Karnataka, India. J Ethnopharmacol 1995;47:149–158. [PubMed: 8569239]
9. Cannon JR, Dampawan P, Lojanapiwatna V, Phuriyakorn B, Sinchai W, Sriirugsa P, Suvatabhandhu K, Wiriyachitra P. A contribution to the Thai phytochemical survey. J Sci Soc Thailand 1980;6:46–53.
10. Cantino PD. Evidence for a polyphyletic origin of the Lamiaceae. Ann Missouri Bot Gard 1992;79:361–379.
11. Cantrell CL, Klun JA, Bryson CT, Kobaisy M, Duke SO. Isolation and identification of mosquito bite deterrent terpenoids from leaves of American (*Callicarpa americana*) and Japanese (*Callicarpa japonica*) beautyberry. J Agric Food Chem 2005;53:5948–5953. [PubMed: 16028979]
12. Casciari JJ, Hollingshead MG, Alley MC, Mayo JG, Malspeis L, Miyauchi S, Grever MR, Weinstein JN. Growth and chemotherapeutic response of cells in a hollow fiber in vitro solid tumor model. J Natl Cancer Inst 1994;86:1846–1852. [PubMed: 7990159]
13. Chatterjee A, Desmukh SK, Chandrasekharan S. Diterpenoid constituents of *Callicarpa macrophylla* Vahl: the structures and stereochemistry of calliterpenone and calliterpenone monoacetate. Tetrahedron 1972;28:4319–4323.
14. Chaudhury A, Bhattacharyya A, Mitra SR, Adityachaudhuri N. Phytochemical investigation on the leaves of *Callicarpa macrophylla* Vahl. J Indian Chem Soc 1978;55:628–629.
15. Chen RS, Lai JS, Wu TS. Studies on the constituents of *Callicarpa formosana* Rolfe. J Chin Chem Soc 1986;33:329–334.
16. Chung PY, Chung LY, Ngeow YF, Goh SH, Imiyabir Z. Antimicrobial activities of Malaysian plant species. Pharm Biol 2004;42:292–300.
17. Crellin, JK.; Philpott, J. A Reference Guide to Medicinal Plants: Herbal Medicine Past and Present. Durham, NC: Duke University Press; 1997.
18. Curtis, MA. Botany; Containing a Catalogue of the Indigenous and Naturalized Plants of the State. Raleigh, NC: North Carolina Institution for the Deaf Dumb and Blind; 1867.
19. Darbour N, Raynaud J. Les aglycones anthocyaniques de *Callicarpa bodinieri* Leveille et *Callicarpa purpurea* Juss. (Verbénacées). Pharmazie 1988;43:143–144. [PubMed: 3393589]
20. de Laszlo H, Henshaw PS. Plant materials used by primitive peoples to affect fertility. Science 1954;119:626–631. [PubMed: 13156639]
21. Dhar ML, Dhar MN, Dhawan BN, Mehrotra BN, Srimal RC, Tandon JS. Screening of Indian plants for biological activity. Part IV. Indian J Exp Biol 1973;11:43–54. [PubMed: 4779295]
22. Fernald, ML.; Kinsey, AC. Edible Wild Plants of Eastern North America. New York: Harper and Brothers; 1958.
23. Gao XL, Li ZM, Zhang RP. Chemical constituents of *Callicarpa pedunculata*. Huaxi Yaoxue Zashi 2000;15:358–359.

24. Goh, SH.; Soepadmo, E.; Chang, P.; Barnerjee, U.; Chan, KC.; Deverre, JR.; Hadi, H.; Loke, SE.; Nasrulhawq, A.; Oo, SL.; Taylor, CE.; Wong, WH.; Zakaria, M. Asian Symposium on Medicinal Plants and Spices. Seoul; Korea: 1984. Studies on Malaysian medicinal plants: preliminary results.
25. Graham JG, Quinn ML, Fabricant DS, Farnsworth NR. Plants used against cancer - an extension of the work of Jonathan Hartwell. J Ethnopharmacol 2000;73:347–377. [PubMed: 11090989]
26. Haddon, AC. Birth and childhood customs, and limitation of children. In: Haddon, AC., editor. Reports of the Cambridge Anthropological Expedition to Torres Straits: Sociology, Magic and Religion of the Eastern Islanders. New York: Johnson Reprint Company; 1971. p. 316
27. Harley, RM.; Atkins, S.; Budantsev, AL.; Cantino, PD.; Conn, BJ.; Grayer, R.; Harley, MM.; de Kok, R.; Krestovskaja, T.; Morales, R.; Paton, AJ.; Ryding, O.; Upson, T. Labiatae. In: Kadereit, JW., editor. Flowering Plants, Dicotyledons: Lamiales, except Acanthaceae, including Avicenniaceae, The Families and Genera of Vascular Plants. New York: Springer; 2004. p. 478
28. Hartwell, JL. A Survey. Lawrence, MA: Quarterman; 1982. Plants Used Against Cancer.
29. Hayashi K, Hayashi T, Otsuka H, Takeda Y. Antiviral activity of 5,6,7-trimethoxyflavone and its potentiation of the antiherpes activity of acyclovir. J Antimicrob Chemother 1997;39:821–824. [PubMed: 9222055]
30. Hedrick, UP. Sturtevant's Notes on Edible Plants. Albany, NY: J. B. Lyon Company; 1919.
31. Holdsworth DK, Hurley CL, Rayner SE. Traditional medicinal plants of New Ireland, Papua New Guinea. Quart J Crude Drug Res 1980;18:131–139.
32. Hosozawa S, Kato N, Munakata K. 5,6,7-Trimethoxyflavone from *Callicarpa japonica*. Phytochemistry 1972;11:2362.
33. Hu Y, Shen Y, Gan F, Hao X. Four diterpenes from *Callicarpa pedunculata*. Biochem System Ecol 2002;30:999–1001.
34. Hu YM, Shen YM, Gu QX, Zuo GY, Hao XJ. Studies on chemical constituents of *Callicarpa pedunculata*. Zhong Cao Yao 2001;32:1063–1065.
35. Jain SP, Puri HS. Ethnomedicinal plants of Jaunsar-Bawar Hills, Uttar Pradesh, India. J Ethnopharmacol 1984;12:213–222. [PubMed: 6521494]
36. Jones WP, Lobo-Echeverri T, Mi Q, Chai HB, Soejarto DD, Cordell Geoffrey A, Swanson SM, Kinghorn AD. Cytotoxic constituents from the fruiting branches of *Callicarpa americana* collected in southern Florida. J Nat Prod 2007;70:372–377. [PubMed: 17279798]
37. Kapoor LD, Singh A, Kapoor SL, Srivastava SN. Survey of Indian plants for saponins, alkaloids and flavonoids. IV. Lloydia 1975;38:221–224. [PubMed: 1143019]
38. Kawazu K, Inaba M, Mitsui T. Fish-killing components of *Callicarpa candicans*. Part I Isolation of callicarpone and its toxicity to fish. Agric Biol Chem 1967;31:494–497.
39. Kawazu K, Inaba M, Mitsui T. Fish-killing components of *Callicarpa candicans*. Part II Structure of callicarpone. Agric Biol Chem 1967;31:498–506.
40. Kawazu K, Mitsui T. Callicarpone, a fish-killing component of *Callicarpa candicans*. Tetrahedron Lett 1966:3519–3524.
41. Khare, CP., editor. Indian Herbal Remedies: Rational Western Therapy, Ayurvedic and Other Traditional Usage, Botany. New York: Springer-Verlag; 2004.
42. Kobaisy M, Tellez MR, Dayan FE, Duke SO. Phytotoxicity and volatile constituents from leaves of *Callicarpa japonica* Thunb. Phytochemistry 2002;61:37–40. [PubMed: 12165300]
43. Koo AK, Sung SH, Park JH, Kim SH, Lee KY, Kim YC. *In vitro* neuroprotective activities of phenylethanoid glycosides from *Callicarpa dichotoma*. Planta Med 2005;71:778–780. [PubMed: 16142646]
44. Kuo YC, Ou JC, Tsai WJ, Wu CL, Sun CM. Evaluation of Chinese herbs that affect the cell-mediated immunity (II). J Chin Med 1996;7:119–131.
45. Kuo YC, Sun CM, Tsai WJ, Ou JC, Chen WP, Lin CY. Blocking of cell proliferation, cytokines production and genes expression following administration of Chinese herbs in the human mesangial cells. Life Sci 1999;64:2089–2099. [PubMed: 10372651]
46. Lama S, Santra SC. Development of Tibetan plant medicine. Sci Cult 1979;45:262–265. [PubMed: 11630911]

47. Lin CC, Kan WS. Medicinal plants used for the treatment of hepatitis in Taiwan. Amer J Chinese Med 1990;18:35–43.
48. Madulid DA, Gaerlan FJM, Romero EM, Agoo EMG. Ethnopharmacological study of the Ati tribe in Nagpana, Barotac Viejo, Iloilo. Acta Manilana 1989;38:25–40.
49. Manandhar NP. An ethnobotanical survey of herbal drugs of Kaski district, Nepal. Fitoterapia 1994;65:7–13.
50. Manandhar NP. Herbal remedies of Surkhet district, Nepal. Fitoterapia 1993;64:266–272.
51. Manandhar NP. An inventory of some vegetable drug resources of Makawanpur district Nepal. Fitoterapia 1995;66:231–238.
52. Manandhar NP. Some less known medicinal plants of Rasuwa district (Nepal). Quart J Crude Drug Res 1980;18:147–151.
53. Manandhar NP. A survey of medicinal plants of Jajarkot district, Nepal. J Ethnopharmacol 1995;48:1–6. [PubMed: 8569241]
54. Martin, CO.; Mott, SP., editors. American Beautyberry (Callicarpa americana): Section 7.5.8, U.S. Army Corps of Engineers Wildlife Resources Management Manual. Vicksburg, MS; U.S. Army Engineer Waterways Experiment Station: 1997.
55. McChesney JD, Kabra PM, Fraher P. Simple analogs of the toxin calliterpenone. J Pharm Sci 1979;68:1116–1120. [PubMed: 501532]
56. Mi HM, Zhang CH, Su ZW, Li CG. A SEM observation on the leaves of the genus *Callicarpa* of 16 Chinese species. Acta Pharm Sin (Yao Xue Xue Bao) 1984;19:381–386.
57. Mi Q, Lantvit D, Reyes-Lim E, Chai HB, Zhao WM, Lee IS, Peraza-Sanchez S, Ngassapa O, Kardono LBS, Riswan S, Hollingshead MG, Mayo JG, Farnsworth NR, Cordell GA, Kinghorn AD, Pezzuto JM. Evaluation of the potential cancer chemotherapeutic efficacy of natural product isolates employing *in vivo* hollow fiber tests. J Nat Prod 2002;65:842–850. [PubMed: 12088425]
58. Moerman, DE. A Reference Dictionary. New York: Garland Publishing; 1977. American Medical Ethnobotany.
59. Nishino C, Kawazu K, Mitsui T. Maingayic acid, a piscicidal constituent of *Callicarpa maingayi*. Tetrahedron Lett 1971:1541–1544.
60. Osawa K, Ueda J, Banba K. Studies on the constituents of *Callicarpa japonica* Thunb. Ann Rep Tohoku Coll Pharm (Tahoku Yakka Deigaku Kenkyu Nempo) 1984;31:167–169.
61. Paijmans, KP., editor. New Guinea Vegetation. New York: Elsevier Scientific Publishing; 1976.
62. Puri HS. Preliminary phytochemical screening of the plants of Silent Valley. I. Bull Med Ethno Bot Res 1980;1:384–392.
63. Radford, AE.; Ahles, HE.; Bell, CR. Manual of the Vascular Flora of the Carolinas. Chapel Hill, NC: University of North Carolina Press; 1968.
64. Rafinesque, CS. Medical Flora; or Manual of the Medical Botany of the United States of North America. Vol. 2. Philadelphia: Atkinson and Alexander; 1830.
65. Ren FZ, Luan XH, Qu HH, Zhao YM. Studies on the chemical constituents of *Callicarpa bodinieri* (II). Chin Pharm J (Zhongguo Yao Xue Za Zhi) 2001;36:445–447.
66. Ren FZ, Luan XH, Zhao YM, Qu H. Studies on flavonoids from leaves of *Callicarpa bodinieri* Levl. Zhongguo Zhong Yao Za Zhi 2001;26:841–844. [PubMed: 12776333]
67. Ren FZ, Qu HH, Luan XH, Zhao YM. Studies on the chemical constituents of *Callicarpa bodinieri* Levl. Nat Prod Res Develop (Tianran Chanwu Yanjiu Yu Kaifa) 2001;13:33–34.
68. Sen M, Pal BC. Chemical investigation of the bark of *Callicarpa arborea* (Verbenaceae). J Indian Chem Soc 1974;51:903.
69. Sen M, Sarkar U. Chemical investigation of the leaves of *Callicarpa arborea* (Verbenaceae). J Indian Chem Soc 1978;55:744–745.
70. Shao Y, Hu LH, Sim KY, Goh SH. Lignanoids and diterpenoids from *Callicarpa furfuracea*. Helv Chim Acta 2006;89:64–72.
71. Siang ST. Use of combined traditional Chinese and western medicine in the management of burns. Panminerva Med 1983;25:197–202. [PubMed: 6669397]
72. Singh AK, Agrawal PK. 16α,17-Isopropylideno-3-oxo-phyllocladane, a diterpenoid from *Callicarpa macrophylla*. Phytochemistry 1994;37:587–588.

73. Singh AK, Bhattachaary AK, Prasad G, Sharma VD, Gupta KC. The essential oil of *Callicarpa macrophylla* Vahl. and its antimicrobial activity. Ind J Microbiol 1982;22:286–288.
74. Spies JR. The toxicity of certain plant extracts to goldfish. II. J Econ Entomol 1933;26:285–288.
75. Su BN, Park EJ, Mbwambo ZH, Santarsiero BD, Mesecar AD, Fong HHS, Pezzuto JM, Kinghorn AD. New chemical constituents of *Euphorbia quinquecostata* and absolute configuration assignment by a convenient Mosher ester procedure carried out in NMR tubes. J Nat Prod 2002;65:1278–1282. [PubMed: 12350147]
76. Subramanian SS, Nair AGR, Vedantham TNC. Terpenoids and flavones of *Callicarpa macrophylla* and *C. longifolia*. Phytochemistry 1974;13:306–307.
77. Suffness M, Abbott BJ, Statz D, Wonilowicz E, Spjut R. The utility of P388 leukemia compared to B16 melanoma and colon carcinoma 38 for *in vivo* screening of plant extracts. Phytother Res 1988;2:89–97.
78. Sullivan GR, Dale JA, Mosher HS. Correlation of configuration and ^{19}F chemical shifts of α-methoxy-α-trifluoromethylphenylacetate derivatives. J Org Chem 1973;38:2143–2147.
79. Talapatra SK, Polley M, Talapatra B. Terpenoids and related compounds. Part 32 Calliphyllin, a new diterpene from the leaves of *Callicarpa macrophylla*. J Indian Chem Soc 1994;71:527–532.
80. Taoubi K, Fauvel MT, Gleye J, Fouraste I. Etude des esters heterosidiques de l'acide cafeique chez des Verbenaceae. (Phenylpropanoid glycosides from Verbenaceae). Bull Liaison Groupe Polyphenols 1992;16:174–177.
81. Taylor, LA. Plants Used as Curatives by Certain Southeastern Tribes. Cambridge, MA: Botanical Museum, Harvard University; 1940.
82. Tellez MR, Dayan FE, Schrader KK, Wedge DE, Duke SO. Composition and some biological activities of the essential oil of *Callicarpa americana* (L.). J Agric Food Chem 2000;48:3008–3012. [PubMed: 10898657]
83. Tingle FC, Mitchell ER. Aqueous extracts from indigenous plants as oviposition deterrents for *Heliothis virescens* (F.). J Chem Ecol 1984;10:101–113.
84. Tiwari KC, Majumder R, Bhattacharjee S. Folklore medicines from Assam and Arunchal Pradesh (District Tirap). Int J Crude Drug Res 1979;17:61–67.
85. Van den Berghe DA, Ieven M, Mertens F, Vlietinck AJ, Lammens E. Screening of higher plants for biological activities. II Antiviral activity. Lloydia 1978;41:463–471. [PubMed: 713708]
86. Vigneron JP. Substances antiappétantes d'origine naturelle. Ann Zool Ecol Anim 1978;10:663–694.
87. Wang X, Wei R, Lu W, Chen J. Chemical composition of *Callicarpa integerrima*. Zhong Cao Yao 1986;17:108.
88. Womersley, JS. Botanical validation in medicinal plant investigations. Noumea, New Caledonia: South Pacific Commission; 1973.
89. Woo ER, Yoon SH, Kwak JH, Kim HJ, Park H. Inhibition of gp 120-CD4 interaction by various plant extracts. Phytomedicine 1997;4:53–58.
90. Xu J, Harrison LJ, Vittal JJ, Xu YJ, Goh SH. Four new clerodane diterpenoids from *Callicarpa pendandra*. J Nat Prod 2000;63:1062–1065. [PubMed: 10978198]
91. Zomlefer, WB. Guide to Flowering Plant Families. Chapel Hill: University of North Carolina; 1994.

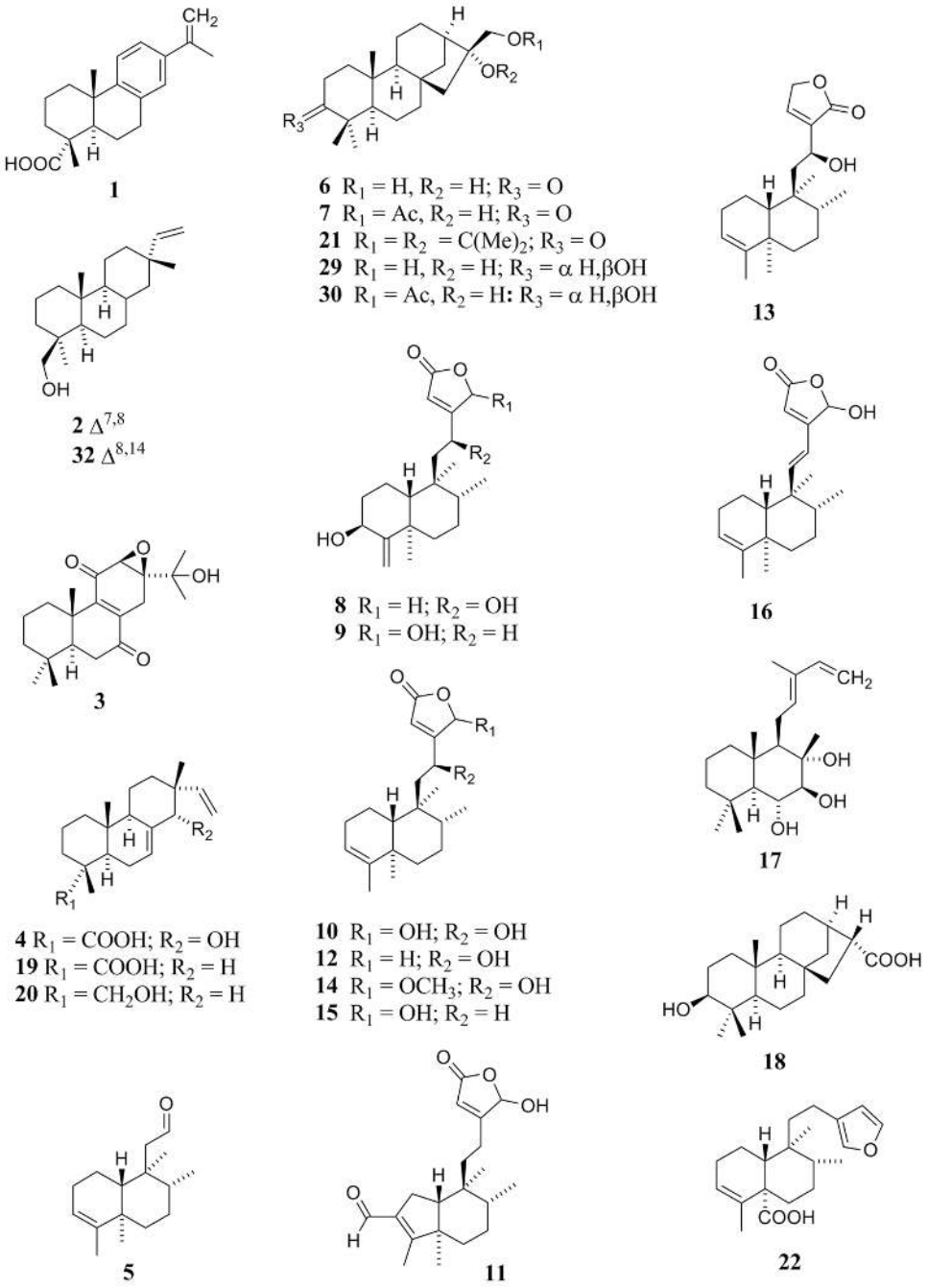


Figure 1.
Diterpenes detected or isolated from *Callicarpa* species.

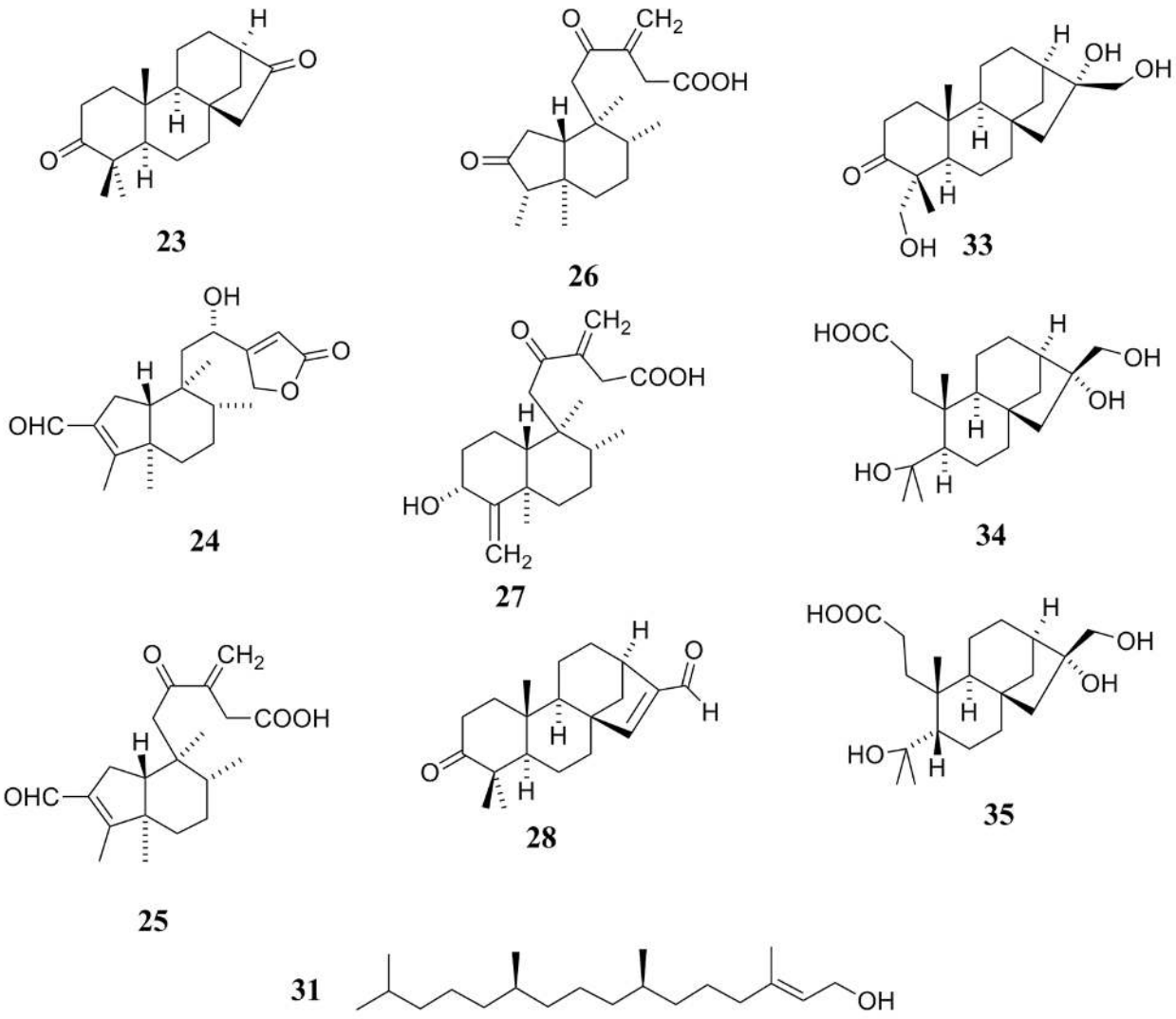
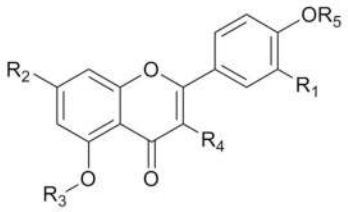
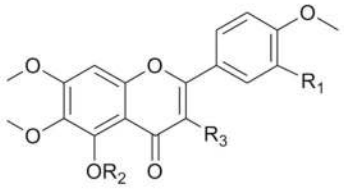


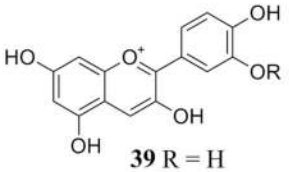
Figure 2.
Diterpenes detected or isolated from *Callicarpa* species (continued).



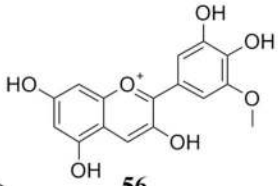


36 $R_1 = R_3 = R_4 = R_5 = H$; $R_2 = OH$
37 $R_1 = R_3 = R_4 = R_5 = H$; R_2 = O-β-D-Glucuronide
38 $R_1 = OCH_3$; $R_2 = R_3 = R_4 = H$; R_5 = O-β-D-Glucoside
40 $R_1 = OH$; R_2 = O-β-D-Glucoside; $R_3 = R_4 = R_5 = H$
41 $R_1 = R_3 = R_4 = R_5 = H$; $R_2 = OCH_3$
42 $R_1 = R_3 = R_5 = H$; $R_2 = R_4 = OCH_3$
43 $R_1 = R_5 = H$; $R_2 = OH$; $R_3 = CH_3$; $R_4 = OCH_3$
44 $R_1 = R_2 = R_4 = OCH_3$; $R_3 = R_5 = H$
45 $R_1 = R_3 = R_4 = H$; $R_2 = OCH_3$; $R_5 = CH_3$
47 $R_1 = R_2 = R_4 = OCH_3$; $R_3 = H$; $R_5 = CH_3$
49 $R_1 = R_3 = H$; $R_2 = R_4 = OCH_3$; $R_5 = CH_3$
51 $R_1 = R_2 = OH$; $R_3 = R_4 = R_5 = H$
52 $R_1 = R_2 = R_4 = OH$; $R_3 = H$; R_5 = O-β-D-Glucoside
53 $R_1 = OH$; $R_3 = R_4 = R_5 = H$; R_2 = O-β-D-Glucuronide
55 $R_1 = R_2 = R_4 = OCH_3$; $R_3 = R_5 = CH_3$
57 $R_1 = R_2 = OCH_3$; $R_4 = H$; $R_3 = R_5 = CH_3$

46 $R_1 = R_2 = H$; $R_3 = OCH_3$
48 $R_1 = OCH_3$; $R_2 = R_3 = H$
50 $R_1 = R_2 = R_3 = H$



39 R = H
54 R = CH_3



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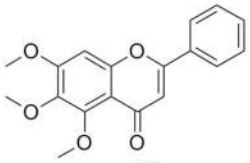

58

Figure 3.
Flavonoids detected or isolated from *Callicarpa* species.

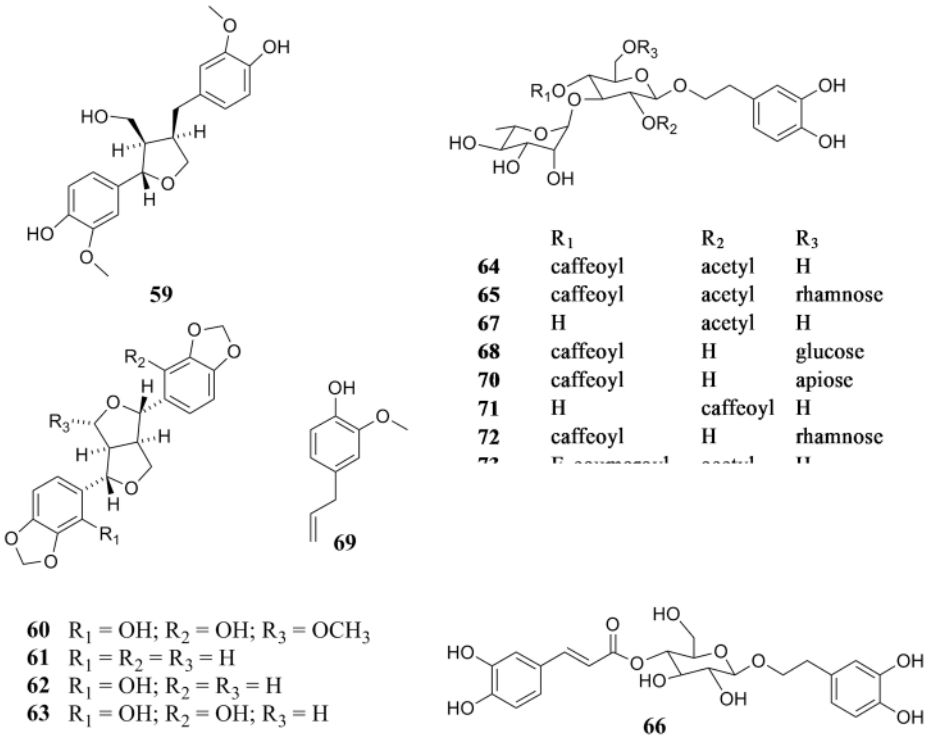

Figure 4.
Phenylethanoids and phenyl propanoids detected or isolated from *Callicarpa* species (including lignans).

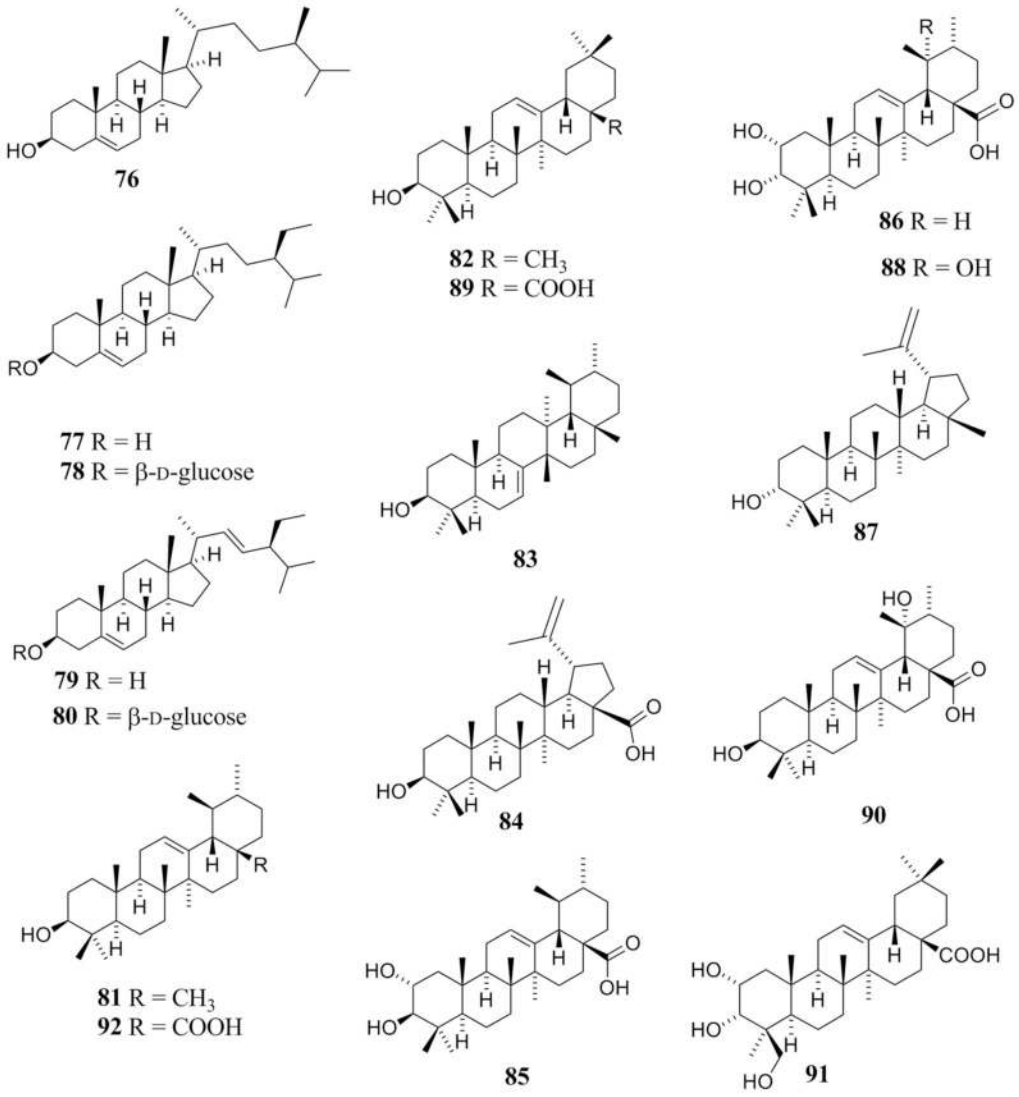

Figure 5.
Triterpenes and phytosterols detected or isolated from *Callicarpa* species.

Table 1

Ethnobotanical uses of the plants in the genus *Callicarpa*

Species	Part Used	Country	Use	Reference
C. americana L.	Bark	United States	Fever	[17]
	Leaves	United States	Dropsy	[64]
	Roots	United States	Skin cancer	[28]
	Roots	United States	Dysentery	[81]
	Roots and berries	United States	Colic	[58]
	Roots and branches	United States	Fever, malaria, rheumatism	[58]
C. arborea Roxb.	Bark	India	Skin disease	[68]
	Bark	Nepal	Fever	[51]
	Bark juice	Nepal	Indigestion	[50]
C. bodinieri H.Lév.	Leaves	China	Wounds	[56]
C. cana L.	Not stated	Papua New Guinea	Antifertility	[61,88]
C. candicans (Burm. f.) Hochr.	Leaves	Palau Islands, Philippines	Fish poison	[55]
	Leaves	Malaysia	Emmenagogue	[24]
C. cathayana Chang	Leaves	China	Wounds	[56]
C. flavida Elmer	Bark	Philippines	Toothache	[48]
C. formosana Rolfe	Entire plant	Taiwan	Hepatitis	[47]
	Not stated	Taiwan	Oral infections, intestinal and stomach disorders	[15]
	Leaves	China	Wounds	[56]
C. giraldii Hesse ex Rehder	Leaves	China	Wounds	[56]
C. giraldii Hesse ex Rehder var. *lyi* (Levl.) C.Y.Wu	Leaves	China	Wounds	[56]
C. integerrima Champ. ex Benth.	Leaves	China	Wounds	[56]
C. japonica Thunb.	Leaves	China	Wounds	[56]
	Leaves	Japan	Fish poison	[32]
C. kochiana Makino	Leaves	China	Wounds	[56]
C. lanata L. (*C. tomentosa* Murr.)[a]	Leaves	India	Anthelmintic	[8]
	Fresh roots	Bangladesh	Fever, malaria	[2]
C. lingii Merr.	Leaves	China	Wounds	[56]
C. longifolia Lam.	Leaves	China	Wounds	[56]
	Not stated	Papua New Guinea	Antifertility	[88]
C. longissima Merr.	Leaves	China	Wounds	[56]
C. macrophylla Vahl.	Fruit juice	Nepal	Fever	[53]
	Leaves	China	Wounds	[56]
	Leaves (smoked)	India	Headache	[84]
	Not stated	China	Fever	[46]
	Fresh roots	India	Fever, mouth ulcers, cough	[35]
	Roots	Nepal	Oral infection	[52]
	Root juice	Nepal	Indigestion	[49]
	Seeds		Infections, rheumatism	[1]
C. pedunculata R.Br.	Not stated	Papua New Guinea	Antifertility	[88]
C. purpurea Juss. (*C. dichotoma* Raeusch.)[a]	Leaves	China	Wounds	[56]
C. reevesii Wall. (*C. nudiflora* Hook. et Arn.)[a]	Leaves	China	Wounds	[56]
C. rubella Lindl.	Bark	India	Tumors of the large intestine	[25]
	Leaves	China	Wounds	[56]
	Entire plant	China	Burns	[71]
Callicarpa sp.[b]	Leaves	Papua New Guinea	Shoulder pain	[31]
Callicarpa sp.[b]	Not stated	Papua New Guinea	Body pain	[61]
Callicarpa sp.[b]	Leaves	Papua New Guinea	Antifertility	[26]
Callicarpa sp.[b]	Leaves	Papua New Guinea	Antifertility	[20]
Callicarpa sp.[b]	Leaves and twigs	Papua New Guinea	Antifertility	[61]

[a] The botanical binomial in parentheses is listed as a synonym for the preceding species name listed in the "International Plant Names Index" online database.

[b] Only the genus was identified in the cited reference.

Table 2

Summary of phytochemical screening of extracts of Callicarpa species

Species	Plant Part	Results	Reference
C. angustifolia King & Gamble	Leaves and twigs	Alkaloids present	[9]
C. bodinieri H.Lév.	Leaves	Flavonoids present	[80]
C. candicans (Burm. f.) Hochr.	Not stated	Alkaloids absent	[24]
	Not stated	Essential oils	[24]
	Not stated	Flavonoids present	[24]
	Not stated	Saponins absent	[24]
	Not stated	Terpenoids present	[24]
C. lanata [a]	Twigs	Alkaloids absent	[62]
	Twigs	Saponins absent	[62]
C. macrophylla Vahl.	Aerial parts	Tannins present (hide test)	[4]
C. tomentosa [a]	Leaves	Flavonoids present	[80]
C. tomentosa [a]	Leaves and twigs	Alkaloids absent	[37]
	Leaves and twigs	Flavonoids absent	[37]
	Leaves and twigs	Saponins absent	[37]
C. reevesii Wall. (*C. nudiflora* Hook. et Arn.) [b]	Not stated	Tannins present	[71]

[a] Taxonomic authority not stated in the cited publication.

[b] The botanical binomial in parentheses is listed as a synonym for the preceding species name listed in the “International Plant Names Index” online database.

Table 3

Phytochemical constituents of the genus *Callicarpa*

Compound Type/Name	Species Studied	Plant Part	Reference
Amino Acids			
Alanine	*C. japonica* Thunb.	Fruits	[60]
Aspartic acid	*C. japonica* Thunb.	Fruits	[60]
Glycine	*C. japonica* Thunb.	Fruits	[60]
Serine	*C. japonica* Thunb.	Fruits	[60]
Threonine	*C. japonica* Thunb.	Fruits	[60]
Benzenoids			
Salicylic acid	*C. integerrima* Champ. ex Benth.	Entire plant	[87]
Syringic acid	*C. integerrima* Champ. ex. Benth	Entire plant	[87]
Vanillic acid	*C. integerrima* Champ. ex Benth.	Entire plant	[87]
Carbohydrates			
D-Glucose	*C. japonica* Thunb.	Fruits	[60]
myo -Inositol	*C. pedunculata* R.Br.	Entire plant	[34]
Diterpenenoids [Fig. (1) and Fig. (2)]			
Abieta-8,11,13,15-tetraen-18-oic acid (**1**)	*C. pedunculata* R.Br.	Entire plant	[34]
	C. pedunculata R.Br.	Leaves	[33]
Akhdarenol (**2**)	*C. acuminata* H.B.K.	Leaves	[3]
Callicarpone (**3**)	*C. candicans* (Burm. f.) Hochr.	Leaves	[40]
Calliphyllin (**4**)	*C. macrophylla* Vahl.	Leaves	[79]
	C. pedunculata R.Br.	Leaves	[33]
Callicarpenal (**5**)	*C. americana* L.	Leaf essential oil	[11]
	C. japonica Thunb.	Leaf essential oil	[11]
Calliterpenone (**6**)	*C. americana* L.	Fruits, leaves, and twigs	[36]
	C. furfuracea Ridl.	Leaves	[70]
	C. longifolia Lam.	Leaves	[76]
	C. macrophylla Vahl.	Aerial parts	[13]
	C. macrophylla Vahl.	Leaves	[72,76]
	C. macrophylla Vahl.	Seeds	[1]
	C. pedunculata R.Br.	Entire plant	[34]
	C. pedunculata R.Br.	Leaves	[33]
Calliterpenone-17-acetate (**7**)	*C. furfuracea* Ridl.	Leaves	[70]
	C. longifolia Lam.	Leaves	[76]
	C. macrophylla Vahl.	Aerial parts	[13]
	C. macrophylla Vahl.	Leaves	[72,76]
	C. macrophylla Vahl.	Seeds	[1]
3β,12(*S*)-Dihydroxycleroda-4(18),13-dien-15,16-olide (**8**)	*C. americana* L.	Fruits, leaves, and twigs	[36]
3β,16ξ-Dihydroxycleroda-4(18),13-dien-15,16- olide (**9**)	*C. americana* L.	Fruits, leaves, and twigs	[36]
12(*S*),16ξ-Dihydroxycleroda-3,13-dien-15,16- olide (**10**)	*C. americana* L.	Fruits, leaves, and twigs	[36]
2-Formyl-16ξ-hydroxy-3-A-norcleroda-2,13-dien-15,16-olide (**11**)	*C. americana* L.	Fruits, leaves, and twigs	[36]
12(*S*)-Hydroxycleroda-3,13-dien-15,16-olide (**12**)	*C. americana* L.	Fruits, leaves, and twigs	[36]
12(*S*)-Hydroxycleroda-3,13-dien-16,15-olide (**13**)	*C. americana* L.	Fruits, leaves, and twigs	[36]
12(*S*)-Hydroxy-16ξ-methoxycleroda-3,13-dien-15,16-olide (**14**)	*C. americana* L.	Fruits, leaves, and twigs	[36]
16ξ-Hydroxycleroda-3,13-dien-15,16-olide (**15**)	*C. americana* L.	Fruits, leaves, and twigs	[36]
16ξ-Hydroxycleroda-3,11(*E*),13-trien-15,16-olide (**16**)	*C. americana* L.	Fruits, leaves, and twigs	[36]
6α-Hydroxynidorellol (**17**)	*C. pedunculata* R.Br.	Entire plant	[34]
	C. pedunculata R.Br.	Leaves	[33]
3β-Hydroxyphyllocladan-17-oic acid (**18**)	*C. furfuracea*	Leaves	[70]
Isopimaric acid (**19**)	*C. acuminata* H.B.K.	Leaves	[3]
	C. pedunculata R.Br.	Entire plant	[33]
Isopimarol (**20**)	*C. japonica* Thunb.	Leaf essential oil	[42]
16α,17-Isopropylideno-3-oxophyllocladane (**21**)	*C. macrophylla* Vahl.	Leaves	[72]
Maingayic acid (**22**)	*C. maingayi* King & Gamble	Leaves	[59]
17-Norphyllocladane-3,16-dione (**23**)	*C. furfuracea* Ridl.	Leaves	[70]
Pentandralactone (**24**)	*C. pentandra* Roxb.	Leaves	[90]
Pentandranoic acid A (**25**)	*C. pentandra* Roxb.	Leaves	[90]
Pentandranoic acid B (**26**)	*C. pentandra* Roxb.	Leaves	[90]
Pentandranoic acid C (**27**)	*C. pentandra* Roxb.	Leaves	[90]
Phylloclad-15-en-3,17-dione (**28**)	*C. furfuracea* Ridl.	Leaves	[70]
3β,16β-Phyllocladane-3,16,17-triol (**29**)	*C. furfuracea* Ridl.	Leaves	[70]
3β,16β-Phyllocladane-3,16,17-triol-17-acetate (**30**)	*C. furfuracea* Ridl.	Leaves	[70]
Phytol (**31**)	*C. japonica* Thunb.	Leaves and twigs	[86]
Sandaracopimaradien-19-ol (**32**)	*C. acuminata* H.B.K.	Leaves	[3]
16α,17,19-Trihydroxyphyllocladan-3-one (**33**)	*C. furfuracea* Ridl.	Leaves	[70]
4,16α,17-Trihydroxy-3,4-secophyllocladan-3-oic acid (**34**)	*C. furfuracea* Ridl.	Leaves	[70]
5β,16α-4,16,17-Trihydroxy-3,4-secophyllocladan-3-oic acid (**35**)	*C. furfuracea* Ridl.	Leaves	[70]
Flavonoids [Fig. (3)]			

Compound Type/Name	Species Studied	Plant Part	Reference
Apigenin (**36**)	*C. longifolia* Lam.	Leaves	[76]
	C. macrophylla Vahl.	Leaves	[76]
Apigenin-7-*O* -β-D-glucuronide (**37**)	*C. longifolia* Lam.	Leaves	[76]
	C. macrophylla Vahl.	Leaves	[76]
Chrysoeriol-4′-*O* -β-D-glucoside (**38**)	*C. bodinieri* H.Lév.	Entire plant	[66]
Cyanidin (**39**)	*C. bodinieri* H.Lév.	Fruits	[19]
	C. purpurea Juss.	Fruits	[19]
Cynaroside (**40**)	*C. bodinieri* H.Lév.	Entire plant	[66]
5,4′-Dihydroxy-7-methoxyflavone (Genkwanin) (**41**)	*C. americana* L.	Fruits, leaves, and twigs	[36]
5,4′-Dihydroxy-3,7-dimethoxyflavone (**42**)	*C. macrophylla* Vahl.	Leaves	[79]
7,4′-Dihydroxy-3,5-dimethoxyflavone (**43**)	*C. pedunculata* R.Br.	Entire plant	[34]
5,4′-Dihydroxy-3,7,3′-trimethoxyflavone (**44**)	*C. macrophylla* Vahl.	Leaves	[14,79]
5-Hydroxy-7,4′-dimethoxyflavone (**45**)	*C. americana* L.	Fruits, leaves, and twigs	[36]
5-Hydroxy-3,6,7,4′-tetramethoxyflavone (**46**)	*C. bodinieri* H.Lév.	Leaves	[67]
5-Hydroxy-3,7,3′,4′-tetramethoxyflavone (**47**)	*C. formosana* Rolfe	Leaves	[15]
5-Hydroxy-6,7,3′,4′-tetramethoxyflavone (**48**)	*C. integerrima* Champ. ex Benth.	Entire plant	[87]
5-Hydroxy-3,7,4′-trimethoxyflavone (**49**)	*C. formosana* Rolfe	Leaves	[15]
	C. pedunculata R.Br.	Entire plant	[34]
5-Hydroxy-6,7,4′-trimethoxyflavone (**50**)	*C. acuminata* H.B.K.	Leaves	[3]
	C. americana L.	Fruits, leaves, and twigs	[36]
Luteolin (**51**)	*C. longifolia* Lam.	Leaves	[76]
	C. macrophylla Vahl.	Leaves	[76]
Luteolin-4′-*O* -β-D-glucoside (**52**)	*C. bodinieri* H.Lév.	Entire plant	[66]
Luteolin-7-*O* -β-D-glucuronide (**53**)	*C. longifolia* Lam.	Leaves	[76]
	C. macrophylla Vahl.	Leaves	[76]
Paeonidin (**54**)	*C. bodinieri* H.Lév.	Fruits	[19]
	C. purpurea Juss.	Fruits	[19]
3,5,7,3′,4′-Pentamethoxyflavone (**55**)	*C. formosana* Rolfe	Leaves	[15]
Petunidin (**56**)	*C. purpurea* Juss.	Fruits	[19]
5,7,3′,4′-Tetramethoxyflavone (**57**)	*C. formosana* Rolfe	Leaves	[15]
5,6,7-Trimethoxyflavone (**58**)	*C. japonica* Thunb.	Not stated	[29,32]
Lignans [Fig. (4)]			
Lariciresinol (**59**)	*C. furfuracea* Ridl.	Leaves	[70]
9α-Methoxysesamin-2,2′-diol (**60**)	*C. furfuracea* Ridl.	Leaves	[70]
(+)-Sesamin (**61**)	*C. furfuracea* Ridl.	Leaves	[70]
(+)-Sesamin-2-ol (**62**)	*C. furfuracea* Ridl.	Leaves	[70]
Sesamin-2,2′-diol (**63**)	*C. furfuracea* Ridl.	Leaves	[70]
Lipids			
Arachidic acid	*C. japonica* Thunb.	Fruits	[60]
(*E*)-2-Hexenal	*C. americana* L.	Leaf essential oil	[42,82]
Lauric acid	*C. japonica* Thunb.	Fruits	[60]
Linoleic acid	*C. japonica* Thunb.	Fruits	[60]
Myristic acid	*C. japonica* Thunb.	Fruits	[60]
1-Octen-3-ol	*C. americana* L.	Leaf essential oil	[42,82]
Oleic acid	*C. japonica* Thunb.	Fruits	[60]
Palmitic acid	*C. japonica* Thunb.	Fruits	[60]
Pentatetracontanoic acid	*C. bodinieri* H.Lév.	Leaves	[67]
N -Pentatriacontane	*C. bodinieri* H.Lév.	Leaves	[67]
Stearic acid	*C. japonica* Thunb.	Fruits	[60]
N -Triacontane	*C. integerrima* Champ. ex Benth.	Entire plant	[87]
Monoterpenoids			
Nopinone	*C. americana* L.	Leaf essential oil	[82]
α-Pinene	*C. americana* L.	Leaf essential oil	[42,82]
β-Pinene	*C. americana* L.	Leaf essential oil	[42,82]
Phenylpropanoids and Phenylethanoids [Fig. (4)]			
2′-Acetylverbascoside (2′-acetylacteoside) (**64**)	*C. purpurea* Juss. (*C. dichotoma* Raeusch.)[a]	Leaves and twigs	[43]
Brandioside (**65**)	*C. purpurea* Juss. (*C. dichotoma* Raeusch.)[a]	Leaves and twigs	[43]
Calceolarioside A (**66**)	*C. bodinieri* H.Lév.	Leaves	[80]
Cistanoside H (**67**)	*C. purpurea* Juss. (*C. dichotoma* Raeusch.)[a]	Leaves and twigs	[43]
Echinacoside (**68**)	*C. purpurea* Juss. (*C. dichotoma* Raeusch.)[a]	Leaves and twigs	[43]
Eugenol (**69**)	*C. japonica* Thunb.	Leaf essential oil	[42]
Forsythoside B (**70**)	*C. purpurea* Juss. (*C. dichotoma* Raeusch.)[a]	Leaves and twigs	[43]
Isoverbascoside (isoacteoside) (**71**)	*C. bodinieri* H.Lév.	Leaves	[80]

Compound Type/Name	Species Studied	Plant Part	Reference
	C. purpurea Juss. (*C. dichotoma* Raeusch.)[a]	Leaves and twigs	[43]
Poliumoside (**72**)	*C. purpurea* Juss. (*C. dichotoma* Raeusch.)[a]	Leaves and twigs	[43]
E -Tubuloside E (**73**)	*C. purpurea* Juss. (*C. dichotoma* Raeusch.)[a]	Leaves and twigs	[43]
Z -Tubuloside E (**74**)	*C. purpurea* Juss. (*C. dichotoma* Raeusch.)[a]	Leaves and twigs	[43]
Verbascoside (acteoside) (**75**)	*C. bodinieri* H.Lév.	Leaves	[80]
	C. tomentosa[b]	Leaves	[80]
	C. purpurea Juss. (*C. dichotoma* Raeusch.)[a]	Leaves and twigs	[43]
Sesquiterpenoids			
Bicyclogermacrene	*C. japonica* Thunb.	Leaf essential oil	[42]
α-Cadinol	*C. americana* L.	Leaf essential oil	[42,82]
Camphor (juniper camphor)	*C. japonica* Thunb.	Leaf essential oil	[42]
Caryophyllene oxide	*C. americana* L.	Leaf essential oil	[82]
Curcuphenol	*C. japonica* Thunb.	Leaf essential oil	[42]
β-Elemene	*C. japonica* Thunb.	Leaf essential oil	[42]
γ-Elemene	*C. japonica* Thunb.	Leaf essential oil	[42]
δ-Elemene	*C. japonica* Thunb.	Leaf essential oil	[42]
7-*epi* -α-Eudesmol	*C. americana* L.	Leaf essential oil	[42,82]
Germacrene B	*C. japonica* Thunb.	Leaf essential oil	[42]
Germacrene D	*C. japonica* Thunb.	Leaf essential oil	[42]
Globulol	*C. japonica* Thunb.	Leaf essential oil	[42]
α-Guaiene	*C. japonica* Thunb.	Leaf essential oil	[42]
α-Humulene	*C. americana* L.	Leaf essential oil	[11,42,82]
	C. japonica Thunb.	Leaf essential oil	[11]
Humulene epoxide II	*C. americana* L.	Leaf essential oil	[11,42,82]
	C. japonica Thunb.	Leaf essential oil	[11]
Intermediol	*C. americana* L.	Leaf essential oil	[11]
	C. japonica Thunb.	Leaf essential oil	[11]
Khusinol	*C. americana* L.	Leaf essential oil	[82]
Ledol	*C. japonica* Thunb.	Leaf essential oil	[42]
Selin-11-en-4-α-ol	*C. japonica* Thunb.	Leaf essential oil	[42]
α-Selinene	*C. americana* L.	Leaf essential oil	[42,82]
7-*epi* -α-Selinene	*C. americana* L.	Leaf essential oil	[42,82]
Seychellene	*C. japonica* Thunb.	Leaf essential oil	[42]
Spathulenol	*C. japonica* Thunb.	Leaf essential oil	[11,42]
Valencene	*C. americana* L.	Leaf essential oil	[42,82]
Viridiflorol	*C. japonica* Thunb.	Leaf essential oil	[42]
Phytosterols [Fig. (5)]			
Campesterol (**76**)	*C. japonica* Thunb.	Fruits	[60]
β-Sitosterol (**77**)	*C. arborea*[b]	Bark	[68]
	C. arborea[b]	Leaves	[14,69]
	C. bodinieri H.Lév.	Entire plant	[66]
	C. formosana Rolfe	Leaves	[15]
	C. integerrima Champ. ex Benth.	Entire plant	[87]
	C. japonica Thunb.	Fruits	[60]
	C. macrophylla Vahl.	Leaves	[79]
	C. pedunculata R.Br.	Entire plant	[34]
β-Sitosterol-d-glucoside (**78**)	*C. formosana* Rolfe	Leaves	[15]
Stigmasterol (**79**)	*C. bodinieri* H.Lév.	Leaves	[67]
	C. formosana Rolfe	Leaves	[15]
	C. japonica Thunb.	Fruits	[60]
Stigmasterol-D-glucoside (**80**)	*C. formosana* Rolfe	Leaves	[15]
Triterpenoids [Fig. (5)]			
α-Amyrin (**81**)	*C. acuminata* H.B.K.	Leaves	[3]
	C. bodinieri H.Lév.	Leaves	[67]
β-Amyrin (**82**)	*C. pedunculata* R.Br.	Fruits	[23]
	C. pedunculata R.Br.	Entire plant	[34]
Bauerenol (**83**)	*C. arborea*[b]	Bark	[68]
Betulinic acid (**84**)	*C. arborea*[b]	Bark	[68]
	C. bodinieri H.Lév.	Entire plant	[66]
	C. macrophylla Vahl.	Leaves	[79]
Corosolic acid (**85**)	*C. bodinieri* H.Lév.	Entire plant	[65]
	C. pentandra Roxb.	Leaves	[90]
2α,3α-Dihydroxyurs-12-en-28-oic acid (**86**)	*C. bodinieri* H.Lév.	Entire plant	[65]

Compound Type/Name	Species Studied	Plant Part	Reference
	C. formosana Rolfe	Leaves	[15]
	C. pentandra Roxb.	Leaves	[90]
Epilupeol (**87**)	*C. arborea* [b]	Leaves	[69]
Euscaphic acid (**88**)	*C. americana* L.	Fruits, leaves, and twigs	[36]
	C. bodinieri H.Lév.	Entire plant	[65]
Oleanolic acid (**89**)	*C. macrophylla* Vahl.	Seeds	[1]
Pomolic acid (**90**)	*C. pentandra* Roxb.	Leaves	[90]
2α,3α,24-Trihydroxyolean-12-en-28-oic acid (**91**)	*C. bodinieri* H.Lév.	Entire plant	[65]
Ursolic acid (**92**)	*C. arborea* [b]	Leaves	[14,69]
	C. bodinieri H.Lév.	Entire plant	[66]
	C. formosana Rolfe	Leaves	[15]
	C. longifolia Lam.	Leaves	[76]
	C. pedunculata R.Br.	Fruits	[23]
	C. pedunculata R.Br.	Entire plant	[34]
	C. pentandra Roxb.	Leaves	[90]

[a] The botanical binomial in parentheses is listed as a synonym for the preceding species name listed in the “International Plant Names Index” online database.

[b] The taxonomic authority was not stated in the cited publication.

Table 4

Biological evaluation of extracts of species of *Callicarpa*

Species	Part Used	Biological Activity	Reference
C. acuminata H.B.K.	Leaves	Plant growth inhibition	[3]
C. americana L.	Freeze-dried leaves	Inactive against several viruses in plaque-inhibition assays	[85]
	Leaves	Insect oviposition deterrent	[83]
	Fresh leaf essential oil	Antialgal	[82]
	Fresh leaf essential oil	Mosquito bite deterrent	[11]
	Fruits, leaves, and twigs	Cytotoxic activity	[36]
C. arborea Roxb. var. *oblongifolia*	Aerial parts	Inactive against 9KB cells at 20 Rg/mL	[7]
		Diuretic	[7]
C. cana [a]	Fruits, leaves, and twigs	Fish poison	[74]
C. cana L. (*C. erioclona*)[b]	Bark	Antibacterial	[16]
C. formosana Rolfe	Leaves	Insect feeding deterrent	[86]
	Not stated	Monocyte antiproliferation	[44]
	Not stated	Inactive in antiproliferation and no effect on IL-1β and TNF-α levels	[45]
	Twigs	Insect feeding deterrent	[86]
C. furfuracea Ridl.	Bark	Antibacterial	[16]
C. fulvohirsuta Merr.	Bark	Antibacterial	[16]
C. havilandii H.J.Lam	Bark and leaves, separately	Antibacterial	[16]
C. japonica Thunb.	Aerial parts	Antiviral activity	[89]
	Entire plant	Insect feeding deterrent	[86]
	Leaves	Phytotoxic	[42]
C. lanata L.	Aerial parts	Inactive against 9KB cells at 20 μg/mL; LD_{50} >1000 mg/kg (i.p., mice)	[21]
C. longifolia Lam.	Leaves	Inactive against *Staphylococcus aureus*	[16]
C. macrophylla Vahl.	Aerial parts	Inactive against 9KB cells at 20 Rg/mL	[7]
	Leaves	Antibacterial	[73]
		Antifungal	[73]
C. pilosissima Maxim.	Dried entire plant	Inactive against Colon 38 tumor	[77]
		Weakly active against P388 tumor	[77]
		Inactive against melanoma-B16 tumor	[77]
		Inactive against 9KB cells	[77]
C. stapfii H.N. Moldenke	Bark and leaves, separately	Antibacterial	[16]

[a] Taxonomic authority not stated in the cited publication.

[b] The botanical binomial in parentheses is listed as a synonym for the preceding species name listed in the “International Plant Names Index” online database.

Table 5

Cytotoxic activity of compounds isolated from *Callicarpa americana* [a,b]

Compound Code	Cell Line[c,d]					
	MCF-7	Lu1	Col2	LNCaP	hTERT-RPE1	HUVEC
10	-	2.4	2.3	4.1	1.9	1.8
11	3.9	8.7	9	4.5	1.9	9.8
13	2.8	2.9	-	3.3	-	-
15	3.5	3.7	-	3.3	-	4.1
16	2.7	2.6	-	2.5	-	1.2
41	-	>20	>20	>20	3.9	>20

[a] Compounds **6**, **8**, **9**, **12**, **14**, **45**, **50**, and **88** were inactive in the cell lines tested.

[b] Adapted from [36].

[c] Cell lines: MCF-7 = breast cancer; Lu1 = lung cancer; Col2 = colon cancer; LNCaP = hormone-dependent prostate cancer; hTERT-RPE1 = human telomerase reverse-transcriptase retinal pigment epithelium; HUVEC = human umbilical vein epithelial cells.

[d] ED_{50} values are given in μg/mL, and values <5 μg/mL are considered to be active.