

Review Article

## A Review on Chemical Constituents and Pharmacological Action of the Genus *Lindera* (Lauraceae)

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### ABSTRACT

The genus *Lindera* consists of approximately 100 species that are widely distributed in tropical and subtropical areas throughout the world. It is represented by widely well-known medicinal and aromatic plants that produce various phytochemicals with potential pharmacological actions. This review attempts to summarize the information on the phytochemicals of *Lindera* species together with their biological properties. The data and information were collected via an electronic search engine which are Scopus, ScienceDirect, Google Scholar, PubMed, and SciFinder. Sesquiterpenes represent the major chemical compounds that have been characterised in *Lindera* species, as well as alkaloids, flavonoids, and phenolics. These compounds were shown to possess anticancer, antifibrotic, anti-inflammatory, antitumor, antioxidant, anti-arthritic, cytotoxic, antiallergic, and antihyperlipidemic properties. The outcome of these studies will further support the therapeutic potential of the genus *Lindera* and provide convincing evidence for its future clinical applications in modern medicine.

**Keywords:** *Lindera*, Lauraceae, sesquiterpenes, phytochemicals, pharmacology

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### 1. INTRODUCTION

Natural products are chemical substances produced by living organisms, predominantly plants. Medicinal plants have historically been utilized to treat various ailments and are considered potential sources for pharmaceuticals. Initially, the ancient medical is based on empirical observations of herbs and natural remedies, and now natural products have undergone millions of years of evolution and chemical diversification, which has led to a variety of biological activities and drug-like qualities (Maria & Christoph, 2020). According to earlier research, the presence of specific phytochemicals has proven to be an effective treatment for a better quality of life. For instance, *Centella asiatica* leaf contains active ingredients, kaempferol and quercetin that can treat skin damage and improve blood circulation (Gray et al., 2018). In addition, *Marinda citrifolia* has the active compounds,

scopoletin and rutin, which can act as antioxidant, anticancer, and anti-inflammatory agents (Jamaludin et al., 2021).

Lauraceae family, considered one of the most ancient plant families within the Magnoliidae subclass, predominantly across Southeast Asia, Madagascar, northern South America, and the east coast of Brazil. In Malaysia, it is known as ‘medang’ that contributes around 213 species from 16 genera, while China hosts 25 genera and 445 species. Identified by specific floral morphology including smooth bark with aromatic sap, plain leaves arranged oppositely, spirally, or alternately, and small, fragrant, trimerous flowers, often with six sepals. Many of its species are utilized for spices, perfume oils, and medicines in traditional practices, such as *Laurus nobilis* for digestive disorders (Alejo Armijo et al., 2017), *Cinnamomum verum* for respiratory and digestive issues (Ranasinghe et al., 2013), and *Persea americana* for topical treatment of skin conditions (Nayak et al., 2008).

The genus *Lindera*, comprising approximately 80-100 species within the Lauraceae family, is distributed worldwide across the tropical, subtropical, and temperate regions of Asia and Midwestern America. *Lindera* species such as *L. aggregate*, *L. akoensis*, and *L. chunii merr* are prevalent in countries like China, Korea, Japan, India, the United States, Nepal, Vietnam, and Malaysia. Known for their aromatic leaves and bark, *Lindera* trees are utilized in traditional medicine, culinary practices, and aromatherapy. Dioecious in nature, *Lindera* species produce small, inconspicuous flowers with six tepals and tiny drupe fruits (Nakamura et al., 2021). With medicinal applications ranging from treating gastrointestinal disorders to respiratory infections, *Lindera* species like *L. radix* and *L. aggregata* hold cultural significance in traditional Chinese medicine for their ability to alleviate discomfort and promote wellness by improving qi circulation and relieving congestion (Cao et al., 2015).

However, further research is necessary to fully explore the medicinal potential of ethnobotanical plants, particularly those within the *Lindera* species, for the development of future herbal medicines and pharmaceuticals.

## **2. CHEMICAL CONSTITUENTS OF THE GENUS *Lindera***

### **2.1. Sesquiterpenes**

Sesquiterpenes (Figure 1) are found particularly in higher plants and in many other living systems. Numerous plants, including fruits, vegetables, herbs, and spices, contain sesquiterpenes. They are frequently found in plants such as chamomile, ginger, and turmeric (Dhifi et al., 2016). Besides, sesquiterpenes are commonly found in fungi and some marine organisms, and known for their diverse range of biological activities and therapeutic properties. Naturally, they occur as hydrocarbons or in oxygenated forms including lactones, alcohols, acids, aldehydes, and ketones (Lv et al., 2023). According to Scopus, there are about 874 documents that relate to *Lindera* sesquiterpenes since 1964. To date, a total of 362 sesquiterpenes have been reported, mostly isolated from the roots, leaves, flowers, and a few obtained from whole plants. Among them, germacrane-, eudesmane- and lindenane-type sesquiterpenoids account for a fairly large proportion (Feng et al., 2022). Table 1 shows several sesquiterpenes that have been isolated and identified from various *Lindera* species. Most of the compounds are reported mainly from *L. aggregata*, *L. strychnifolia*, and *L. glauca*. Furthermore, there that were 165 compounds were classify as bisobolane, elemene, eudesme, gemacrane, guaiane, as well as 46 compounds from lindenane and sesquiterpenes dimers.

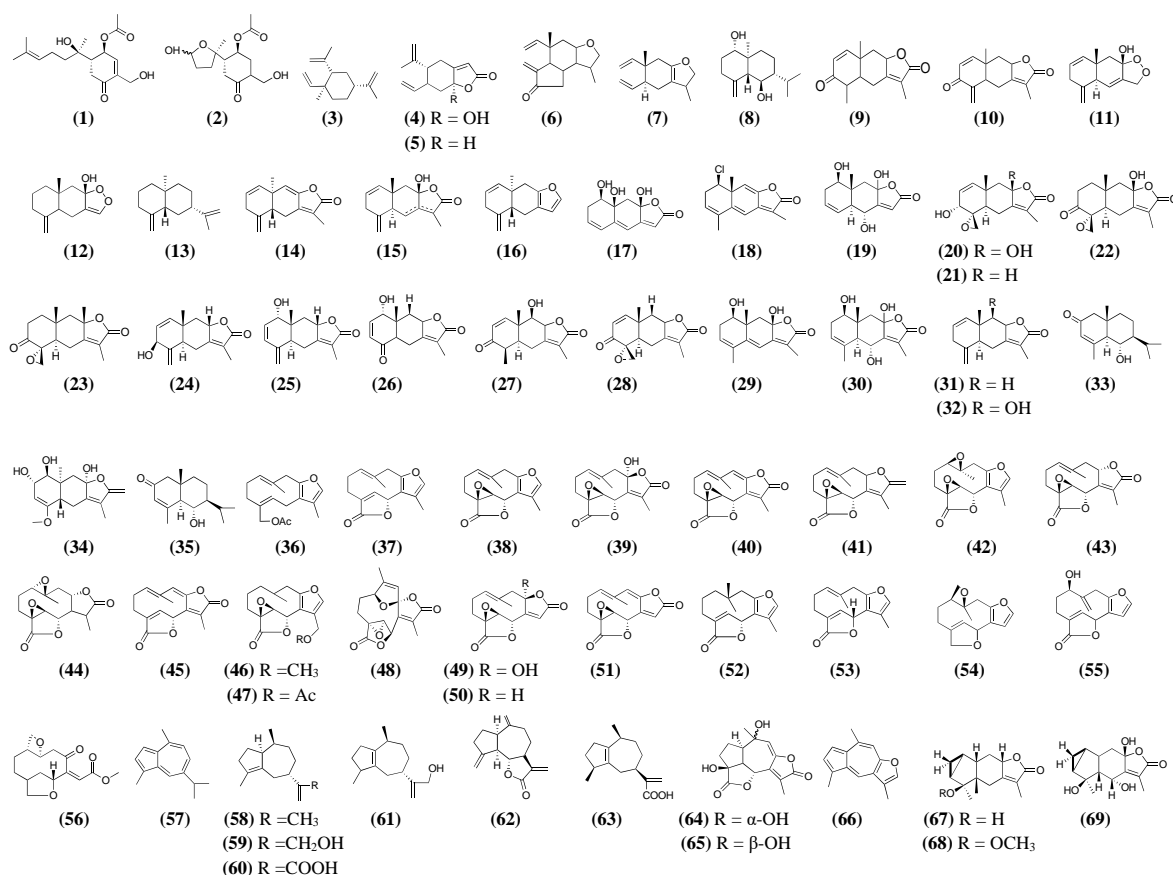
**Table 1.** Sesquiterpenes isolated from several *Lindera* species

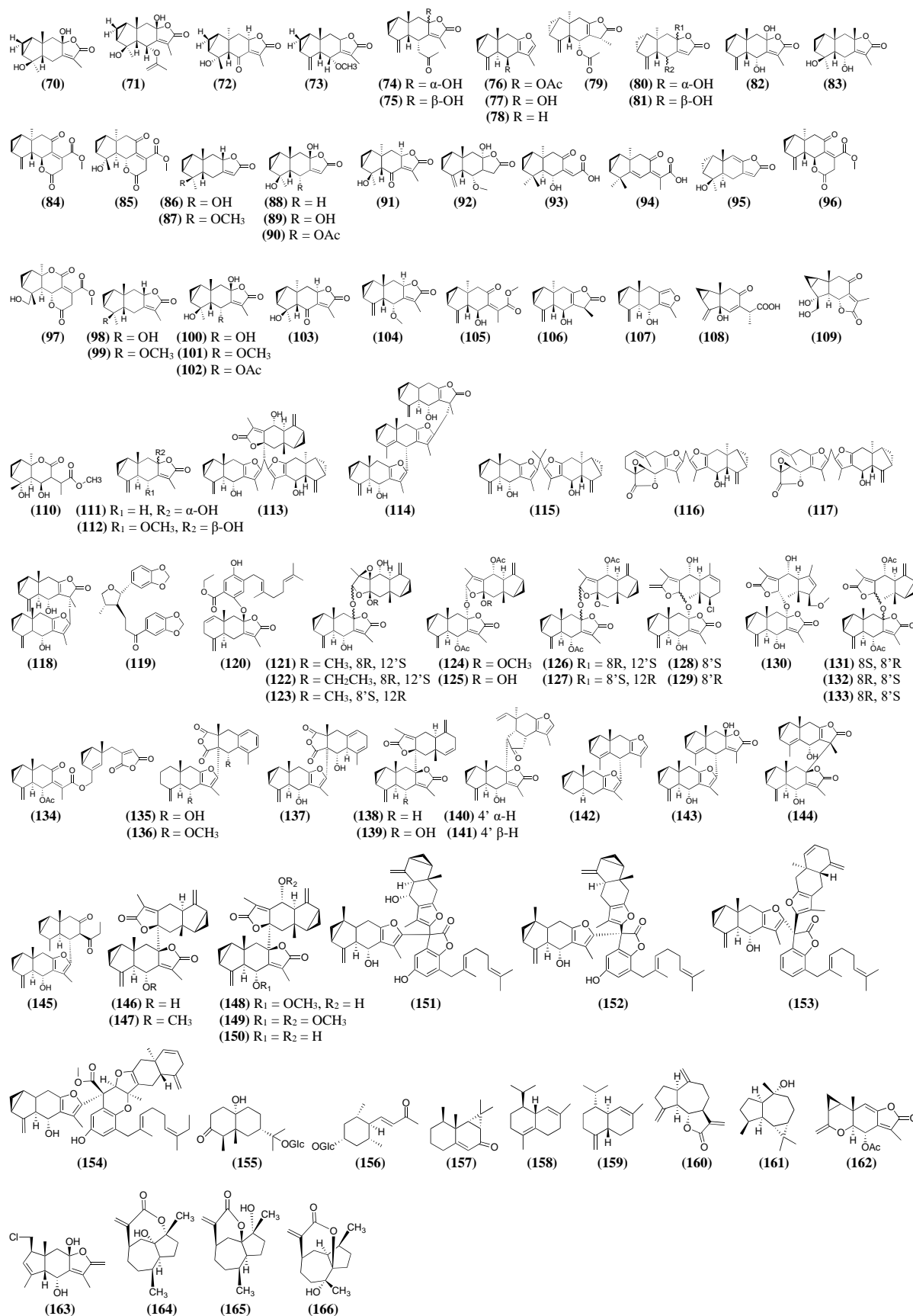
Compounds	Species	Part	References
<b>BISOBOLANE</b>			
3-(Hydroxymethyl)-6-(5-(2-hydroxypropan-2-yl)-2-methyltetrahydrofuran-2-yl)-4-oxocyclohex-2-en-1-yl acetate (1)	<i>L. blume</i>	Leaves	Ryen et al., 2020
6-(2-Hydroxy-6-methylhept-5-en-2-yl)-3-(hydroxymethyl)-4-oxocyclohex-2-en-1-yl acetate (2)	<i>L. blume</i>	Leaves	Ryen et al., 2020
<b>ELEMENE</b>			
$\beta$ -Elemene (3)	<i>L. strychnifolia</i>	Roots	Lv et al., 2023
Hydroxyisogermafurenolide (4)	<i>L. strychnifolia</i>	Roots	Gan et al., 2009b
Isogermafurenolide (5)	<i>L. strychnifolia</i>	Roots	Lv et al., 2023
Isolinderalactone (6)	<i>L. strychnifolia</i>	Roots	Yen et al., 2016
	<i>L. aggregata</i>	Roots	Yang et al., 2020b
Isogermafurene (7)	<i>L. strychnifolia</i>	Roots	Lv et al., 2023
<b>EUDESME</b>			
ent-4(15)-Eudesmene-1b,6, $\alpha$ -diol (8)	<i>L. aggregata</i>	Roots	Yang et al., 2020b
3-Oxo-4, 5 $\alpha$ H, 8 $\beta$ H-eudesma-1,7(11)-dien-8, 12-olide (9)	<i>L. strychnifolia</i>	Roots	Ohno et al., 2005
3-Oxo-5 $\alpha$ H, 8 $\beta$ H-eudesma-1,4(15), 7(11)-trien-8, 12-olide (10)	<i>L. strychnifolia</i>	Roots	Ohno et al., 2005
8-Hydroxylindestenolide (11)	<i>L. aggregata</i>	Roots	Sumioka et al., 2011
Atractylenolide III (12)	<i>L. aggregata</i>	Roots	Gan et al., 2009
Eudesma-4(14),11-diene (13)	<i>L. strychnifolia</i>	Roots	Liu et al., 2016
Dehydrolindestrenolide (14)	<i>L. aggregata</i>	Roots	Yang et al., 2020
Hydroxylindestenolide (15)	<i>L. aggregata</i>	Roots	Li et al., 2002
Lindestrene (16)	<i>L. strychnifolia</i>	Roots	Liu et al., 2013
Linderagalactone D (17)	<i>L. aggregata</i>	Roots	Wu et al., 2010
Linderagalactone E (18)	<i>L. aggregata</i>	Roots	Gan et al., 2009b
Linderaggredin A (19)	<i>L. aggregata</i>	Aerial	Kuo et al., 2020
Linderolide A (20)	<i>L. aggregata</i>	Roots	Sumioka et al., 2011
Linderolide C (21)	<i>L. aggregata</i>	Roots	Sumioka et al., 2011
Linderolide B (22)	<i>L. aggregata</i>	Roots	Sumioka et al., 2011
Linderolide D (23)	<i>L. aggregata</i>	Roots	Sumioka et al., 2011
Linderolide E (24)	<i>L. aggregata</i>	Roots	Sumioka et al., 2011
Linderolide G (25)	<i>L. aggregata</i>	Roots	Liu et al., 2013
Linderolide H (26)	<i>L. aggregata</i>	Roots	Liu et al., 2013
Linderolide I (27)	<i>L. aggregata</i>	Roots	Liu et al., 2013
Linderolide J (28)	<i>L. aggregata</i>	Roots	Liu et al., 2013
Linderagalactones D (29)	<i>L. aggregata</i>	Roots	Gan et al., 2009b
Linderagalactones E (30)	<i>L. aggregata</i>	Roots	Gan et al., 2009b
Lindestrenolide (31)	<i>L. strychnifolia</i>	Roots	Sumioka et al., 2011
	<i>L. aggregata</i>	Roots	Liu et al., 2013
Hydroxylindestrenolide (32)	<i>L. aggregata</i>	Roots	Liu et al., 2013
Linerenone (33)	<i>L. communis</i>	Fruits	Deng et al., 2011
Myrrhalindenane C (34)	<i>L. myrrha</i>	Roots	Nguyen et al., 2023
Polydactin B (35)	<i>L. communis</i>	Fruits	Deng et al., 2011
<b>GEMACRANE</b>			
Neosericenyl acetate (36)	<i>L. aggregata</i>	Roots	Lv et al., 2023
Linderalactone (37)	<i>L. strychnifolia</i>	Roots	Li et al., 2002
	<i>L. chunii</i>	Roots	Liu et al., 2013
	<i>L. aggregata</i>	Roots	Yang et al., 2020

Linderane (38)	<i>L. aggregata</i>	Roots	Wu et al., 2010
	<i>L. strychnifolia</i>	Roots	Li et al., 2002
Linderanines A (39)	<i>L. aggregata</i>	Roots	Qiang et al., 2011
Linderanines B (40)	<i>L. aggregata</i>	Roots	Qiang et al., 2011
Linderanines C (41)	<i>L. aggregata</i>	Roots	Qiang et al., 2011
Linderadine (42)	<i>L. strychnifolia</i>	Roots	Qiang et al., 2011
Lideranlide A (43)	<i>L. aggregata</i>	Roots	Qiang et al., 2011
Lideranlide B (44)	<i>L. aggregata</i>	Roots	Qiang et al., 2011
Lideranlide C (45)	<i>L. aggregata</i>	Roots	Qiang et al., 2011
Lideranlide D (46)	<i>L. aggregata</i>	Roots	Qiang et al., 2011
Lideranlide E (47)	<i>L. aggregata</i>	Roots	Qiang et al., 2011
Linderoline (48)	<i>L. strychnifolia</i>	Roots	Liu et al., 2013
Lideranine A (49)	<i>L. aggregata</i>	Roots	Qiang et al., 2011
Lideranine C (50)	<i>L. aggregata</i>	Roots	Qiang et al., 2011
Eudeglaucone (51)	<i>L. glauca</i>	Twigs	Yu et al., 2016
Neolinderane (52)	<i>L. strychnifolia</i>	Roots	Liu et al., 2013
Neolinderalactone (53)	<i>L. strychnifolia</i>	Roots	Liu et al., 2013
	<i>L. aggregata</i>	Roots	Gan et al., 2009b
Pseudoneolinderane (54)	<i>L. strychnifolia</i>	Roots	Li et al., 2002
	<i>L. chunii</i>	Roots	Zhang et al., 2002
	<i>L. aggregata</i>	Roots	Liu et al., 2021
Parvigemone (55)	<i>L. aggregata</i>	Roots	Liu et al., 2016
Neolindenenonelactone (56)	<i>L. aggregata</i>	Roots	Gan et al., 2009b
<b>GUAIANE</b>			
1,4-Dimethyl-7-ethylazulene (57)	<i>L. strychnifolia</i>	Roots	Liu et al., 2013
Aciphyllene (58)	<i>L. glauca</i>	Leaves	Nii et al., 1983
Glaucyl alcohol (59)	<i>L. glauca</i>	Roots	Nii et al., 1983
Aciphyllic acid (60)	<i>L. glauca</i>	Roots	Nii et al., 1983
Aciphyllyl alcohol (61)	<i>L. glauca</i>	Leaves	Nii et al., 1983
Dehydrocostuslactone (62)	<i>L. aggregata</i>	Roots	Wen et al., 2021
Glaucic acid (63)	<i>L. glauca</i>	Roots	Nii et al., 1983
Lindenanolides C (64)	<i>L. aggregata</i>	Roots	Wen et al., 2021
Lindenanolides D (65)	<i>L. aggregata</i>	Roots	Wen et al., 2021
Linderazulene (66)	<i>L. strychnifolia</i>	Roots	Lv et al., 2023
<b>LINDENANE</b>			
(1 <i>R</i> , 3 <i>S</i> , 4 <i>R</i> , 5 <i>S</i> , 8 <i>S</i> , 10 <i>S</i> )-4-Hydroxy-1,3-cycloedesma-7(11)-en-12,8-olide (67)	<i>L. strychnifolia</i>	Roots	Liu et al., 2016
(1 <i>R</i> , 3 <i>S</i> , 4 <i>R</i> , 5 <i>R</i> , 8 <i>S</i> , 10 <i>S</i> )-4-Methoxy-1,3-cycloedesma-7(11)-en-12,8-olide (68)	<i>L. strychnifolia</i>	Roots	Liu et al., 2016
(1 <i>R</i> , 3 <i>S</i> , 4 <i>R</i> , 5 <i>R</i> , 8 <i>S</i> , 10 <i>S</i> )-4,8-Dihydroxy-1,3-cycloedesma-7(11)-en-12,8-olide (69)	<i>L. strychnifolia</i>	Roots	Liu et al., 2016
(1 <i>R</i> , 3 <i>S</i> , 4 <i>R</i> , 5 <i>R</i> , 6 <i>R</i> , 8 <i>S</i> , 10 <i>S</i> )-4,6,8-Trihydroxy-1,3-cyclo-eudesma-7(11)-en-12,8-olide (70)	<i>L. strychnifolia</i>	Roots	Liu et al., 2016
(1 <i>R</i> , 3 <i>S</i> , 4 <i>R</i> , 5 <i>R</i> , 6 <i>R</i> , 8 <i>S</i> , 10 <i>S</i> )-4,8-Dihydroxy-6-acetoxy- 1,3-cycloedesma-7(11)-en-12,8-olide (71)	<i>L. strychnifolia</i>	Roots	Liu et al., 2016
(1 <i>R</i> , 3 <i>S</i> , 4 <i>S</i> , 5 <i>S</i> , 8 <i>R</i> , 10 <i>R</i> )-4-Hydroxy-6-oxo-1,3-cycloedesma-7(11)-en-12,8-olide (72)	<i>L. strychnifolia</i>	Roots	Liu et al., 2016
(1 <i>R</i> , 3 <i>S</i> , 5 <i>R</i> , 6 <i>R</i> , 8 <i>R</i> , 10 <i>S</i> )-6-Methoxy-8-hydroxy-1,3-cyclo-eudesma-4(15),7(11)-dien-12,8-olide (73)	<i>L. strychnifolia</i>	Roots	Liu et al., 2016
6 $\alpha$ -Acetyl-lindenanolide B1 (74)	<i>L. aggregata</i>	Roots	Wen et al., 2021
6 $\alpha$ -Acetyl-lindenanolide B2 (75)	<i>L. aggregata</i>	Roots	Wen et al., 2021
Lindenenyl acetate (76)	<i>L. aggregata</i>	Roots	Li et al., 2009
Isolinderoxide (77)	<i>L. strychnifolia</i>	Roots	Wen et al., 2021
Lindenene (78)	<i>L. aggregata</i>	Roots	Wen et al., 2021
Lindenanolide A (79)	<i>L. aggregata</i>	Roots	Wen et al., 2021
Lindenanolide B1 (80)	<i>L. aggregata</i>	Roots	Wen et al., 2021
Lindenanolide B2 (81)	<i>L. aggregata</i>	Roots	Wen et al., 2021
Lideranlide F (82)	<i>L. aggregata</i>	Roots	Qiang et al., 2011

Linderanlide K (83)	<i>L. aggregata</i>	Roots	Liu et al., 2013
Linderanlide L (84)	<i>L. aggregata</i>	Roots	Liu et al., 2013
Linderanlide M (85)	<i>L. aggregata</i>	Roots	Liu et al., 2013
Linderanlide N (86)	<i>L. aggregata</i>	Roots	Liu et al., 2016
Linderanlide O (87)	<i>L. aggregata</i>	Roots	Liu et al., 2016
Linderanlide P (88)	<i>L. aggregata</i>	Roots	Liu et al., 2016
Linderanlide Q (89)	<i>L. aggregata</i>	Roots	Liu et al., 2016
Linderanlide R (90)	<i>L. aggregata</i>	Roots	Liu et al., 2016
Linderanlide S (91)	<i>L. aggregata</i>	Roots	Liu et al., 2016
Linderanlide T (92)	<i>L. aggregata</i>	Roots	Liu et al., 2016
Linderagalactone B (93)	<i>L. aggregata</i>	Roots	Gan et al., 2009b
Linderagalactone C (94)	<i>L. aggregata</i>	Roots	Gan et al., 2009b
Linderaggredin B (95)	<i>L. aggregata</i>	Aerial	Kuo et al., 2020
Linderolide L (96)	<i>L. strychnifolia</i>	Roots	Liu et al., 2013
Linderolide M (97)	<i>L. strychnifolia</i>	Roots	Liu et al., 2013
Linderolide N (98)	<i>L. strychnifolia</i>	Roots	Cao et al., 2016
Linderolide O (99)	<i>L. strychnifolia</i>	Roots	Cao et al., 2016
Linderolide P (100)	<i>L. strychnifolia</i>	Roots	Cao et al., 2016
Linderolide Q (101)	<i>L. strychnifolia</i>	Roots	Cao et al., 2016
Linderolide R (102)	<i>L. strychnifolia</i>	Roots	Cao et al., 2016
Linderolide S (103)	<i>L. strychnifolia</i>	Roots	Cao et al., 2016
Linderolide T (104)	<i>L. strychnifolia</i>	Roots	Cao et al., 2016
Linderolide U (105)	<i>L. aggregata</i>	Roots	Kim et al., 2021
Linderolide V (106)	<i>L. aggregata</i>	Roots	Kim et al., 2021
Lindenenol (107)	<i>L. aggregata</i>	Roots	Liu et al., 2013
	<i>L. strychnifolia</i>	Roots	Li et al., 2002
Myrrhalindenane A (108)	<i>L. myrrha</i>	Roots	Duong et al., 2023
Myrrhalindenane B (109)	<i>L. myrrha</i>	Roots	Duong et al., 2023
Strychnilactone (110)	<i>L. aggregata</i>	Roots	Li et al., 2002
Strychnistenolide (111)	<i>L. aggregata</i>	Roots	Li et al., 2002
Strychnistenolide 6-O-acetate (112)	<i>L. strychnifolia</i>	Roots	Liu et al., 2016
<b>SESQUITERPENE DIMERS</b>			
Aggreganoid A (113)	<i>L. aggregata</i>	Roots	Liu et al., 2019a
Aggreganoid B (114)	<i>L. aggregata</i>	Roots	Liu et al., 2019a
Aggreganoid C (115)	<i>L. aggregata</i>	Roots	Liu et al., 2019a
Aggreganoid D (116)	<i>L. aggregata</i>	Roots	Liu et al., 2019a
Aggreganoid E (117)	<i>L. aggregata</i>	Roots	Liu et al., 2019a
Aggreganoid F (118)	<i>L. aggregata</i>	Roots	Liu et al., 2019a
Linderin A (119)	<i>L. aggregata</i>	Roots	Wen et al., 2021
Linderin B (120)	<i>L. aggregata</i>	Roots	Wen et al., 2021
Linderaggrenolide A (121)	<i>L. aggregata</i>	Roots	Liu et al., 2021b
Linderaggrenolide B (122)	<i>L. aggregata</i>	Roots	Liu et al., 2021b
Linderaggrenolide C (123)	<i>L. aggregata</i>	Roots	Liu et al., 2021b
Linderaggrenolide D (124)	<i>L. aggregata</i>	Roots	Liu et al., 2021b
Linderaggrenolide E (125)	<i>L. aggregata</i>	Roots	Liu et al., 2021b
Linderaggrenolide F (126)	<i>L. aggregata</i>	Roots	Liu et al., 2021b
Linderaggrenolide G (127)	<i>L. aggregata</i>	Roots	Liu et al., 2021b
Linderaggrenolide H (128)	<i>L. aggregata</i>	Roots	Liu et al., 2021b
Linderaggrenolide I (129)	<i>L. aggregata</i>	Roots	Liu et al., 2021b
Linderaggrenolide J (130)	<i>L. aggregata</i>	Roots	Liu et al., 2021b
Linderaggrenolide K (131)	<i>L. aggregata</i>	Roots	Liu et al., 2021b
Linderaggrenolide L (132)	<i>L. aggregata</i>	Roots	Liu et al., 2021b
Linderaggrenolide M (133)	<i>L. aggregata</i>	Roots	Liu et al., 2021b
Linderaggrenolide N (134)	<i>L. aggregata</i>	Roots	Liu et al., 2021b
Linderanoid A (135)	<i>L. aggregata</i>	Roots	Liu et al., 2021a
Linderanoid B (136)	<i>L. aggregata</i>	Roots	Liu et al., 2021a
Linderanoid C (137)	<i>L. aggregata</i>	Roots	Liu et al., 2021a
Linderanoid D (138)	<i>L. aggregata</i>	Roots	Liu et al., 2021a
Linderanoid E (139)	<i>L. aggregata</i>	Roots	Liu et al., 2021a
Linderanoid F (140)	<i>L. aggregata</i>	Roots	Liu et al., 2021a

Linderanoid G (141)	<i>L. aggregata</i>	Roots	Liu et al., 2021a
Linderanoid H (142)	<i>L. aggregata</i>	Roots	Liu et al., 2021a
Linderanoid I (143)	<i>L. aggregata</i>	Roots	Liu et al., 2021a
Linderanoid J (144)	<i>L. aggregata</i>	Roots	Liu et al., 2021a
Linderanoid K (145)	<i>L. aggregata</i>	Roots	Liu et al., 2021a
Linderanoid L (146)	<i>L. aggregata</i>	Roots	Liu et al., 2021a
Linderanoid M (147)	<i>L. aggregata</i>	Roots	Liu et al., 2021a
Linderanoid N (148)	<i>L. aggregata</i>	Roots	Liu et al., 2021a
Linderanoid O (149)	<i>L. aggregata</i>	Roots	Liu et al., 2021a
Lindenaneolide F (150)	<i>L. aggregata</i>	Roots	Liu et al., 2021a
Linderalide A (151)	<i>L. aggregata</i>	Roots	Liu et al., 2019a
Linderalide B (152)	<i>L. aggregata</i>	Roots	Liu et al., 2019a
Linderalide C (153)	<i>L. aggregata</i>	Roots	Liu et al., 2019a
Linderalide D (154)	<i>L. aggregata</i>	Roots	Liu et al., 2019a
<b>OTHERS</b>			
10,11-Dihydroxyeremophilan-3-one 11-O- $\beta$ -D-glucopyranoside (155)	<i>L. strychnifolia</i>	Roots	Mimura et al., 2009
Alangioside L (156)	<i>L. umbellata</i>	Stems	Kuroda et al., 2011
Aristofone (157)	<i>L. communis</i>	Fruits	Deng et al., 2011
Cadinene (158)	<i>L. aggregata</i>	Seeds	Lv et al., 2023
Cadina-4,10 (15)-diene (159)	<i>L. aggregata</i>	Seeds	Lv et al., 2023
Dehydrocostuslactone (160)	<i>L. aggregata</i>	Root	Qiang et al., 2011
Epiglobulol (161)	<i>L. communis</i>	Fruits	Deng et al., 2011
Linderaggregin C (162)	<i>L. aggregata</i>	Aerial	Kuo et al., 2020
Linderagalactone A (163)	<i>L. aggregata</i>	Aerial	Kuo et al., 2020
Pseudoguaianelactones A (164)	<i>L. glauca</i>	Roots	Ruan et al., 2020
Pseudoguaianelactones B (165)	<i>L. glauca</i>	Roots	Ruan et al., 2020
Pseudoguaianelactone C (166)	<i>L. glauca</i>	Roots	Ruan et al., 2020





**Figure 1.** Chemical structures of isolated sesquiterpenes.

## 2.2. Alkaloids

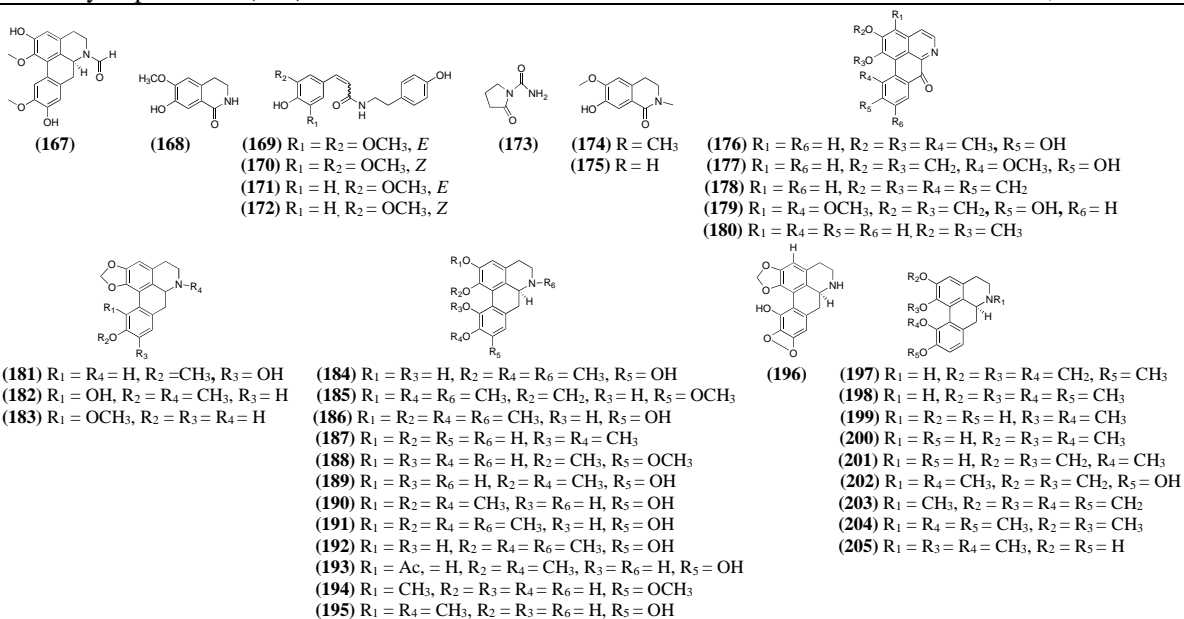
Alkaloids are one of the most diverse groups of secondary metabolites found in living organisms and have an array of structure types, biosynthetic pathways, and pharmacological activities. Alkaloids are a group of naturally occurring organic compounds which contain at least one nitrogen atom in an amine-type structure. Alkaloids are divided into several classes based on their sources, pharmacokinetics, and chemical structures such as isoquinoline, quinoline, indole, indolizidine, pyrroloindole, pyrrole and pyrrolidine, imidazole or glyoxaline, pyridine, piperidine, aporphine, pyrrolizidine, tropane, and purine (Azzeme & Zaman, 2019). Several studies on the alkaloids of *Lindera* species (Figure 2) were documented starting from 1994 to 2023. Eight *Lindera* species have been reported on alkaloids which were from *L. aggregata*, *L. glauca*, *L. chunii*, *L. megaphylla*, *L. reflexa*, *L. radix*, *L. myrrha*, and *L. oldhanii* with a total of 65 alkaloids. They were identified as amides, aporphines, benzyl-tetrahydroisoquinolines, bis-benzyltetrahydroisoquinolines, and isoquinolines. These isolated compounds were tabulated in Table 2.

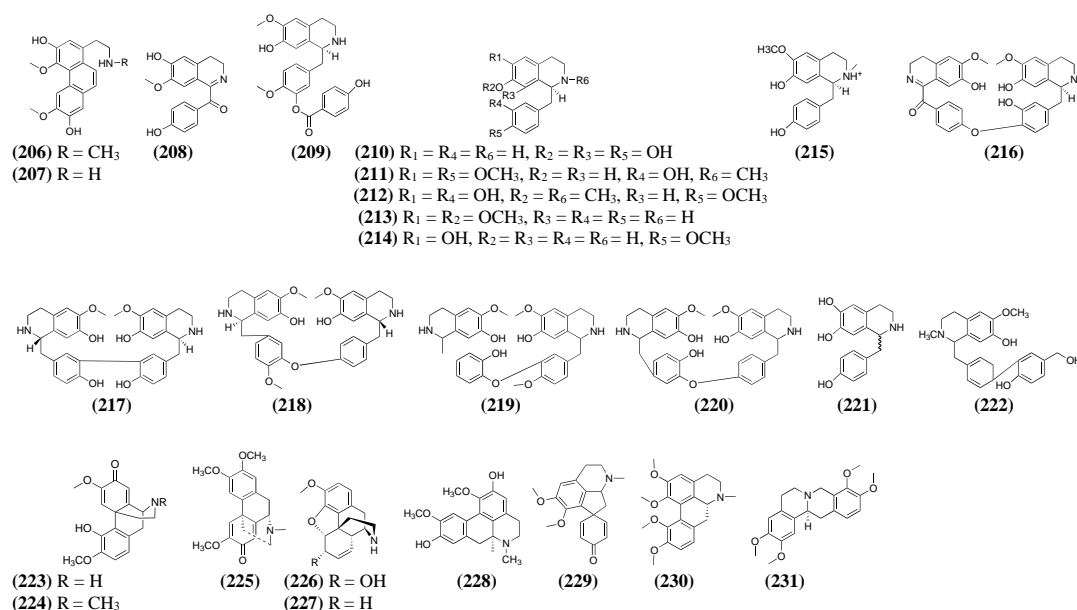
**Table 2.** Alkaloids isolated from several *Lindera* species

Compounds	Species	Part	References
<b>AMIDES</b>			
Linderaggrine B (167)	<i>L. aggregata</i>	Roots	Kuo et al., 2020
Northalifoline (168)	<i>L. glauca</i>	Aerial	Ma et al., 2015
N-cis-sinapoyltyramine (169)	<i>L. glauca</i>	Aerial	Chang et al., 2000
N-trans-sinapoyltyramine (170)	<i>L. glauca</i>	Aerial	Chang et al., 2000
N-cis-feruloyltyramine (171)	<i>L. glauca</i>	Aerial	Chang et al., 2000
N-trans-feruloyltyramine (172)	<i>L. glauca</i>	Aerial	Chang et al., 2000
Squamolone (173)	<i>L. glauca</i>	Aerial	Chang et al., 2000
Northalifoline (174)	<i>L. glauca</i>	Aerial	Chang et al., 2000
Thalifoline (175)	<i>L. glauca</i>	Aerial	Ma et al., 2015
<b>APORPHINE</b>			
7-Oxohernagine (176)	<i>L. chunii</i>	Roots	Zhang et al., 2002
7-Oxohernangerine (177)	<i>L. chunii</i>	Roots	Zhang et al., 2002
Hernandonine (178)	<i>L. chunii</i>	Roots	Zhang et al., 2002
Lindechunine A (179)	<i>L. chunii</i>	Roots	Zhang et al., 2002
Lycicamine (180)	<i>L. glauca</i>	Aerial	Chang et al., 2000
Actinodaphnine (181)	<i>L. aggregata</i>	Roots	Yang et al., 2020
Bulbocapnine (182)	<i>L. aggregata</i>	Roots	Lv et al., 2023
Hernangerine (183)	<i>L. aggregata</i>	Roots	Cao et al., 2016
Boldine (184)	<i>L. aggregata</i>	Roots	Gan et al., 2009a
	<i>L. glauca</i>	Aerial	Chang et al., 2001
D-dicentrine (185)	<i>L. megaphylla</i>	Roots	Huang et al., 1998
Isoboldine (186)	<i>L. aggregata</i>	Roots	Ma et al., 2015
Linderaline (187)	<i>L. aggregata</i>	Roots	Chou et al., 2005
Laetanine (188)	<i>L. glauca</i>	Aerial	Zhu et al., 2016
	<i>L. reflexa</i>	Roots	Chen et al., 2015
Laurolistine (189)	<i>L. chunii</i>	Roots	Zhang et al., 2002
Laurotetanine (190)	<i>L. aggregata</i>	Roots	Gan et al., 2009a
N-methylaurotetanine (191)	<i>L. aggregata</i>	Roots	Gan et al., 2009a
	<i>L. chunii</i>	Roots	Zhang et al., 2002
Norboldine (192)	<i>L. aggregata</i>	Roots	Gan et al., 2009a
Norboldine acetate (193)	<i>L. aggregata</i>	Roots	Gan et al., 2009a
Norbracteoline (194)	<i>L. glauca</i>	Aerial	Zhu et al., 2016
	<i>L. reflexa</i>	Roots	Chen et al., 2015
Norisoboldine (195)	<i>L. aggregata</i>	Roots	Yang et al., 2020
Lindechunine B (196)	<i>L. chunii</i>	Roots	Zheng et al., 2002
Launobine (197)	<i>L. reflexa</i>	Roots	Chen et al., 2015
Norisocorydine (198)	<i>L. glauca</i>	Aerial	Zhu et al., 2016
Hernovine (199)	<i>L. myrrha</i>	Roots	Phan et al., 1994



Hernavine (200)	<i>L. myrrha</i>	Roots	Phan et al., 1994
Hernangerine (201)	<i>L. myrrha</i>	Roots	Phan et al., 1994
N-Methylhernangerine (202)	<i>L. chunii</i>	Leaves	Zhang et al., 2002
N-Methylovigerine (203)	<i>L. chunii</i>	Leaves	Zhang et al., 2002
O-Methylbulbocapnine (204)	<i>L. megaphylla</i>	Flower	Chen et al., 1995
N-Methylhernovine (205)	<i>L. megaphylla</i>	Flower	Chen et al., 1995
Secoboldine (206)	<i>L. aggregata</i>	Roots	Yang et al., 2020
Secolaurolitsine (207)	<i>L. aggregata</i>	Roots	Yang et al., 2020
Linderine A (208)	<i>L. aggregata</i>	Roots	Lv et al., 2023
<b>BENZYL TETRAHYDROISOQUINOLINE</b>			
(1 <i>S</i> )-5'-O-p-Hydroxy benzoyl norreticuline (209)	<i>L. aggregata</i>	Roots	Yang et al., 2020
Norjuziphine (210)	<i>L. aggregata</i>	Roots	Yang et al., 2020
Reticuline (211)	<i>L. aggregata</i> <i>L. megaphylla</i>	Roots Flower	Yang et al., 2020 Chen et al., 1995
Protosinomenine (212)	<i>L. aggregata</i>	Roots	Yang et al., 2020
Norcinnamolaurine (213)	<i>L. glauca</i>	Aerial	Zhu et al., 2016
Argemexirine (214)	<i>L. aggregata</i>	Roots	Lv et al., 2023
Magnocurarine (215)	<i>L. aggregata</i>	Roots	Gan et al., 2009a
<b>BIS-BENZYL TETRAHYDROISOQUINOLINE</b>			
(1' <i>S</i> )-12'-Hydroxyl-linderegatine (216)	<i>L. aggregata</i>	Roots	Yang et al., 2020
(1 <i>R</i> , 1' <i>R</i> )-11,11'-Biscoclaurine (217)	<i>L. aggregata</i>	Roots	Yang et al., 2020
Costaricine (218)	<i>L. aggregata</i>	Roots	Yang et al., 2020
Linderegatine (219)	<i>L. aggregata</i>	Roots	Zhu et al., 2016
<b>Compounds</b>	<b>Species</b>	<b>Part</b>	<b>References</b>
Lindoldhamine (220)	<i>L. glauca</i> <i>L. aggregata</i>	Aerial Roots	Zhu et al., 2016 Yang et al., 2020
<b>ISOQUINOLINE</b>			
Demethylcoclaurine-7-O-glucoside (221)	<i>L. aggregata</i>	Roots	Peng et al., 2020
Karakoramine (222)	<i>L. aggregata</i>	Roots	Peng et al., 2020
Pallidine (223)	<i>L. aggregata</i>	Roots	Peng et al., 2020
Salutaridine (224)	<i>L. aggregata</i>	Roots	Yang et al., 2020
N-Methylflavinantine (225)	<i>L. glauca</i>	Aerial	Chang et al., 2013
<b>OTHER</b>			
Norcodeine (226)	<i>L. radix</i>	Roots	Zou et al., 2021
6-O-methyl codeine (227)	<i>L. radix</i>	Roots	Zou et al., 2021
Boldine n-oxide (228)	<i>L. aggregata</i>	Roots	Chou et al., 2005
Pronuciferine (229)	<i>L. aggregata</i>	Roots	Gan et al., 2009
Reticuline n-oxide (230)	<i>L. aggregata</i>	Roots	Chou et al., 2005
Tetrahydropalmatine (231)	<i>L. radix</i>	Roots	Zou et al., 2021





**Figure 2.** Chemical structures of isolated alkaloids.

### 2.3. Flavonoids

Flavonoids are divided into several classes based on their sources, pharmacokinetics, and chemical structures such as flavones, flavonols, flavanones, catechins, anthocyanidins and isoflavones (Panche et al., 2016). The various classes of flavonoids differ in oxidation level and substitution pattern of the C ring, while the individual compounds within a class differ in the pattern of substitution of A and B rings (Kumar & Pandey, 2013). Several studies on the flavonoids of *Lindera* species (Figure 3) were documented starting from 1985 to 2022. Seven *Lindera* species have been reported with flavonoids which were from *L. aggregata*, *L. erythrocarpa*, *L. umbellata*, *L. lucida*, *L. oxyphylla*, *L. glauca*, and *L. obtusiloba*. There were 42 compounds that was classified to flavonoids isolated from *Lindera* species. They were known as chalcones, dihydrochalcones, flavanones, flavonols, and flavones. These isolated compounds were tabulated in Table 3.

**Table 3.** Flavonoids isolated from several *Lindera* species

Compounds	Species	Part	References
<b>CHALCONE</b>			
Flavokawain B (232)	<i>L. oxyphylla</i>	Bark	Hosseinzadeh et al., 2013
Kanakugiol (233)	<i>L. erythrocarpa</i>	Aerial	Kim et al., 2011
Pedicellin (234)	<i>L. lucida</i>	Twigs	Leong et al., 1998
Linderachalcone (235)	<i>L. umbellata</i>	Leaves	Ichino et al., 1989
Neolinderatin (236)	<i>L. umbellata</i>	Leaves	Ichino et al., 1989
<b>DIHYDROCHALCONE</b>			
3',5'-Dihydroxy-2',4',6'- trimethoxy-dihydrochalcone (237)	<i>L. erythrocarpa</i>	Leaves	Kim et al., 2011
Dihydrokanakugiol (238)	<i>L. erythrocarpa</i>	Leaves	Kim et al., 2011
Dihydropashanone (239)	<i>L. erythrocarpa</i>	Leaves	Kim et al., 2011
Linderatin (240)	<i>L. umbellata</i>	Leaves	Ichino et al., 1989
Methylinderatin (241)	<i>L. umbellata</i>	Leaves	Ichino et al., 1989
Kanakugin (242)	<i>L. erythrocarpa</i>	Leaves	Kim et al., 2011
Nubigenol (243)	<i>L. aggregata</i>	Leaves	Zhang et al., 2003
Onysilin (244)	<i>L. oxyphylla</i>	Bark	Hosseinzadeh et al., 2013
Pinostrobin (245)	<i>L. erythrocarpa</i>	Leaves	Kim et al., 2011
Pinocembrin (246)	<i>L. oxyphylla</i>	Bark	Hosseinzadeh et al., 2013

**FLAVANONES**

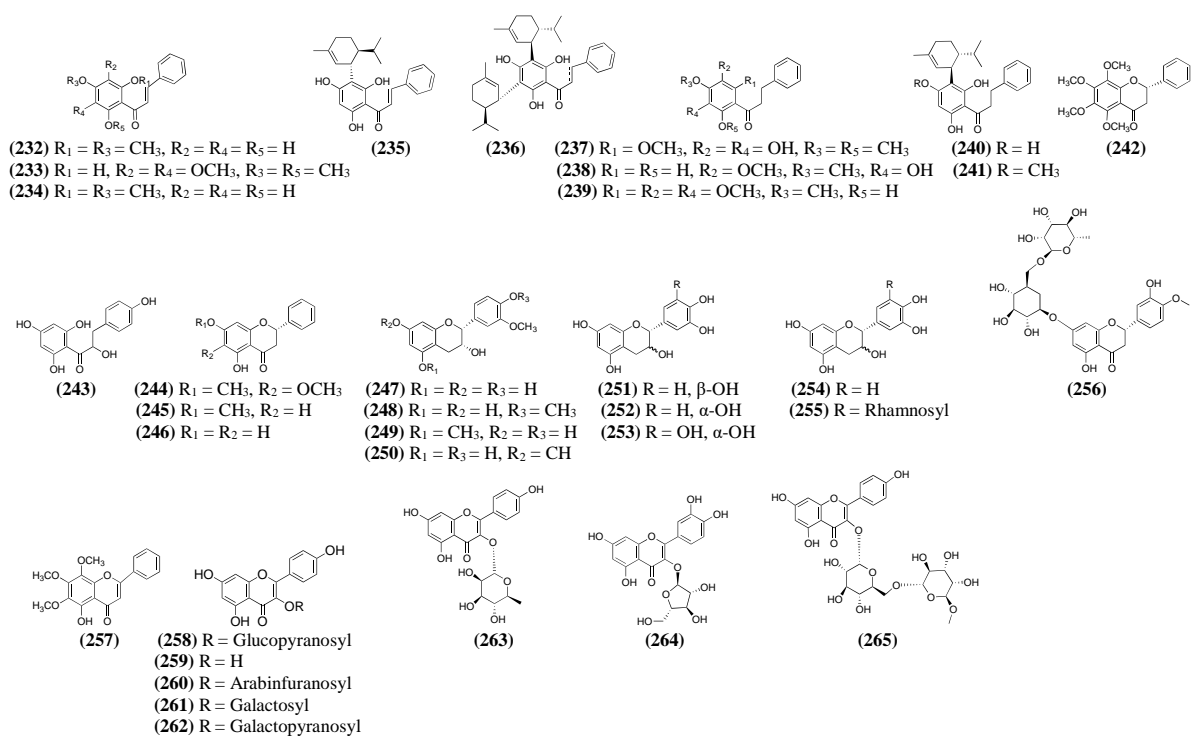
3'-O-methyl(-)-epicatechin (247)	<i>L. umbellata</i>	Twigs	Morimoto et al., 1985
3',4'-Di-O-methyl(-)-epicatechin (248)	<i>L. umbellata</i>	Twigs	Morimoto et al., 1985
5,3'-Di-O-methyl(-)-epicatechin (249)	<i>L. umbellata</i>	Twigs	Morimoto et al., 1985
5,7,3'-Tri-O-methyl(-)-epicatechin (250)	<i>L. umbellata</i>	Twigs	Morimoto et al., 1985
Catechin (251)	<i>L. umbellata</i>	Stems	Ichino et al., 1989
	<i>L. aggregata</i>	Stems	Zhang et al., 2003
Epicatechin (252)	<i>L. umbellata</i>	Stems	Ichino et al., 1989
	<i>L. erythrocarpa</i>	Aerial	Kim et al., 2011
	<i>L. strychnifolia</i>	Stems	Kobayashi et al., 2002
Epigallocatechin (253)	<i>L. aggregata</i>	Leaves	Zhang et al., 2003
Dihydrokaempferol (254)	<i>L. aggregata</i>	Leaves	Xiao et al., 2011
Dihydrokaempferol-3-O-l-rhamnoside (255)	<i>L. aggregata</i>	Leaves	Xiao et al., 2011
Hesperidin (256)	<i>L. aggregata</i>	Leaves	Xiao et al., 2011

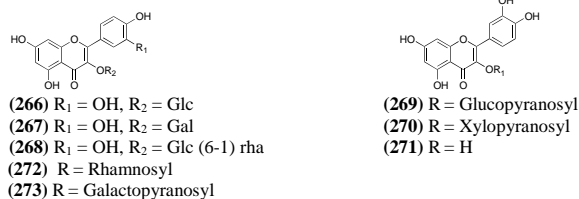
**FLAVONE**

5-Hydroxy-6,7,8-trimethoxyflavone (257)	<i>L. lucida</i>	Twigs	Leong et al., 1998
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**FLAVONOLS**

Astragaline (258)	<i>L. aggregata</i>	Leaves	Zhang et al., 2003
Kaempferol (259)	<i>L. nessiana</i>	Aerial	Chang et al., 2000
Kaempferol-3-O-L-arabinopyranoside (260)	<i>L. glauca</i>	Aerial	Chang et al., 2000
Kaempferol-3-O-β-d-galactoside (261)	<i>L. aggregata</i>	Leaves	Chang et al., 2000
Kaempferol-3-O-β-d-galactopyranoside (262)	<i>L. aggregata</i>	Leaves	Chang et al., 2000
Afzelin (263)	<i>L. aggregata</i>	Leaves	Luo et al., 2009
Avicularin (264)	<i>L. obtusiloba</i>	Stems	Lee et al., 2011
Kaempferol-3-O-(2"-O-β-d-glucopyranosyl)-α-l-rhamnopyranoside (265)	<i>L. aggregata</i>	Leaves	Luo et al., 2009
Isoquercitrin (266)	<i>L. umbellata</i>	Branches	Lee et al., 2011
Hyperin (267)	<i>L. obtusiloba</i>	Stems	Lee et al., 2011
Rutin (268)	<i>L. umbellata</i>	Branches	Zhang et al., 2003b
Kaempferol-3-O-α-d-glucopyranoside (269)	<i>L. glauca</i>	Aerial	Zhang et al., 2001
Kaempferol-3-O-β-d-xylopyranoside (270)	<i>L. aggregata</i>	Leaves	Luo et al., 2009
Quercetin (271)	<i>L. aggregata</i>	Leaves	Zhang et al., 2001
Quercetin-3-O-rhamnoside (272)	<i>L. aggregata</i>	Leaves	Zhang et al., 2001
Quercetin-3-O-β-d-galacto-pyranoside (273)	<i>L. aggregata</i>	Leaves	Zhang et al., 2001





**Figure 3.** Chemical structures of isolated flavonoids.

## 2.4. Phenolics

Phenolic compounds are the most widely distributed secondary metabolites, ubiquitously present in the plant kingdom. They contain benzene rings with one or more hydroxyl substituents, and range from simple phenolic molecules to highly polymerized compounds (Lin et al., 2016). Several studies on the phenolics of *Lindera* species (Figure 4) were documented starting from 2006 to 2021. There were 37 compounds classified to phenolics isolated from *Lindera* species. Overall, four *Lindera* species have been reported with phenolics which were from *L. fruticosa*, *L. aggregata*, *L. nacusua*, and *L. obtusiloba*. The most reported phenolic compounds are from *L. aggregata* and *L. obtusiloba*, each with eight reports. Besides, *L. fruticosa* and *L. radix* each with seven reports. The root part is the most common part that contains abundant of phenolic compounds. These isolated compounds as tabulated in Table 4.

**Table 4.** Phenolics isolated from several *Lindera* species

Compounds	Species	Part	References
$\beta$ -D-(3,4-Disinapoyl) fructofuranosyl- $\alpha$ -D-(6-sinapoyl) glucopyranoside (274)	<i>L. fruticosa</i>	Roots	Song et al., 2008
$\beta$ -D-(3-Sinapoyl) fructofuranosyl- $\alpha$ -D-(6-sinapoyl) glucopyranoside (275)	<i>L. fruticosa</i>	Roots	Song et al., 2008
p-Hydroxybenzoic acid (276)	<i>L. aggregata</i>	Roots	Ma et al., 2015
1-O-3-Hydroxyphenyl-4,5-dimethoxy-(6'-O-3'',5''-dimethoxygalloyl)- $\beta$ -d-glucopyranoside (277)	<i>L. nacusua</i>	Bark	Lei et al., 2017
1-O-3-Hydroxyphenyl-4,5-dimethoxy-(6'-O-vanilloyl)- $\beta$ -d-glucopyranoside (278)	<i>L. nacusua</i>	Bark	Lei et al., 2017
1-O-3-Hydroxyphenyl-5-methoxyphenol-(6'-O-vanilloyl)- $\beta$ -d-glucopyranoside (279)	<i>L. nacusua</i>	Bark	Lei et al., 2017
4,6-Dihydroxy-2-methoxyphenyl-1-O- $\beta$ -D-glucopyranoside (280)	<i>L. obtusiloba</i>	Stems	Choi et al., 2013
6'-O-Vanilloyltachioside (281)	<i>L. aggregata</i>	Roots	Ma et al., 2015
6-Hydroxy-4-methoxyphenol 1-O- $\beta$ -d-(6'-O-syringoyl) glucopyranoside (282)	<i>L. nacusua</i>	Bark	Lei et al., 2017
2-Methoxy-3,4-methylenedioxybenzophenone (283)	<i>L. fruticosa</i>	Roots	Song et al., 2006
(S)-2-Methoxy-3,4-methylenedioxybenzhydryl alcohol (284)	<i>L. fruticosa</i>	Roots	Song et al., 2008
3-Hydroxy-5-methoxybiphenyl (285)	<i>L. fruticosa</i>	Roots	Song et al., 2008
3,5-Dimethoxybiphenyl (286)	<i>L. fruticosa</i>	Roots	Song et al., 2008
1-Methoxy-2,5,7-trihydroxyxanthone (287)	<i>L. fruticosa</i>	Roots	Song et al., 2006
1,7-Dihydroxyxanthone (288)	<i>L. fruticosa</i>	Roots	Song et al., 2006
Benzyl 2-hydroxy-6-methoxybenzoate (289)	<i>L. fruticosa</i>	Roots	Song et al., 2006
Tyrosol (290)	<i>L. aggregata</i>	Roots	Ma et al., 2015
2-(4-Hydroxy-3-methoxyphenyl)-ethanol (291)	<i>L. aggregata</i>	Roots	Ma et al., 2015
2-(4-Hydroxy-3,5-dimethoxyphenyl)-ethanol (292)	<i>L. aggregata</i>	Roots	Ma et al., 2015
2,6-Dimethoxy-p-benzoquinone (293)	<i>L. aggregata</i>	Roots	Ma et al., 2015
2,6-Dimethoxy-4-hydroxyphenyl-1-O- $\beta$ -D-glucopyranoside (294)	<i>L. obtusiloba</i>	Stems	Choi et al., 2013
4,6-Dihydroxy-2-methoxyphenyl-1-O- $\beta$ -D-glucopyranoside	<i>L. obtusiloba</i>	Stems	Choi et al., 2013

(295)	<i>L. obtusiloba</i>	Stems	Choi et al., 2013
Isotachioside (296)	<i>L. obtusiloba</i>	Stems	Choi et al., 2013
Koaburaside (297)	<i>L. obtusiloba</i>	Stems	Choi et al., 2013
Tachioside (298)	<i>L. radix</i>	Roots	Zou et al., 2021
Cryptochlorogenic acid (299)	<i>L. aggregata</i>	Roots	Ma et al., 2015
3-Hydroxy-1-(4-hydroxyphenyl)propan-1-one (300)	<i>L. aggregata</i>	Roots	Ma et al., 2015
4-Hydroxy-3-methoxy acetophenone (301)	<i>L. glauca</i>	Aerial	Chang et al., 2000
3-(3,4-Dihydroxyphenyl)propionic acid (302)	<i>L. radix</i>	Roots	Zou et al., 2021
Ferulic acid (303)	<i>L. obtusiloba</i>	Stems	Choi et al., 2013
Erigeside C (304)	<i>L. radix</i>	Roots	Zou et al., 2021
Neochlorogenic acid (305)	<i>L. radix</i>	Roots	Zou et al., 2021
Protocatechualdehyde (306)	<i>L. radix</i>	Roots	Zou et al., 2021
Salidroside (307)	<i>L. obtusiloba</i>	Stems	Choi et al., 2013
Syringic acid (308)	<i>L. radix</i>	Roots	Zou et al., 2021
Vanillic acid (309)	<i>L. aggregata</i>	Roots	Ma et al., 2015

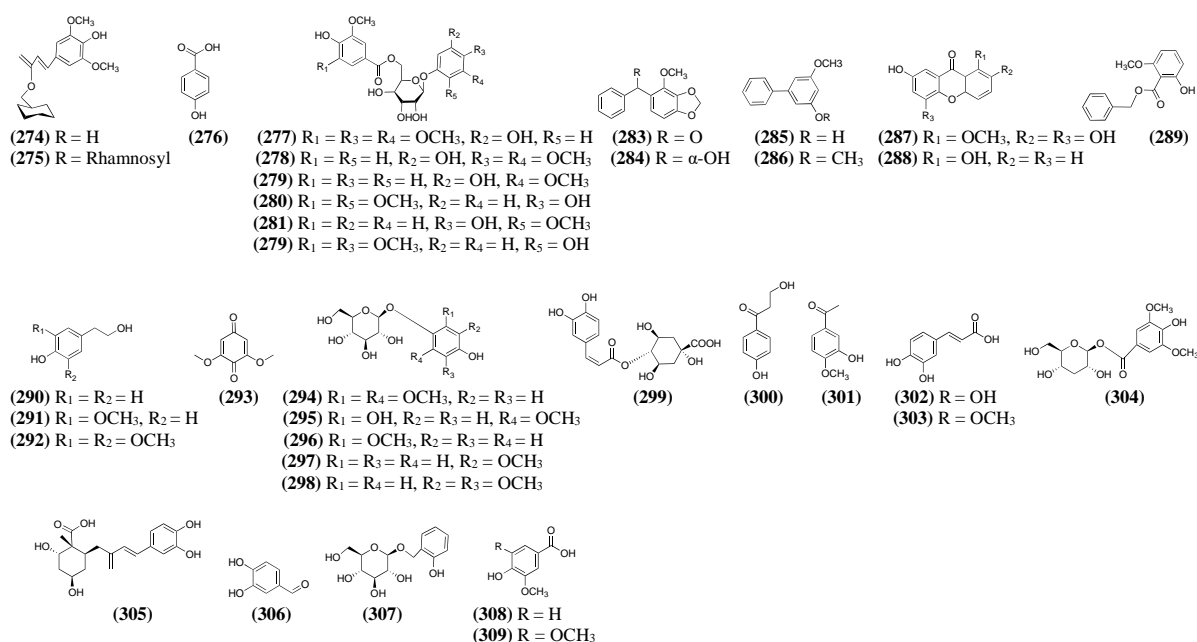


Figure 4. Chemical structures of isolated phenolics.

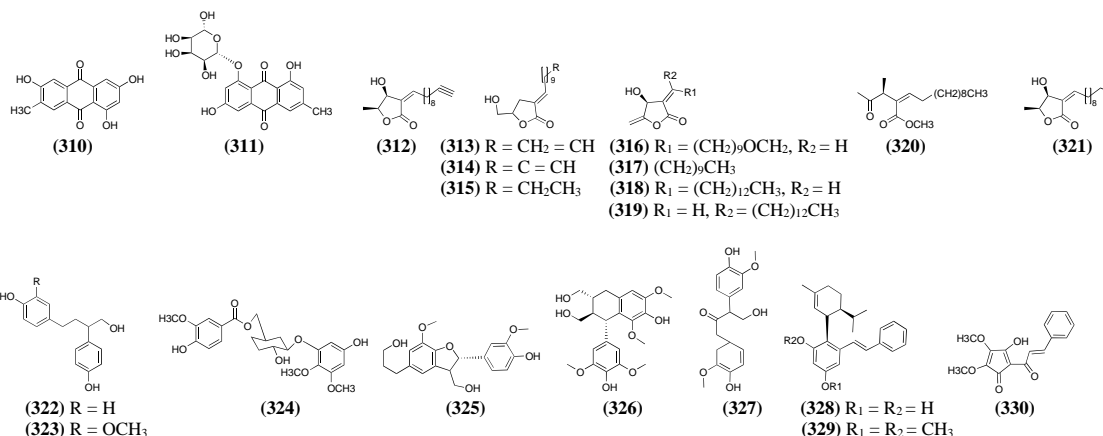
## 2.5. Miscellaneous Constituents

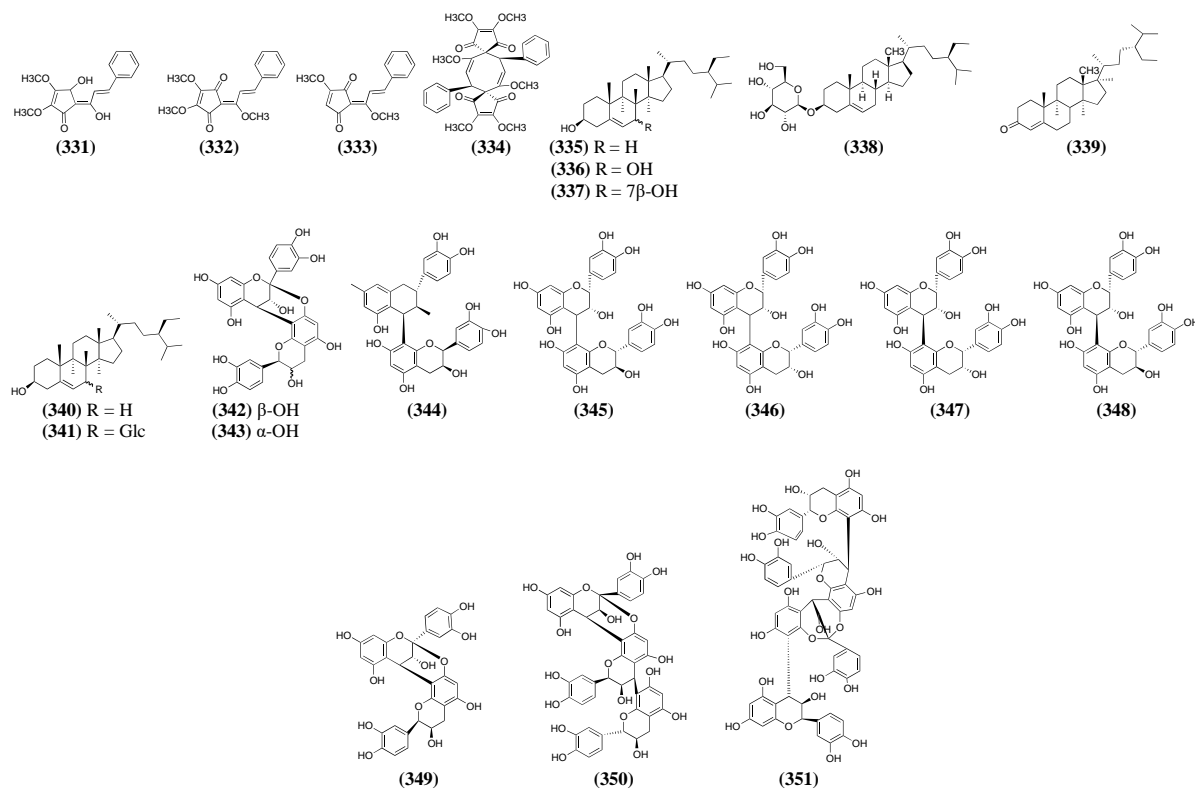
Another secondary metabolite compounds that have been identified from *Lindera* species are anthraquinones, butanolides, benzoids, benzoids glycosides, lignans, lucidones, steroids, and tannins (Figure 5). These compounds are tabulated in Table 5.

Table 5. Miscellaneous isolated from several *Lindera* species

Compounds	Species	Part	References
<b>ANTHRAQUINONES</b>			
Demethylmacrorporine I (310)	<i>L. nacusua</i>	Bark	Wei et al., 2016
Emodin-6-O- $\beta$ -D-glucopyranoside (311)	<i>L. nacusua</i>	Bark	Wei et al., 2016
<b>BUTENOLIDES</b>			
(2Z,3R,4S)-2-(dodec-11-ynylidene)-3-hydroxy-4-methylbutanolide (312)	<i>L. nacusua</i>	Bark	Wei et al., 2016
Majorenolide (313)	<i>L. akoensis</i>	Roots	Chang et al., 2008
Majorynolide (314)	<i>L. akoensis</i>	Roots	Chang et al., 2008
Majoranolide (315)	<i>L. akoensis</i>	Roots	Chang et al., 2008

Obtusilactone (316)	<i>L. akoensis</i>	Roots	Chang et al., 2008
Isoobtusilactone (317)	<i>L. akoensis</i>	Roots	Chang et al., 2008
Obtusilactone A (318)	<i>L. obtusiloba</i>	Roots	Kwon et al., 2000
Isoobtusilactone A (319)	<i>L. obtusiloba</i>	Roots	Kwon et al., 2000
Secoaggregatalactone A (320)	<i>L. aggregata</i>	Roots	Lin et al., 2007
Litsenolide (321)	<i>L. nacusua</i>	Bark	Lei et al., 2017
<b>BENZENOIDS</b>			
Linderagatin A (322)	<i>L. aggregata</i>	Roots	Ma et al., 2015
Linderagatin B (323)	<i>L. aggregata</i>	Roots	Ma et al., 2015
<b>BENZENOIDS GLYCOSIDE</b>			
6'-O-vanilloyl-5-hydroxy-2,3-dimethoxyphenol 1-O- $\beta$ -d-glucopyranoside (324)	<i>L. aggregata</i>	Roots	Kuo et al., 2020
<b>LIGNANS</b>			
rel-(2 $\alpha$ ,3 $\beta$ )-7-O-methylcedrusin (325)	<i>L. aggregata</i>	Roots	Ma et al., 2015
Lyoniresinol (326)	<i>L. aggregata</i>	Roots	Ma et al., 2015
Evofolin B (327)	<i>L. aggregata</i>	Roots	Ma et al., 2015
Reflexanbene A (328)	<i>L. reflexa</i>	Leaves	Fu et al., 2022
Reflexanbene C (329)	<i>L. reflexa</i>	Leaves	Fu et al., 2022
<b>LUCIDONES</b>			
Linderone A (330)	<i>L. oxyphylla</i>	Bark	Hosseinzadeh et al., 2013
Lucidone (331)	<i>L. erythrocarpa</i>	Fruits	Kim et al., 2011
Methylinderone (332)	<i>L. erythrocarpa</i>	Fruits	Kim et al., 2011
Methylucidone (333)	<i>L. erythrocarpa</i>	Fruits	Kim et al., 2011
Linderaspirone (334)	<i>L. aggregata</i>	Roots	Wang et al., 2010
<b>STEROIDS</b>			
$\beta$ -Sitosterol (335)	<i>L. glauca</i>	Stem	Huh et al., 2011
7-Ketositosterol (336)	<i>L. glauca</i>	Stem	Huh et al., 2011
7 $\beta$ -Hydroxysitosterol (337)	<i>L. glauca</i>	Stem	Huh et al., 2011
$\beta$ -Sitosteryl-D-glucoside (338)	<i>L. glauca</i>	Stem	Huh et al., 2011
$\beta$ -Sitostenone (339)	<i>L. glauca</i>	Stem	Huh et al., 2011
Stigmasterol (340)	<i>L. communis</i>	Wood	Tsai et al., 2002
Daucosterol (341)	<i>L. glauca</i>	Stem	Huh et al., 2011
<b>TANNINS</b>			
Epicatechin-(4 $\beta$ -8,2-O-7)-epicatechin (342)	<i>L. aggregata</i>	Roots	Zhang et al., 2003c
Epicatechin-(4 $\beta$ -8,2-O-7)-catechin (343)	<i>L. aggregata</i>	Roots	Zhang et al., 2003c
Epicatechin-(4 $\beta$ -8)-catechin (344)	<i>L. aggregata</i>	Roots	Zhang et al., 2003c
Procyanidin B1 (345)	<i>L. aggregata</i>	Roots	Zhang et al., 2003c
Procyanidin B2 (346)	<i>L. aggregata</i>	Roots	Zhang et al., 2003c
Procyanidin B3 (347)	<i>L. aggregata</i>	Roots	Zhang et al., 2003c
Procyanidin B4 (348)	<i>L. aggregata</i>	Roots	Zhang et al., 2003c
Proanthocyanidins (349)	<i>L. aggregata</i>	Roots	Zhang et al., 2003c
Cinnamtannin B1 (350)	<i>L. glauca</i>	Stem	Huh et al., 2011
Cinnamtannin B2 (351)	<i>L. glauca</i>	Stem	Huh et al., 2011





**Figure 5.** Chemical structures of miscellaneous constituents.

### 3. PHARMACOLOGICAL ACTION

Numerous biologically active compounds have been isolated from *Lindera* species previously by several researchers. Sesquiterpenes, flavonoids, phenolics, and alkaloids are among the compounds which reported mainly on anticancer, antifibrotic, anti-inflammatory, antitumor, antioxidant, anti-arthritic, cytotoxic, anti-allergic, and antihyperlipidemic properties. Isolinderalactone (**6**) has been reported to inhibit antitumor, anticancer, and anti-inflammatory activities. Chuang et al. (2018) discovered that isolinderalactone was able to trigger apoptosis or programmed cell death in a variety of cancer cells, including breast cancer cells and lung cancer cells. Fu et al. (2022) was found that isolinderalactone have a strong inhibitory effect on tumor cell lines MGC803 and SMMC-7721 with  $IC_{50}$  values 2.65 and 4.13  $\mu$ M, respectively. Kwak et al. (2022) managed to discover isolinderalactone to exhibit human-resistant colorectal cancer (CRC) cells with  $IC_{50}$  value 7.80  $\mu$ M. Besides, isolinderalactone was also able to inhibit the expression of multiple genes involved in tumour growth and angiogenesis, which it can lead the formation of new blood vessels that can give nutrition to the tumours. In alkaloid type, the most reported compound was norisoboldine (**195**). Norisoboldine (**195**) helps by preventing the release of cytokines that promote inflammation. In addition, it has been demonstrated that norisoboldine prevents the synthesis of prostaglandin E2 (PGE2) and nitric oxide (NO), both are essential for the inflammatory response. Additionally, Yang et al. (2020) reported the compound induced production of nitric oxide by lipopolysaccharide in RAW 264.7 cells ( $IC_{50}$  value 9.6  $\mu$ M) as well as vascular endothelial growth factor (VEGF)-induced endothelial cell migration ( $IC_{50}$  value 15.1  $\mu$ M) (Lu et al., 2013). In flavonoids type, quercetin-3-*O*-rhamnosides (**272**) are the most reported compound that can act as an antioxidant agent. September-Malaterre et al. (2022) was reported, the compound can control the activities of superoxide dismutase (SOD) and glutathione (GSH). In addition, it is also found extremely effective at increasing the body's

antioxidant capacity by controlling and regulating glutathione levels (Xu et al., 2019). Koaburaside (**297**) is one of the most reported compounds in phenolic type with mainly for antiallergic effect. Moreover, there were other biological activities of phytochemicals from *Lindera* species that have been reported as described in Table 6.

**Table 6.** Biological activities of several *Lindera* phytochemicals

Compounds	Species	Biological activities
<b>SESQUITEPENOIDS</b>		
Isolinderalactone ( <b>6</b> )	<i>L. aggregata</i>	<b>Anticancer:</b> Exhibited human resistant colorectal cancer (CRC) cells with IC <sub>50</sub> value 7.80 μM (Kwak et al., 2022) <b>Antitumor:</b> Exhibited in breast cancer cell lines by lowering the cell proliferation to the concentration of 30-100 μM (Yen et al., 2015) <b>Antitumor:</b> Exhibited in human ovarian cancer (OC) cells and inhibit several cancer cell line growth by reducing mitochondrial superoxide and cell proliferation with a dose concentration of 5-50 μM for 24 h (Rajina et al., 2020) <b>Anti-inflammatory:</b> Inhibit the invasion and migration of A549 cancer cells by involving the inhibition of MMP-2 and β-catenin protein expression with the range dose concentration 1-10 μM for 24-48 h (Chuang et al., 2018)
	<i>L. reflexa</i>	<b>Anticancer:</b> Strong inhibitory effect on tumor cell lines MGC803 and SMMC-7721 with IC <sub>50</sub> values 2.65 and 4.13 μM, respectively (Fu et al., 2019)
	<i>L. strychnifolia</i>	<b>Antitumor:</b> Decreased G2/M phase cell cycle arrest and reactive oxygen species (ROS) generation triggered apoptotic cell death of colorectal cancer (CRC) cells with a dose concentration of 3-9 μM (Kwak et al., 2022)
Linderalactone ( <b>37</b> )	<i>L. aggregate</i>	<b>Anticancer:</b> Strong inhibition in the proliferation of lung cancer cells A-549 with IC <sub>50</sub> value 15 μM (Deng et al., 2019) <b>Anti-inflammatory:</b> Exhibited liver protection by reducing swelling with EC <sub>50</sub> value 67.0 μM (Gan et al., 2009b)
Lindenene ( <b>78</b> )	<i>L. communis</i>	<b>Anticancer:</b> Showed significant activity against H460, ES2, and DU145 cancer cells with IC <sub>50</sub> value 2.1, 2.8, and 3.0 μg/mL, respectively (Deng et al., 2011)
Linderaggrenolide H ( <b>128</b> )	<i>L. aggregate</i>	<b>Anticancer:</b> Exhibit significant transforming growth factor-β inhibitory activity with IC <sub>50</sub> value 25.9 μM (Liu et al., 2021b)
Linderanoid E ( <b>139</b> )	<i>L. aggregate</i>	<b>Anticancer:</b> Induced TGF-β smad2 phosphorylation at a concentration of 25 μM and have low activity against A549 cells with IC <sub>50</sub> value 49.9 μM (Liu et al., 2021a)
Linderalide D ( <b>154</b> )	<i>L. aggregata</i>	<b>Anticancer:</b> Moderate NF-κB inhibitory activity with the inhibitory rate reaching almost 40% at a concentration of 50 μM with IC <sub>50</sub> value 18.0 (Liu et al., 2019a)
Linderaggrenolide I ( <b>129</b> )	<i>L. aggregata</i>	<b>Anticancer:</b> Transforming growth factor-β inhibitory activity with IC <sub>50</sub> value 21.5 μM (Liu et al., 2021b)
(1R,3S,4R,5R,8S,10S)-4-Methoxy-1,3-cycloedesma-7(11)-en-12,8-olide ( <b>68</b> )	<i>L. strychnifolia</i>	<b>Anti-inflammatory:</b> Strongly inhibit lipopolysaccharide-stimulated nitric oxide production in murine RAW 264.7 macrophage cells, with IC <sub>50</sub> value of 6.3 μM (Liu et al., 2016)
(1R,3S,4R,5R,8S,10S)-4,8-Dihydroxy-1,3-cycloedesma-7(11)-en-12,8-olide ( <b>69</b> )	<i>L. strychnifolia</i>	<b>Anti-inflammatory:</b> Strongly inhibit lipopolysaccharide-stimulated nitric oxide production in murine RAW 264.7 macrophage cells, with IC <sub>50</sub> value of 6.3 of 9.6 μM (Liu et al., 2016)
Linderane ( <b>38</b> )	<i>L. aggregata</i>	<b>Anti-inflammatory:</b> Showed activity against H <sub>2</sub> O <sub>2</sub> -



		induced oxidative damage on HepG2 cells with EC <sub>50</sub> value of 167.0 (Gan et al., 2009b)
Linderagalactone D (17)	<i>L. aggregata</i>	<b>Anti-inflammatory:</b> Exhibit liver protection by reducing swelling with EC <sub>50</sub> value 98.0 μM (Gan et al., 2009b) <b>Anti-inflammatory:</b> Exhibit of H <sub>2</sub> O <sub>2</sub> -induced oxidative damage on HepG2 cells with EC <sub>50</sub> value 67.5 μM (Gan et al., 2009b)
Linderolide C (21)	<i>L. aggregata</i>	<b>Anti-inflammatory:</b> Exhibited in LPS-induced RAW264.7 macrophage cells with IC <sub>50</sub> value 37.8 μM (Sumioka et al., 2011)
Linderagalactone E (18)	<i>L. aggregata</i>	<b>Anti-inflammatory:</b> Exhibit of H <sub>2</sub> O <sub>2</sub> -induced oxidative damage on HepG2 cells with EC <sub>50</sub> value 42.4 μM (Gan et al., 2009b)
Hydroxylindestenolide (15)	<i>L. aggregata</i>	<b>Anti-inflammatory:</b> Exhibit of H <sub>2</sub> O <sub>2</sub> -induced oxidative damage on HepG2 cells with EC <sub>50</sub> value of 42.4 μM (Gan et al., 2009b)
8-Hydroxy-lindestenolide (11)	<i>L. aggregata</i>	<b>Anti-inflammatory:</b> Exhibit of H <sub>2</sub> O <sub>2</sub> -induced oxidative damage on HepG2 cells with EC <sub>50</sub> value 67.5 μM (Gan et al., 2009b)
Linderolide D (23)	<i>L. aggregata</i>	<b>Anti-inflammatory:</b> Exhibited in LPS-induced RAW264.7 macrophage cells with IC <sub>50</sub> value 38.7 μM (Sumioka et al., 2011)
Linderolide E (24)	<i>L. strychnifolia</i>	<b>Anti-inflammatory:</b> Showed strong activity towards nitric oxide production in RAW264.7 cells with IC <sub>50</sub> value 18.3 μM (Sumioka et al., 2011)
Linderaggredin A (19)	<i>L. aggregata</i>	<b>Anti-inflammatory:</b> Exhibited human neutrophils with IC <sub>50</sub> value 7.45 μM (Kuo et al., 2020)
Linerenone (33)	<i>L. communis</i>	<b>Anti-inflammatory:</b> Significant activity against H460, ES2, and DU145 cancer cells with IC <sub>50</sub> values 2.1, 2.8, and 3.0 μg/mL, respectively (Deng et al., 2011)
Linderaggredin C (162)	<i>L. aggregata</i>	<b>Anti-inflammatory:</b> Inhibit the superoxide anion generation in human neutrophils with IC <sub>50</sub> value 7.45 μM (Kuo et al., 2020)
Linderolide O (99)	<i>L. aggregata</i>	<b>Anti-inflammatory:</b> Exhibited by reducing redness, swelling, and pain in the body parts with IC <sub>50</sub> value 6.3 μM (Lv et al., 2023)
Linderolide P (100)	<i>L. aggregata</i>	<b>Anti-inflammatory:</b> Exhibited by reducing redness, swelling, and pain in the body parts with IC <sub>50</sub> value 9.6 μM (Lv et al., 2023)
3-Oxo-4, 5αH, 8βH-eudesma- 1,7(11)-dien-8, 12-olide (9)	<i>L. aggregata</i>	<b>Antitumor:</b> Showed strong activity against non-small cell lung cancer (A549) with IC <sub>50</sub> value 7.2 μM (Ohno et al., 2005)
Eudeglaucone (51)	<i>L. glauca</i>	<b>Anti-neuroinflammatory:</b> Inhibited nitric oxide production by lipopolysaccharide with IC <sub>50</sub> value 15.9 μM (Yu et al., 2016)
Linderagalactone E (18)	<i>L. aggregata</i>	<b>Cytotoxicity:</b> Active in HepG2 cells with IC <sub>50</sub> value 67.5 μM (Gan et al., 2009b)
<b>ALKALOIDS</b>		
Norisoboldine (195)	<i>L. aggregata</i>	<b>Anti-arthritic:</b> Strong agents in the development of Treg cells through promoting fatty acid oxidation with IC <sub>50</sub> value 10 μM (Wei et al., 2015)
D-dicentrine (185)	<i>L. megaphylla</i>	<b>Antitumor:</b> Exhibited hepatoma, melanoma, lung/colon carcinoma, oesophageal carcinoma, lymphoma, and leukaemia cell lines with IC <sub>50</sub> value range of 0.41-29.04 μM (Huang et al., 1998)
Isoboldine (186)	<i>L. aggregata</i>	<b>Anti-inflammatory:</b> Reducing the expression of bone matrix-degrading enzymes with IC <sub>50</sub> value 6.8 μM (Lv et al., 2023)

Norboldine (192)	<i>L. aggregata</i>	<b>Anticancer:</b> Exhibited BxPC-3 pancreatic cancer cell with IC <sub>50</sub> value 27.0 μM (Zahari et al., 2014) <b>Anti-inflammatory:</b> Inhibited lipopolysaccharide (LPS)-stimulated nitric oxide production in murine RAW 264.7 macrophage cells with IC <sub>50</sub> value 9.6 μM (Yang et al., 2020)
<i>N</i> -methyl-laurotetanine (191)	<i>L. aggregata</i>	<b>Anti-inflammatory:</b> Inhibit the superoxide anion generation in human neutrophils with IC <sub>50</sub> value 8.36 μM (Kuo et al., 2020)
Boldine (184)	<i>L. aggregata</i>	<b>Anti-inflammatory:</b> Induced production of NO by lipopolysaccharide in RAW 264.7 cells with IC <sub>50</sub> value 8.7 μM (Yang et al., 2020) <b>Anti-inflammatory:</b> Reducing the expression of bone matrix-degrading enzymes with IC <sub>50</sub> value 9.5 μM (Lv et al., 2023)
Linderaggrine B (167)	<i>L. aggregata</i>	<b>Anti-inflammatory:</b> Exhibited superoxide anion generation in human neutrophils with IC <sub>50</sub> value 9.2 μM (Kuo et al., 2020)
Laurolistine (189)	<i>L. aggregata</i>	<b>Cytotoxic:</b> Exhibited human colon carcinoma (HCT-116) cell line with IC <sub>50</sub> value 27.1 μM (Yang et al., 2019)
Costaricine (218)	<i>L. aggregata</i>	<b>Cytotoxic:</b> Exhibited human colon carcinoma (HCT-116) cell line with IC <sub>50</sub> value 51.4 μM (Yang et al., 2020)
Norisoboldine (195)	<i>L. aggregata</i>	<b>Anti-inflammatory:</b> Induced production of NO by lipopolysaccharide in RAW 264.7 cells with IC <sub>50</sub> value 7.8 μM (Yang et al., 2020) <b>Anti-inflammatory:</b> Inhibit vascular endothelial growth factor (VEGF)-induced endothelial cell migration with IC <sub>50</sub> value 15.1 μM (Lu et al., 2013) <b>Anti-inflammatory:</b> Increase the Treg cells in CD4 <sup>+</sup> T cells and decrease Th17 cells, thus it can help in preventing autoimmune disease with IC <sub>50</sub> value 18.4 μM (Lv et al., 2015)
<b>FLAVONOIDS</b>		
Flavokawain B (234)	<i>L. oxyphylla</i>	<b>Anticancer:</b> Strong activity in MCF-7 human breast adenocarcinoma cells with inhibition of 79.7% (Hosseinzadeh et al., 2013) <b>Anti-inflammatory:</b> Acts on DPPH radical scavenging activity with IC <sub>50</sub> value 8.5 ± 0.004 μg/mL (Hosseinzadeh et al., 2013)
Avicularin (264)	<i>L. erythrocarpa</i>	<b>Anti-inflammatory:</b> Reduced releasing of LDH in H9c2 cells with IC <sub>50</sub> value 0.7 μM (Kim et al., 2011)
Quercetin (271)	<i>L. erythrocarpa</i> <i>L. aggregata</i>	<b>Anti-inflammatory:</b> Reduced releasing of LDH in H9c2 cells with IC <sub>50</sub> value 22.3 μM (Kim et al., 2011) <b>Antivirus:</b> Interact and target the S2 domain in SARS-CoV-2 spike proteins with IC <sub>50</sub> value 93.0 μM (Kumar & Pandey, 2013)
Quercetin-3-O-rhamnoside (272)	<i>L. aggregata</i>	<b>Antioxidant:</b> Strong antioxidant capacity and modulation of the Nrf-2 pathway with IC <sub>50</sub> value 7.5 μM (Haque et al., 2020)
Kaempferol (259)	<i>L. neesiana</i>	<b>Antivirus:</b> Act as a 3C protease (3Cpro) inhibitor against enterovirus A71 with IC <sub>50</sub> value 85.0 μM (Adhikari et al., 2019)
<b>PHENOLICS</b>		
2,6-Dimethoxy-4-hydroxyphenyl-1-O-β-D-glucopyranoside (294)	<i>L. obtusifolia</i>	<b>Anti-allergic:</b> Inhibit histamine release and proinflammatory cytokine production in mast cells with inhibition 68.1% (Choi et al., 2013) <b>Anti-allergic:</b> Highly suppressed release of histamine

Koaburaside (297)	<i>L. obtusiloba</i>	from mast cells with IC <sub>50</sub> value 10.80 μM (Haque et al., 2023) <b>Anti-allergic:</b> Inhibit histamine release and proinflammatory cytokine production in mast cells with inhibition 66.9% (Choi et al., 2013) <b>Anti-allergic:</b> Highly suppressed release of histamine from mast cells with IC <sub>50</sub> value 9.0 μM (Haque et al., 2023)
1-Methoxy-2,5,7-trihydroxyxanthone (287)	<i>L. fruticose</i>	<b>Antioxidant:</b> Moderate to low-density lipoprotein activity with IC <sub>50</sub> value 25.5 μM (Song et al., 2006)
3-Hydroxy-5-methoxybiphenyl (285)	<i>L. fruticose</i>	<b>Antioxidant:</b> Moderate to low-density lipoprotein activity with IC <sub>50</sub> value 15.5 μM (Song et al., 2006)
3,5-Dimethoxy-biphenyl (286)	<i>L. fruticose</i>	<b>Antioxidant:</b> Moderate to low-density lipoprotein activity with IC <sub>50</sub> value 48.1 μM (Song et al., 2006)
<b>MISCELLANEOUS</b>		
Epicatechin (342)	<i>L. erythrocarpa</i>	<b>Anti-inflammatory:</b> Reduced releasing of LDH in H9c2 cells with IC <sub>50</sub> value 0.7 μM (Kim et al., 2011)
Proanthocyanidins (349)	<i>L. aggregata</i>	<b>Antivirus:</b> Inhibited HIV-1 integrase with IC <sub>50</sub> value 5.2 to 31.3 μM (Zhang et al., 2003c)
Cinnamtannin B1 (350)	<i>L. glauca</i>	<b>Antioxidant:</b> Inhibit low-density lipoprotein properties with IC <sub>50</sub> value 2.0 mg/mL (Huh et al., 2014)
Cinnamtannin B2 (351)	<i>L. glauca</i>	<b>Antioxidant:</b> Inhibit low-density lipoprotein properties with IC <sub>50</sub> value 1.1 mg/mL (Huh et al., 2014)
Procyanidin B1 (345)	<i>L. aggregata</i>	<b>Antioxidant:</b> Inhibitory activities against HIV-1 integrase with IC <sub>50</sub> value 25.3 μM (Zhang et al., 2003c)
Procyanidin B2 (346)	<i>L. aggregata</i>	<b>Antioxidant:</b> Inhibitory activities against HIV-1 integrase with IC <sub>50</sub> value 27.1 μM (Zhang et al., 2003c)
Litsenolide (321)	<i>L. nacusua</i>	<b>Antitumor:</b> Moderate against HL-60 and MCF-3 cell lines with respective IC <sub>50</sub> values of 20.9 and 17.7 μM (Lei et al., 2017)
Reflexanbene A (328)	<i>L. reflexa</i>	<b>Cytotoxic:</b> Moderate against MGC803 and SMMC-7721 cell lines with IC <sub>50</sub> values 29.6 and 34.3 μM, respectively (Fu et al., 2019)
Reflexanbene C (329)	<i>L. reflexa</i>	<b>Cytotoxic:</b> Moderate against MGC803 and SMMC-7721 cell lines with IC <sub>50</sub> values 47.5 and 54.9 μM, respectively (Fu et al., 2019)

#### 4. CONCLUSION

Numerous biologically active compounds have been isolated from *Lindera* species previously by several researchers. Sesquiterpenes, flavonoids, phenolics, and alkaloids are among the compounds which reported mainly on anticancer, antifibrotic, anti-inflammatory, antitumor, antioxidant, anti-arthritic, cytotoxic, anti-allergic, and antihyperlipidemic properties. Future studies related to ethnopharmacological research should focus on exploring the traditional uses of *Lindera* species among different locations. These studies should also compile information about their formulation and mode of administration in traditional medicine, which we found lacking in most of the reviewed literature. On the other hand, scientific studies should focus on bioassay-guided drug discovery based on the existing traditional knowledge. Mechanism-based *in vitro* and *in vivo* studies should be performed to understand the underlying mechanisms linked to ethnopharmacological uses.

#### Declaration of Interest

The authors hereby declare that there is no conflict of interest.

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