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An Update on Phytochemistry and Biological Activities of *Cinnamomum*

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Abstract: The genus Cinnamomum belongs to the family Lauraceae and contains about 250 species. Cinnamomum plants have great economic value and have been widely used in the pharmaceutical, chemical, food and cosmetic industries. A great deal of research on the chemical constituents and their various biological activities has been conducted on only 20 species of Cinnamomum. We have already summarized the chemical structures and bioactivities of terpenoids from Cinnamomum. Herein, we give an update on other types of compounds and their biological activities. According to the findings, 380 chemical compounds obtained from Cinnamomum, including lignans, butanolides, flavonoids, phenylpropanoids, alkaloids and other compounds are summarized, and their corresponding unique chemical structures and significant biological activities are introduced in this paper.

Keywords: *Cinnamomum*; phytochemistry; immunomodulatory; anti-inflammatory; antioxidant activity.

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1. Introduction

The family Lauraceae contains about 45 genera and 2500 species that are economically important in the pharmaceutical, chemical, food and cosmetic industries. As one of the largest genera of Lauraceae, *Cinnamomum* comprises approximately 250 species, which is represented by evergreen trees and shrubs. *Cinnamomum* plants are mainly distributed in tropical and subtropical Asia, Australia and the Pacific islands [1]. There are about 46 species in China, which are endemic in the southern religions, with the most species in Yunnan province, followed by Guangdong and Sichuan [2].

Cinnamomum species have been used as important sources of traditional medicine, timber, edible fruits, spices, and perfumes in China for a long history [3]. Some *Cinnamomum* species, such as *C. cassia*, *C. zeylanicum*, *C. tamala* and *C. wilsonii*, are famous herbs that have a long history of being used as medicine. Cinnamomi cortex, which is obtained from some *Cinnamomum* species, has been used for treating cardiovascular, chronic gastrointestinal and inflammatory diseases [4, 5]. The extracts from *Cinnamomum* plants have been reported to show various biological activities, including immunomodulatory, anti-inflammatory, anticancer and other activities; moreover, many studies have also been done on the activity of monomer compounds [6-10] However, the relationship between the activities of the extracts from *Cinnamomum* and those of the monomer compounds has not been fully elucidated Therefore, this paper aims to reveal the activity relationship between extracts and compounds from the genus, which may provide a theoretical basis for the discovery of active ingredients from *Cinnamomum* and better utilization of *Cinnamomum* plants.

To date, the research on bioactive constituents from *Cinnamomum* is a research focus in China and many experiments have been done. There have been over 500 compounds isolated from *Cinnamomum* with various pharmaceutical activities. Many constituents have been confirmed to be effective in *in vivo* experiments or even clinically used in treatment for various diseases, such as cinnamaldehyde, cinnamic acid, sesamin, camphor, borneol and so on. There are many lead compounds that are under research and development and many new compounds with unique structures under activity screening tests. Therefore, a summary of the active ingredients of *Cinnamomum* is necessary, which will help to explore more valuable lead compounds.

Among the *Cinnamomum* species, *C. cassia* is the most important species in the genus *Cinnamomum* and has been thoroughly studied. Around 300 constituents with many new skeletons have been found in this species. There are also many studies on phytochemistry of other species, such as *C. burmannii*, *C. camphora*, *C. kotoense* and *C. subavenium.* And the constituents obtained from *Cinnamomum* have shown a variety of biological activities, which provides a lot of bioactive ingredients for the development of new drugs.

We have previously introduced the structures of terpenoids from *Cinnamomum* and their biological activities [11]. Herein, we summarized other types of constituents from *Cinnamomum* plants in this paper, including lignans, butanolides, flavonoids, phenylpropanoids, alkaloids, and other compounds. Also, their pharmacological activities are also introduced in this review, which covers antioxidant, immunomodulatory, anti-inflammatory, anticancer and other effects. Many compounds have been proved to be potent bioactive constituents through a lot of assays and thus are promising treatment for many diseases.

2. Chemical Constituents and Their Biological Activities

A great deal of phytochemical research has been conducted on a few species. Excluding the studies that only give focus on volatile oils, we have summarized a total of 380 constituents from 17 *Cinnamomum* species, which include 82 lignans, 46 butanolides, 65 flavonoids, 76 phenylpropanoids, 19 alkaloids and 92 other compounds.

2.1. Lignans

Lignans are an important part of the secondary metabolites of *Cinnamomum* species, which have high content and abundant structural types. There are 82 lignans isolated from *Cinnamomum*

plants (Table 1 & Figure 1), including five diarylbutanes (**1**-**5**), ten arylnaphthalenes (**6**-**15**), eleven tetrahydrofurans (**16**-**26**), sixteen bis-tetrahydrofurans (**27**-**42**), sixteen benzofurans (**43**-**58**), eight 8-O-4'-neolignan (**59**-**66**), four spirodienones (**67**-**70**), two biphenyls (**71**-**72**), three norlignans (**73**-**75**), four sesquilignans (**76**-**79**), one dimer (**80**), and two neolignans (**81**-**82**).

Spirolignans can be rarely found in natural products. Herein, Lai *et al*. [12] separated two pairs of spirodienone neolignan racemates (**67**-**70**) with a rare 2-oxaspiro[4.5]deca-6,9-dien-8-one motif from *C. subavenium*. It was the first time to report spirodienone neolignans with this rare skeleton. Moreover, these compounds showed significant inhibitory effects against NO production in RAW264.7 mouse macrophages, with IC_{50} values of 17.9, 5.6, 15.1, and 4.3 μM, respectively. Among the four lignans, **70** exhibited strongest inhibitory effects while **67** weakest. Thus, the methoxy substituent at C-5 enhanced the inhibitory effects of the compound. In addition, **69** and **70** showed much stronger inhibitory effects than **67** and **68**, respectively. Thus, the chirality of the spirolignans significantly affected the inhibitory effects on the NO production in the RAW264.7 mouse macrophages.

The lignans obtained from *Cinnamomum* contains two glycosides (**47**, **58**), both of which were isolated from the bark of *C. cassia*, and **58** is a unique compound of *Cinnamomum* plants [2, 13]. It is noteworthy that hydroxyl groups at the 9-positions of some lignans (**3**-**4**, **12**-**13**) formed ester groups with ferulyl groups. This special structure was only found in *C. osmophloeum* [14]. Moreover, C-7, C-7', C-8 and C-8' of compound **82** isolated from *C. balansae* formed a cyclobutane, which is also a relatively rare structure [15].

Biphenyllignans are common in separation, such as magnolol analogues [16]. However, according to Liu *et al*. [17], the C-7 and C-8 positions of biphenyl lignans (**71**-**72**) formed peroxy bonds, which are rare in natural products. Moreover, both the compounds have not been found in other genera and have showed certain neuroprotective activities.

Sesamin (**34**) has high content in *Cinnamomum* plants, especially in the leaves of *Cinnamomum camphora* [7], which has showed various biological activities *in vivo* and *in vitro*. Treatment with **34** could accelerate wound healing by promoting the proliferation, adherence, migration in human umbilical vein endothelial cells. It could also promote neogenesis of granulation tissue and deposition and remodeling of the collagen matrix in a rat model [18]. According to Majdalawieh *et al* [19], the anti-hyperlipidemic activities of **34** have been proven in many *in vivo* studies. It mainly exerts the anti-hyperlipidemic effects by downregulating the activity of Δ5 desaturase, suppressing the activity of SREBP-1, and inhibiting the process of PUFA chain elongation via sesamin-dependent upregulation of PPARα regulatory pathways. Moreover, many other *in vivo* experiments of sesamin have been conducted and **34** has the potential to treat or prevent intestinal ischemia, cardiovascular diseases, lung inflammation and many other diseases [20-22]. In a clinical trial, sesamin supplement could relieve clinical symptoms and pathological changes that were caused by inflammatory impairment in patients with rheumatoid arthritis [23].

Many lignans from different plant sources have been reported to show good neuroprotective activities and some have been used in treatment of neurodegenerative diseases [24]. Lignans **17**, **71**, **72** and **85** were tested for their neuroprotective effects against tunicamycin-induced cell death in SH-SY5Y cells. All these complounds exhibited strong neuroprotective effects with EC_{50} values ranging from 21 to 75 μM [17].

Table 1. Lignans from *Cinnamomum* genus

No.	Compounds	Plants	Ref.	No.	Compounds	Plants	Ref.
1	secoisolariciresinol	c,o	[25, 28]	**42**	4-ketopinoresinol	c	[28]
2	methoxysecoisolariciresinol	c	[28]	**43**	(7S,8R)-lawsonicin	c	[25]
3	Secoisolariciresinol diferuloyl ester	o	[14]	**44**	urolignoside	z	[29]
4	9,9′-Di-O-feruloyl-(+)-5,5′-dimethoxy secoisolariciresinol	o	[14]	**45**	9,9′-dihydroxy-3,4-methylenedioxy-3′-methoxy[7-O-4′,8,5′]neolignan	c	[17]
5	cinnacassoside A	c	[13]	**46**	(7R,8S)-ficusal	c	[17]
6	(6R,7R,8R)-7a-[(β-D-glucopryanosyl)oxy] lyoniresinol	c	[2]	**47**	samwiside	c	[30]
7	(6S,7R,8R)-7a-[(β-D-glucopryanosyl)oxy] lyoniresinol	c	[2]	**48**	(+)-leptolepisol C	c	[25]
8	(6R,7S,8S)-7a-[(β-D-glucopryanosyl)oxy] lyoniresinol	c	[2]	**49**	cinncassin D	c	[25]
9	isolariciresinol	c	[25]	**50**	picrasmalignan A	c	[25]
10	5-methoxy-isolariciresinol	c	[28]	**51**	spicatolignan B	c	[13]
11	(−)-lyoniresinol	c	[31]	**52**	balanophonin	c	[17]
12	(7′S,8′R,8R)-Lyoniresinol-9-O-(E)-feruloyl ester	o	[14]	**53**	5-methoxybalanophonin	c	[17]
13	(7′S,8′R,8R)-lyoniresinol-9,9′-di-O-(E)-feruloyl ester	o	[14]	**54**	hierochin B	c	[17]
14	(-)-lyoniresinol 3*α*-O-β-D-glucopyranoside	c	[32]	**55**	simulanol	c	[17]
15	schizandriside	d	[33]	**56**	salvinal	c	[17]
16	cinnacassin G	c	[17]	**57**	herpetal	c	[17]
17	cinnacassin H	c	[17]	**58**	cinnacassoside B	c	[13]
18	(+)-(7'R,8R,8'R)-5,5'-dimethoxylariciresinol	c	[25]	**59**	(-)-erythro-(7R,8S)-guaiacylglycerol-β-O-4'-sinapoyl ether	c	[25]
19	(+)-(7'S,8R,8'R)-5,5'-dimethoxylariciresinol	c	[25]	**60**	(-)-erythro-(7S,8R)-syringylglycerol-β-O-4′-sinapyl ether	c	[25]
20	5'-methoxylariciresinol	c	[34]	**61**	cinncassin E	c	[25]
21	cinnacassin M	c	[17]	**62**	(+)-threo-(7S,8S)-guaiacylglycerol-β-coniferyl aldehyde ether	c	[25]
22	(+)-episesaminone	d	[35]	**63**	(+)-erythro-(7S,8R)-guaiacylglycerol-β-coniferyl aldehyde ether	c	[25]
23	dehydroxycubebin	p	[36]	**64**	1-(4-hydroxy-3-methoxyphenyl)-2-[3-(3-hydroxy-1-propenyl)-5-methoxyphenoxy]-1,3-propanediol	c	[17]
24	cubebin	p	[36]	**65**	(+)-erythro-(7R,8S)-guaiacylglycerol-8-vanillin ether	c	[25]
25	hinokinin	p	[36]	**66**	1,2,3-propanetriol, 1-[4-(1R,2R)-2-hydroxy-(4-hydroxy-3-methoxy-phneyl)-1-(hydroxymethyl)ethoxy]-3-methoxyphneyl	c	[37]
26	(7′S,8S,8′R)-4,4′-dihydroxy-3,3′,5,5′-tetramethoxy-7′,9-epoxylignan-9′-ol-7-one	c	[17]	**67**	(+)-subaveniumin A	s	[12]
27	(+)-syringaresinol	b,c,k,m,r,s,t	[38-40]	**68**	(+)-subaveniumin B	s	[12]
28	(+)-yangambin	b,c	[28, 38]	**69**	(-)-subaveniumin A	s	[12]
29	clemaphenol A	k	[41]	**70**	(-)-subaveniumin B	s	[12]
30	cinnacassin F	c	[17]	**71**	Cinnacassin I	c	[17]
31	(+)-pinoresinol	b,c,d	[28, 31, 42]	**72**	cinnacassin J	c	[17]
32	(+)-medioresinol	b,c	[28, 43]	**73**	6-hydroxy-2-(4-hydroxy-3,5-dimethoxy-phenyl)-3,7-dioxabicyclo-[3.3.0]-octane	c	[13]
33	pinoresinol methyl ether	d	[42]	**74**	zhebeiresinol	c	[17]
34	sesamin	b,d,j,k,n,s,t	[27, 44-47]	**75**	(-)-(7R,8R,8'R)-acuminatolide	d	[42]
35	(+)-diasesamin	d,j,n	[27, 47]	**76**	buddlenol A	c	[17]
36	(+)-episesamin	d,j	[27, 47]	**77**	erythro-buddlenol B	c	[17]
37	pluviatilol	k	[41]	**78**	ficusesquilignan A	c	[28]
38	piperitol	d	[42]	**79**	buddlenol C	c	[28]

39	9*α*-hydroxysesamin	d	[48]	**80**	hedyotisol A	c	[17]
40	9*β*-hydroxysesamin	d	[48]	**81**	cinnaburmanin A	b	[49]
41	l-asarinin	d	[48]	**82**	cinbalansan	a	[15]

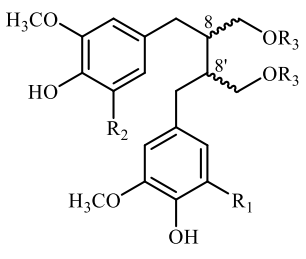
a-*C. balansae*, b-*C. burmannii*, c-*C. cassia*, d-*C. camphora*, i-*C. inunctum*, j-*C. insulari-montanum*, k-*C. kotoense*, m-*C. macrostemon*, o-*C. osmophloeum*, p-*C. parthenoxylon*, q-*C. philippinense*, n-*C. randaiense*, r-*C. reticulatum*, s-*C. subavenium*, t-*C. tenuifolium*, u-*C. trichophyllum*, z-*C. zeylanicum*. The same as below.

The anti-inflammatory activities of the isolated lignans were evaluated on production of nitric oxide (NO) induced by lipopolysaccharide (LPS) in BV-2 microglial cells. Compounds including **19** and **61**-**63** showed significant inhibition activities with IC_{50} values of 17.5, 17.6, 17.7 and 18.7 μM, respectively. Other compounds exhibited moderate inhibitory activities, including **18**, **20, 27, 43**, **59**, **60** and **65**. In addition, it was noticed that 8-*O*-4'-lignans showed significant inhibition with IC_{50} values ranging from 17.6 to 42.0 μM. And among them, lignans with acrylaldehyde group at C-1' exhibited highest anti-inflammatory activities [25].

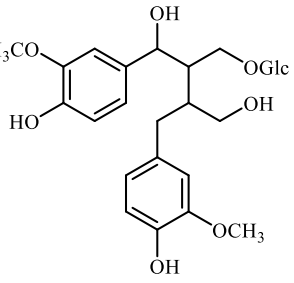
Compound **50** significantly inhibited NO production and suppress TNF-α and IL-6 release at three doses (10, 30 and 100 μM) in LPS-activated macrophage RAW 264.7 cells. Furthermore, the inhibitive action of **50** was more potent than that of the positive control hydrocortisone, a commonly used anti-inflammatory drug. The substance can also inhibit the overexpression of iNOS and COX-2 and the activity of iNOS and COX-2 enzymes in the assays [26].

Three lignan esters, including compounds **4**, **12** and **13**, were tested for their cytotoxicities against HepG2, Hep3B, and Ca9-22 cancer cells. Compounds **12** and **13** have significant cytotoxicities on three cancer cell lines with EC_{50} values of less than 20 and 10 μg/mL respectively, while compound 4 showed moderate effect. The structure-activity relationships are as followed: (a) The cyclolignans (**12** and **13**) demonstrated stronger effects than the dibenzylbutane lignan (**4**) on these three cancer cell lines. (b) The lignan with two feruloyl groups (**13**) showed stronger activities than that with only one (**12**). Thus, both C-9 and C-9′ feruloyl groups significantly increased the cytotoxicity of the compounds [14].

In another assay, the cytotoxicity of **34** on Hep G2 was investigated. The percentage of Hep G2 cells in the S phase decreased from 40% to 30% after treatment with 200 μM **34** for 24 hours, showing a slight cytotoxic effects [27]. Moreover, the lignan **8** was reported to show significant inhibitory effects on ConA-induced T cell proliferation with an inhibition ratio of 80.1% at a concentration of 200 μM, whilst at low doses of 25 and 12.5 μM, stimulated the proliferation of T cells. Some compounds exhibited weak inhibition, including compounds **6**, **238** and **362** [2].



	R_1	R_2	R_3	
1	H	H	H	8R, 8'R
2	OCH_3	OCH_3	H	8R, 8'R
3	H	H	feruloyl	8R, 8'R
4	OCH_3	OCH_3	feruloyl	8S, 8'S



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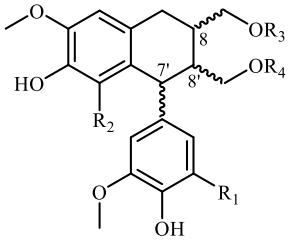
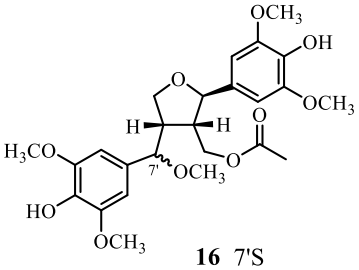
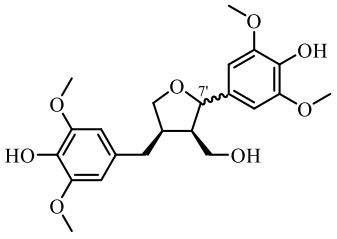


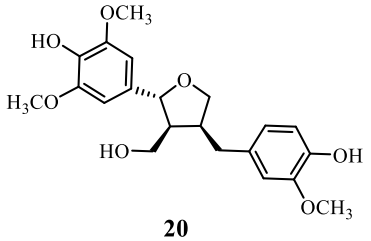
	R_1	R_2	R_3	R_4	
6	OCH_3	OCH_3	H	Glc	7'R, 8'R, 8R
7	OCH_3	OCH_3	H	Glc	7'R, 8'R, 8S
8	OCH_3	OCH_3	H	Glc	7'S, 8'S, 8R
9	H	H	H	H	7'R, 8'S, 8S
10	OCH_3	H	H	H	7'R, 8'S, 8S
11	OCH_3	OCH_3	H	H	7'R, 8'S, 8S
12	OCH_3	OCH_3	feruloyl	H	7'S, 8'R, 8R
13	OCH_3	OCH_3	feruloyl	feruloyl	7'S, 8'R, 8R
14	OCH_3	OCH_3	H	Glc	7'R, 8'S, 8S
15	H	H	H	Xyloside	



16 7'S
17 7'R



18 7'R
19 7'S



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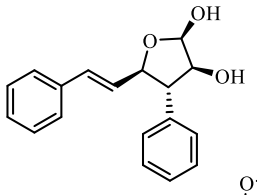

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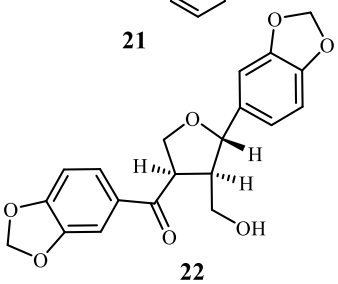

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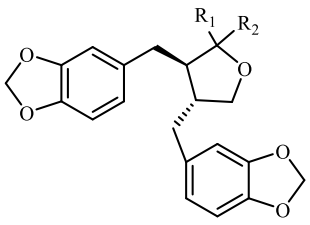
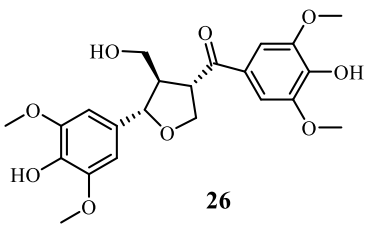


	R_1	R_2
23	H	H
24	OH	H
25	=O	



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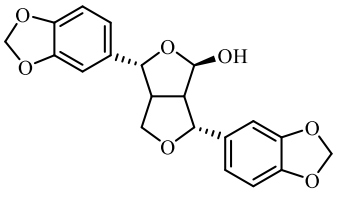

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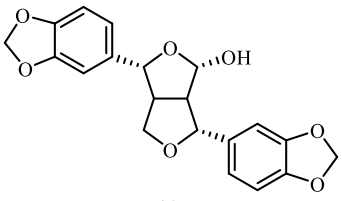

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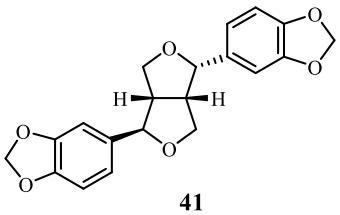

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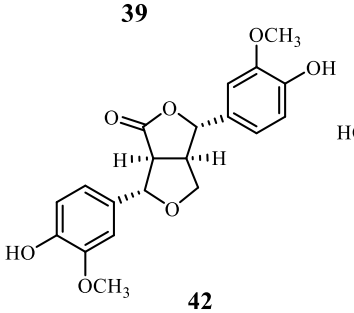

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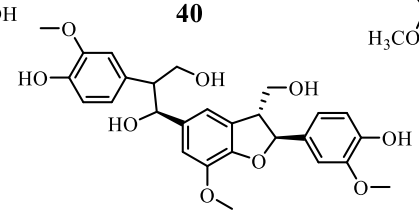

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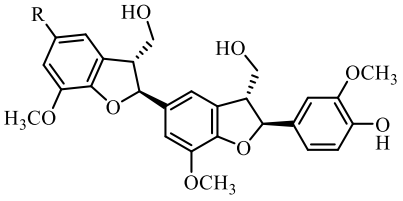
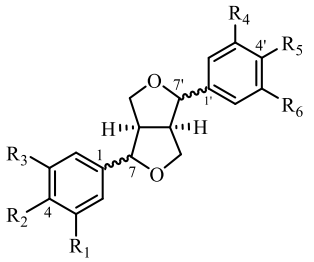
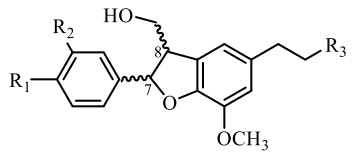


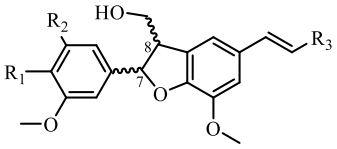
49 R = CHO
50 R = CH=CHCHO



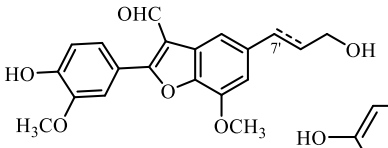
	R_1	R_2	R_3	R_4	R_5	R_6	
27	OCH_3	OH	OCH_3	OCH_3	OH	OCH_3	7S, 7'S
28	OCH_3	OCH_3	OCH_3	OCH_3	OCH_3	OCH_3	7S, 7'S
29	OH	OCH_3	H	OH	OCH_3	H	7S, 7'S
30	OCH_3	OH	OCH_3	OCH_3	OH	OH	7S, 7'S
31	OCH_3	OH	H	OCH_3	OH	H	7S, 7'S
32	OCH_3	OH	OCH_3	OCH_3	OH	H	7S, 7'S
33	OCH_3	OCH_3	H	OCH_3	OH	H	7S, 7'S
34	$-OCH_2O-$		H	$-OCH_2O-$		H	7S, 7'S
35	$-OCH_2O-$		H	$-OCH_2O-$		H	7R, 7'R
36	$-OCH_2O-$		H	$-OCH_2O-$		H	7R, 7'S
37	$-OCH_2O-$		H	OCH_3	OH	H	7R, 7'S
38	$-OCH_2O-$		H	OCH_3	OH	H	7S, 7'S



	R_1	R_2	R_3	
43	OH	OCH_3	CH_2OH	7S, 8R
44	OGlc	OCH_3	CH_2OH	7S, 8R
45	$-OCH_2O-$		CH_2OH	7S, 8R
46	OH	OCH_3	CHO	7R, 8S
47	OH	OCH_3	CH_2OGlc-Api	7S, 8R

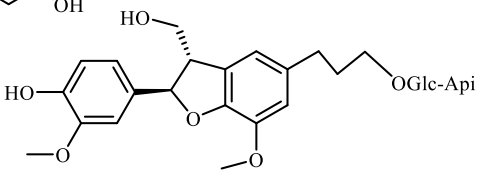


	R_1	R_2	R_3	
51	OH	H	COOH	7R, 8S
52	OH	H	CHO	7R, 8S
53	OH	OCH_3	CHO	7R, 8S
54	OCH_3	H	CH_2OH	7S, 8R
55	OH	OCH_3	CH_2OH	7S, 8R



56

57 $D^{7'}$



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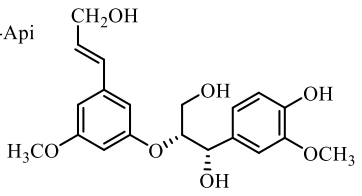

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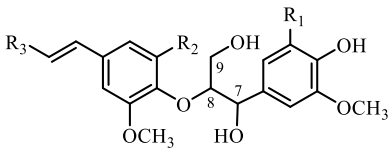
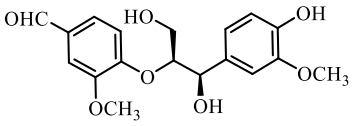


	R_1	R_2	R_3	
59	H	OCH_3	CH_2OH	7R, 8S
60	OCH_3	OCH_3	CH_2OH	7S, 8R
61	OCH_3	H	CHO	7R, 8R
62	H	H	CHO	7S, 8S
63	H	H	CHO	7S, 8R



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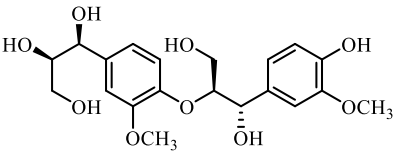

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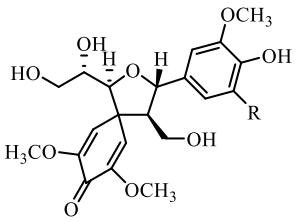
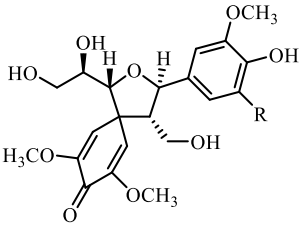


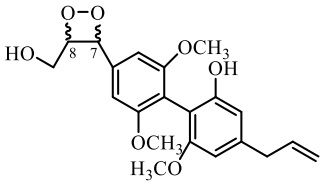
67 R=H

68 $R=OCH_3$



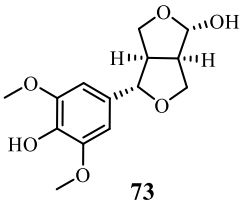
69 R=H

70 $R=OCH_3$



71 7R, 8S

72 7S, 8R



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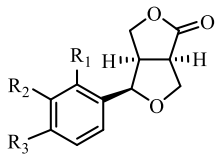
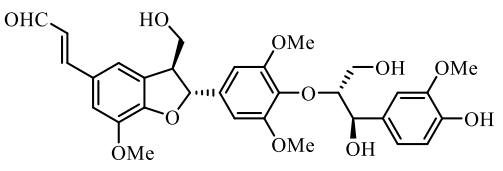


	R_1	R_2	R_3
74	OCH_3	OH	OCH_3
75	-OCHO-		H



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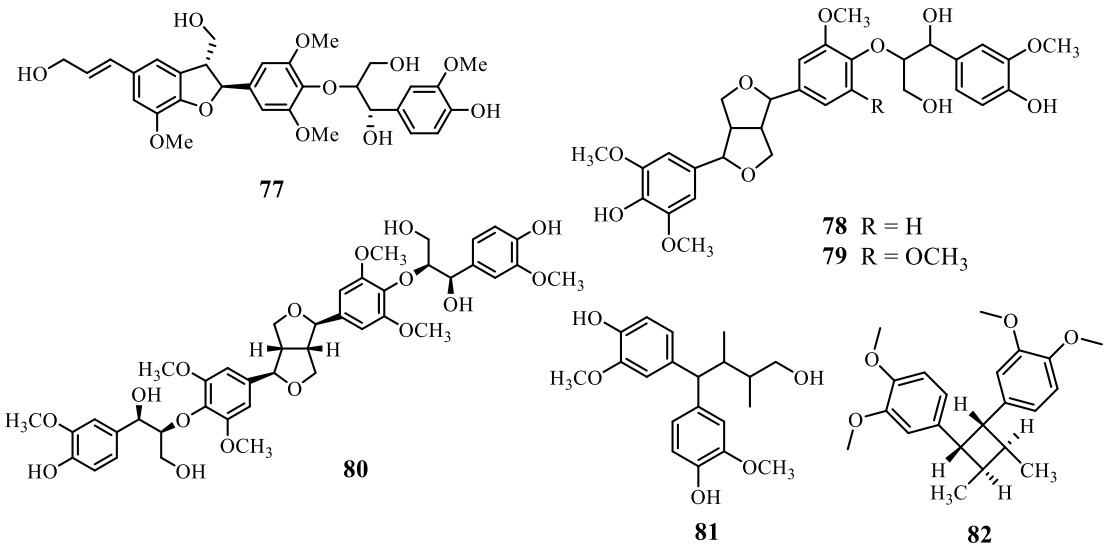


Figure 1. The structures of lignans from *Cinnamomum*

2.2. Butanolides

Butanolides are not very common in the separation of natural products. However, there have been 46 butanolides obtained from the genus *Cinnamomum* (Table 2 & Figure 2), which are important active ingredients with a variety of structure types. Furthermore, some extracts from *Cinnamomum* plants have been reported to show potent anticancer effects and butanolides may be the major active ingredients [50].

The butanolides isolated from the *Cinnamomum* include two simple γ-butyrolactones (**83**, **84**), ten *α,β*-diphenyl-γ-butyrolactones (**85-94**), twenty-nine long-chain fatty alkyl-substituted *γ*-lactone (**95-123**) and five secobutanolides (**124-128**).

According to Liu *et al*. [17], the *α,β*-diphenyl-γ-butyrolactones (**85-94**) are a class of unique natural compounds that have only been isolated from *C. cassia* and thus could be used as potential chemotaxonomic markers for this species. Among these compounds, **85**, **88** and **90** has shown significant neuroprotective activities.

Compounds **96, 99** and **100** were firstly obtained from *Cinnamomum kotoense* in 2006 and showed significant anti-proliferation activity [41, 51]. Isoobtusilactone A (**97**) and obtusilactone A (**98**) are common in *Cinnamomum* plants and both have been found in seven *Cinnamomum* species. Isophilippinolide A (**103**) and philippinolide A (**104**) were firstly found in the roots of *Cinnamomum philippinense* and also showed potent anticancer activities [52]. Compounds **97--110** share the same β-hydroxy-γ-methylene-*α,β*-unsaturated-γ-lactone skeleton.

According to the findings, many butanolides from the genus were proved to exhibit potent anticancer effects and it is illustrated as follows. It was reported that **112**, **113**, **116** and **127** can induce significant cell death in the human colorectal cancer line SW480. At a dose of 50 μM, SubG1 levels were increased to 25.4% and 23.7% respectively, showing that **112** and **113** induced significant DNA damage. The subG1 population in cells treated with **116** and **127** was 11.0% and 9.1%, respectively. All these compounds caused DNA damage in a dose-dependent manner and at a dose of 75 μM, SubG1

expression was increased up to 23.4%-47.2% [44]. In another assay, **106** and **116** also showed potent cytotoxicity, with SubG1 levels of 47.2 and 27.4%, respectively [53].

Subamolide A (**112**), only obtained from *Cinnamomum subavenium*, showed significant effects in the screening of anti-cancer activities *in vivo* [54]. The compound was demonstrated to selectively induce apoptosis in two cancerous human urothelial carcinoma cell lines (NTUB1 and T24) by triggering the mitochondria-dependent apoptotic pathways and p53 and ERK1/2 activation [55]. Compound **112** induced apoptosis in human lung cancer cells A549 and NCI-H460 resulting from triggering mitotic catastrophe with apoptosis and caused a dramatic 70% reduction in tumor size in an animal model [56].

Table 2. Butanolides from *Cinnamomum* genus.

No.	Compounds	Plants	Ref.	No.	Compounds	Plants	Ref.
83	(R)-3-hydroxybutanolide	c	[37]	**106**	subamolide D	s	[50]
84	3-hydroxy-4,4-dimethyl-4-butyrolactone	i	[57]	**107**	subamolide E	s	[50]
85	cinncassin A	c	[17]	**108**	Linderanolide B	s	[44, 50]
86	Cinncassin A_1	c	[17]	**109**	Isolinderanolide B	k,s	[51, 53]
87	Cinncassin A_2	c	[17]	**110**	isoreticulide	r	[58]
88	Cinncassin A_3	c	[17]	**111**	lincomolide B	k	[40]
89	Cinncassin A_4	c	[17]	**112**	subamolide A	s	[44, 50]
90	Cinncassin A_5	c	[17]	**113**	subamolide B	s	[44, 50]
91	Cinncassin A_6	c	[17]	**114**	philippinolide B	q	[52]
92	Cinncassin A_7	c	[17]	**115**	tenuifolide B	t	[45]
93	cinnamomulactone	c	[17]	**116**	subamolide C	s	[44, 50]
94	cinnamomumolide	c	[31]	**117**	kotomolide B	k	[41]
95	5R-methyl-3-heptatriacontyl-2(5H)-furanone	c	[34, 59]	**118**	kotomolide	k	[60]
96	Cinnakotolactone	k	[51]	**119**	5-dodecanyl-4-hydroxy-4-methyl-2-cyclopentenone	d	[60]
97	isoobtusilactone A	d,j,k,n,r,s,t	[39, 45, 47]	**120**	Kotolactone A	k	[40]
98	obtusilactone A	d,j,n,k,r,s,t	[39, 45, 47]	**121**	kotolactone B	k	[40]
99	isokotomolide A	k	[41]	**122**	2-acetyl-5-dodecylfuran	k	[40]
100	kotomolide A	k	[41]	**123**	2-acetyl-5-methylfuran	k	[40]
101	tenuifolide A	t	[45]	**124**	secokotomolide A	k	[40]
102	isotenuifolide A	t	[45]	**125**	secokotomolide	k	[40, 60]
103	isophilippinolide A	q	[52]	**126**	secotenuifolide A	t	[45]
104	philippinolide A	q	[52]	**127**	secosubamolide	s	[44, 50]
105	isomahubanolide	d	[48]	**128**	secosubamolide A	s	[50]

Compound **124** was also found to have significant cytotoxic effects on the human HeLa cell line. Compared to the vehicle control group, incubation with **124** at 0, 25, 50, and 100 μM for 24 h induced apoptosis in sub-G1 phase at 1.4, 68.8, 75.6, and 81.8% [41]. Moreover, **126** showed cytotoxic activity against two human prostate cancer epithelial cell lines, DU145 and LNCaP, with EC_{50} values of less than 7 μM (equal to 3.45 μg/mL) [45]. Inhibitory effects of **103** against the A375.S2 melanoma cell line were evaluated. Compared with untreated cells, treatment with 10, 25, 50, and 100 μM **103** for 24 h resulted in a dose-dependent increase in the subG1 accumulation, extending from 2.34 to 3.92, 4.27, 8.79 and 14.11%, respectively [52].

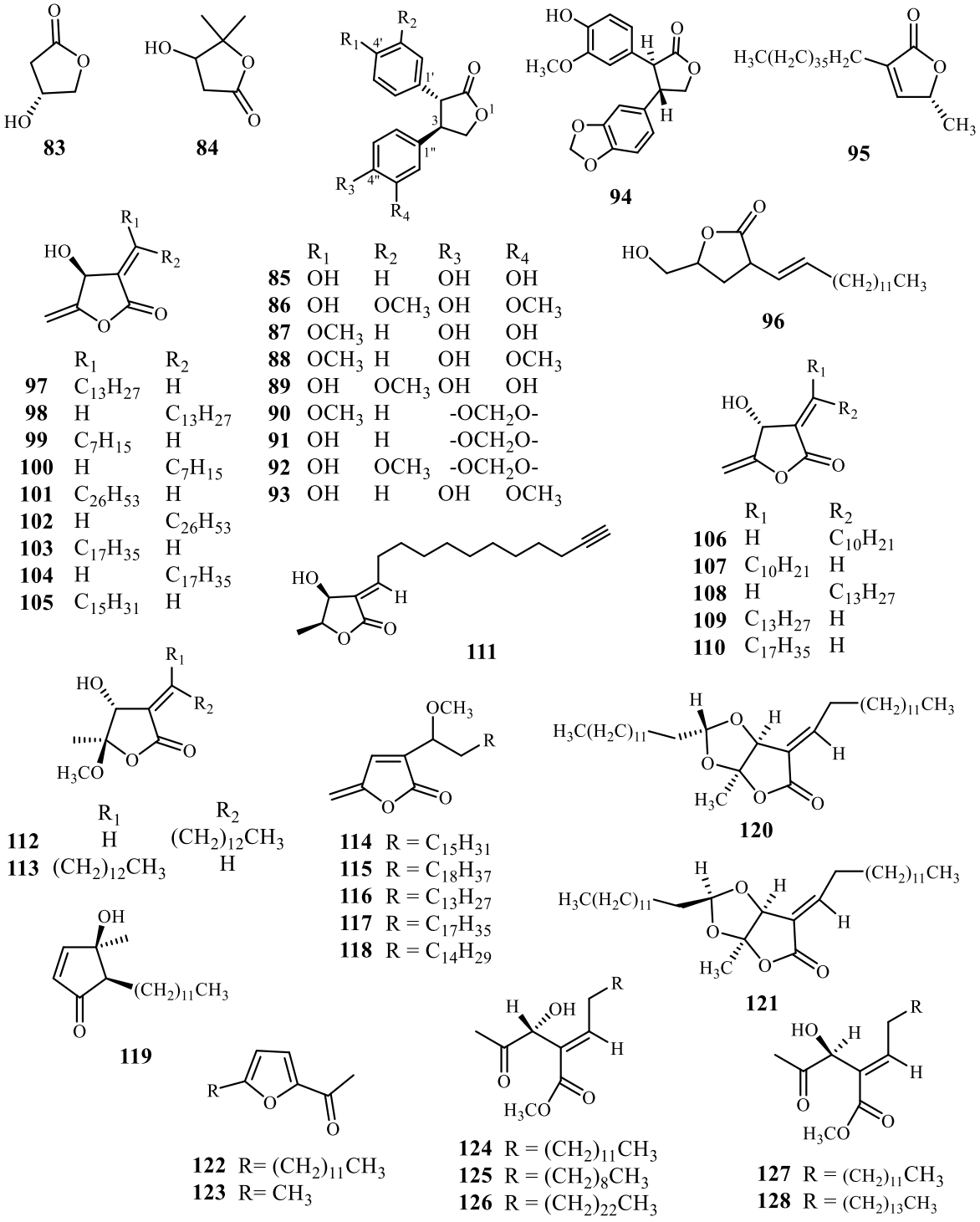


Figure 2. The structures of butanolides from *Cinnamomum*

2.3. Flavonoids

Leaves are mostly used as a medicinal part in traditional Chinese medicine, which undoubtedly have high content of flavonoids. There have been 65 flavonoids (**129**-**193**) isolated from *Cinnamomum* plants (Table 3 & Figure 3), including seven simple flavones (**129**-**135**), thirty-one flavonols (**136**-**166**), one dihydroflavones **(167**), two dihydroflavonols (**168**, **169**), one chalcone (**170**), seventeen flavanes (**171**-**187**) and seven anthocyanidins (**188**-**193**). Flavonoids are representative constituents of *Cinnamomum* plants, exemplified by quercetin (**142**), kaempferol (**136**) and their glycosides. Flavonoids from *Cinnamomum* mostly share similar types with other genus, but some of them have uncommon skeletons and show many biological activities, especially antioxidant activities.

Compound **193** is a flavonol galactoside-lignan ester. The compound has a rare skeleton, in which the kaempferol moiety was connected to a diacyl moiety with a cyclobutane ring bearing two 4-hydroxyphenyl through a sugar moiety.

Many flavonoids are natural antioxidants. It was confirmed that the hydroxy group at the C-3′ position of the B ring is essential for the antioxidant activity, which accounts for higher effect of rutin (**146**) compared to nicotiflorin (**147**) and isorhoifolin (**133**) in both concentrations of 10 and 20 μM, respectively [61].

Compound **140**, isolated from *C. osmophloeum*, was proved to have antioxidant capacity through DPPH and NBT Assays, with the EC_{50} values of 26.9 and 68.1 μM, respectively [62]. Compound **155** exhibited stronger radical scavenging activity (65.21%) than **156** (17.40%) at 60 μmol/L concentration in a DPPH assay, mostly because of the difference of coumaroyl group positions in the compounds [63]. The *in vitro* IC_{50} values against DPPH for tiliroside (**158**) was found to be 60.40 μg/mL and the ferric ion (Fe^{3+}) reducing ability of **158** were 0.324 at the dose of 50 mg/mL [64].

Furthermore, DPPH assays were performed to evaluate the antioxidative potential of some compounds. Compound **358** exerted moderate antioxidant effect with IC_{50} value of 75.03 μM [65]. In another assay, compounds **44**, **144**, **146**, **188** and **320** showed free radical scavenging activities of 30.4, 60.3, 44.7, 39.3 and 77.3%, respectively, at 12.5 ppm concentration. Among these compounds, **320** showed the highest antioxidant activity in the β-carotenelinolate system [29].

In addition to antioxidant effects, some flavonoids were demonstrated to show other activities, including anti-inflammatory, anti-cancer, immunomodulatory and anti-hyperglycemic activities.

Four kaempferol glycosides (**160**-**162** and **166**) from *C. osmophloeum* leaves exerted a dose-dependent inhibition on the production of NO, TNF-a and IL-12 from LPS/IFNc-activated macrophages. Among them, compound **162** showed the highest inhibitory activity, with significant inhibition at 10 μM, and 41% of TNF-a production and 35% of IL-12 production of the positive control at 20 μM [66].

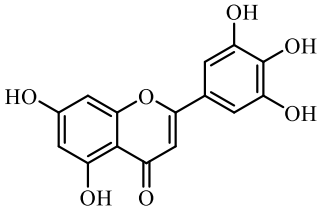
Two flavonoids (**155** and **156**) were repeorted to show potent inhibitory activities in lung cancer cell line (A549 and NCI-H460) and breast cancer cell line (MCF-7 and MDA-MB-231), with IC_{50} values ranging from 1.6 to 8.4 μg / mL. Both of them show highest inhibition on NCI-H460 cell line, with IC_{50} vallues of 4.6 and 1.6 μg/mL, respectively [67].

In vitro tests conducted by Liu *et al.* showed that compound **187** stimulated cell proliferation of splenocytes and peritoneal macrophages, significantly enhanced the cytotoxicity of natural killer cells and increased CD^{4+} and CD^{8+} cell populations, showing good immunomodulatory activity. Moreover, **187** also induced effective phagocytic activation in macrophages [68].

Proanthocyanidins from *C. osmophloeum* twig extracts, including **188** and **190**, were found to be associated with anti-hyperglycemic capacity. Moreover, it was also found that the higher the degree of polymerization of the proanthocyanidins, the better the inhibition of *α*-Glucosidase [37]. Proanthocyanidins were also reported to show inhibitory effects against cyclooxygenase-2 (COX-2). In the assay, compounds **188**-**191** were tested for their inhibitory activities against the COX-2 enzyme isolated from human recombinant Sf9 cells and all of them exerted significant inhibition at doses of 10, 100, and 1000 μg/mL. Moreover, the tetramers (**190**, **191**) showed stronger inhibition than the trimers (**188**, **189**) [69].

Table 3. Flavonoids from *Cinnamomum* genus.

No.	Compounds	Plants	Ref.	No.	Compounds	Plants	Ref.
129	tricetin-7-methyl ether	d	[70]	**162**	kaempferol 3-O-β-D-apiofuranosyl-(1→2)- α-L arabinofuranosyl-7-O-α-L-rhamnopyranoside	o	[1]
130	4',6,7-trimethoxyflavone	d	[42]	**163**	herbacetin	p	[71]
131	apigenin	k	[40]	**164**	kaempferol-3-O-β-D-glucose(6→1)-α-L-rhamnoside	d	[48]
132	genkwanin	k	[40]	**165**	kaempferol-3-O-α-L-rhamnopyranosyl-(1→2)-α-L rhamnopyranoside	o	[1]
133	isorhoifolin	p	[61]	**166**	kaempferol 3-O-β-D-apiofuranosy-(1→4)-α-L-rhamnopyranosyl-7-O-α-L-rhamnopyranoside	o	[1]
134	luteolin	d	[70]	**167**	naringenin 5-O-β-D-glucopyranoside	s	[72]
135	luteolin-7-O-β-D glucoside	d	[70]	**168**	taxifolin	d	[73]
136	kaempferol	j,k	[40, 60]	**169**	dihydrokaempferol	d	[42]
137	kaempferol 3-O-ß-D-glucopyranoside	c,d,s	[28, 72]	**170**	phloridzin	s	[72]
138	kaempferol-3-0-α-L-rhamnopyranoside	d,o,p,s	[1, 71, 72]	**171**	3'-methoxyl-(-)-epicatechin	c	[37]
139	kaempferol-3-0-β-rutinoside	d	[72]	**172**	(-)-epicatechin	c,k,p,s	[44, 60]
140	kaempferol-7-O-α-L-rhamnopyranoside	o	[1]	**173**	5,7-dimethyl-3',4'-di-O-methylene-(±)-epicatechin	c	[31, 32]
141	kaempferol-3-O-α-L-rhamnopyranoside-7-O-α-L rhamnopyranoside	o	[1]	**174**	5,3',dimethoxyl-(-)-epicatechin	c	[37]
142	quercetin	d,k,z	[1, 42, 60]	**175**	(-)-(2R,3R)-4′-hydroxy-5,7,3′-trimethoxyflavan-3-ol	b,c,k	[31, 40, 43]
143	quercetin 3-O-ß-D-glucopyranoside	c,d	[28, 70]	**176**	4'-methoxyl-(+)-catechin	c	[37]
144	quercetin 3-O-α-L-rhamnopyranoside	c,d,p,z	[1, 28, 29, 71]	**177**	7,4' -dimethoxyl-(+)-catechin	c	[37]
145	quercetin 3-O-α-D-arabinopyranoside	c	[28]	**178**	5,7,4' -trimethoxyl-(+)-catechin	c	[37]
146	rutin	d,p,z	[29, 61]	**179**	(+)-catechin	k,s,t	[40, 41, 45]
147	nicotiflorin	p	[61]	**180**	(-)-catechin	k,t	[40, 74]
148	isorhamnetin-3-O-β-D-glucopyranoside	d	[33]	**181**	(-)-afzelechin	c	[37]
149	isorhamnetin-3-O-β-rutinoside	d	[48]	**182**	(2S,3S)-3'-hydroxy-5,7,4'-trimethoxy-flavan-3-ol	d	[32]
150	quercetin 3-O-(3″,4″-di-trans-p-coumaroyl)-α-L-rhamnopyranoside	c	[28]	**183**	(-)-(2R,3R)-5,7-dimethoxy-3',4'-methylenedioxy-flavan-3-ol	d	[42]
151	quercetin 3-O-(2″,4″-di- trans-p-coumaroyl)-α-L-rhamnopyranoside	c	[28]	**184**	(-)-epicatechin-3-O-β-glucoside	c	[37]
152	3″-trans-p-coumaroylquercitrin	c	[28]	**185**	(-)-epicatechin-6-β-glucoside	c	[37]
153	4″-trans-p-coumaroyl-kaempferol-3-O-α-L-rhamnoside	c	[28]	**186**	(-)-epicatechin-8-β-glucoside	c	[37]
154	4″-cis-p-coumaroyl-kaempferol-3-O-α-L-rhamnoside	c	[28]	**187**	proanthocyanidin A-1	c	[37]
155	kaempferol-3-O-(2",4"-di-E-p-coumaroyl)-α-L-rhamnopyranoside	r	[63]	**188**	cinnamtannin B-1	c,s,z	[29, 69, 72]
156	kaempferol-3-O-(3",4"-di-E-p-coumaroyl)-α-L-rhamnopyranoside	r	[63]	**189**	cinnamtannin D-1	c,s	[69, 72]
157	kaempferol 3-O-(3″,6″-di-trans-p-coumaroyl)-ß-D-glucopyranoside	c	[28]	**190**	parameritannin A-1	c	[69]
158	tiliroside	c	[28]	**191**	cassiatannin A	c	[69]
159	kaempferol 3-O-(3″,6″-di-trans-p-coumaroyl)-ß-D-galactopyranoside	c	[28]	**192**	epicatechin-(4β→8)-epicatechin-(4β→8)-epicatechin	c	[34]
160	kaempferitrin	j,o	[1, 75]	**193**	cinnamomoside A	c	[17]
161	kaempferol 3-O-β-D-glucopyranosyl-(1→4)- α-L-rhamnopyranosyl-7-O-α-L-rhamnopyranoside	o	[1]				



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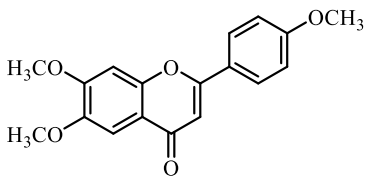

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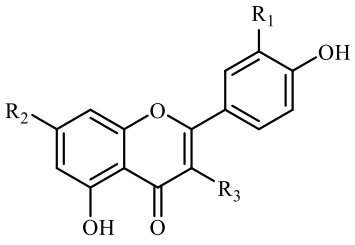
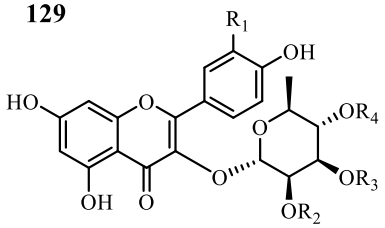
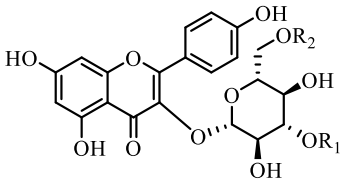


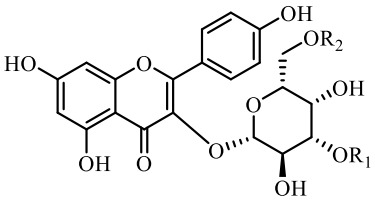
	R_1	R_2	R_3
131	H	OH	H
132	H	OCH_3	H
133	H	O-Rutinose	H
134	OH	OH	H
135	OH	OGlc	H
136	H	OH	OH
137	H	OH	OGlc
138	H	OH	ORha
139	H	OH	O-Rutinose
140	H	ORha	OH
141	H	ORha	ORha
142	OH	OH	OH
143	OH	OH	OGlc
144	OH	OH	ORha
145	OH	OH	OAra
146	OH	OH	O-Rutinose
147	H	OH	O-Rutinose
148	OCH_3	OH	OGlc
149	OCH_3	OH	O-Rutinose



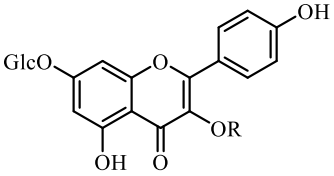
150 R_1=OH R_2=H R_3=R_4=*trans-p*-coumaroyl
151 R_1=OH R_3=H R_2=R_4=*trans-p*-coumaroyl
152 R_1=OH R_2=R_4=H R_3=*trans-p*-coumaroyl
153 R_1=H R_2=R_3=H R_4=*trans-p*-coumaroyl
154 R_1=H R_2=R_3=H R_4=*cis-p*-coumaroyl
155 R_1=H R_3=H R_2=R_4=*trans-p*-coumaroyl
156 R_1=H R_2=H R_3=R_4=*trans-p*-coumaroyl



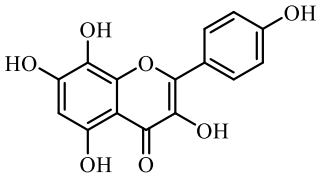
157 R_1=R_2=*trans-p*-coumaroyl
158 R_1=H R_2=*trans-p*-coumaroyl



159 R_1 = R_2 = *trans-p*-coumaroyl



160 R = Rha
161 R = Ara^{6}?$_{1}$Api**16**
2 R = Rha^{4}?$_{1}$Api



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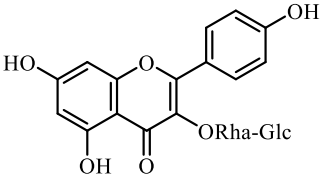

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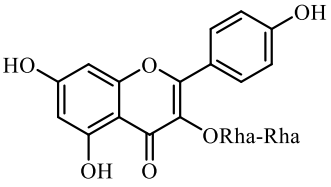

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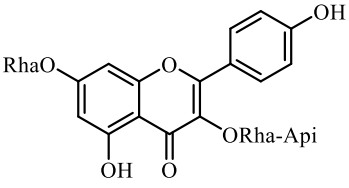

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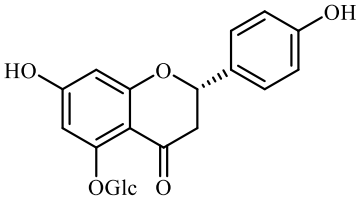

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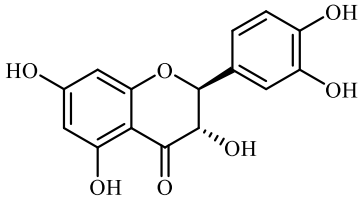

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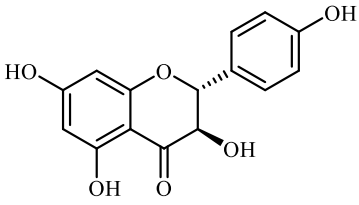

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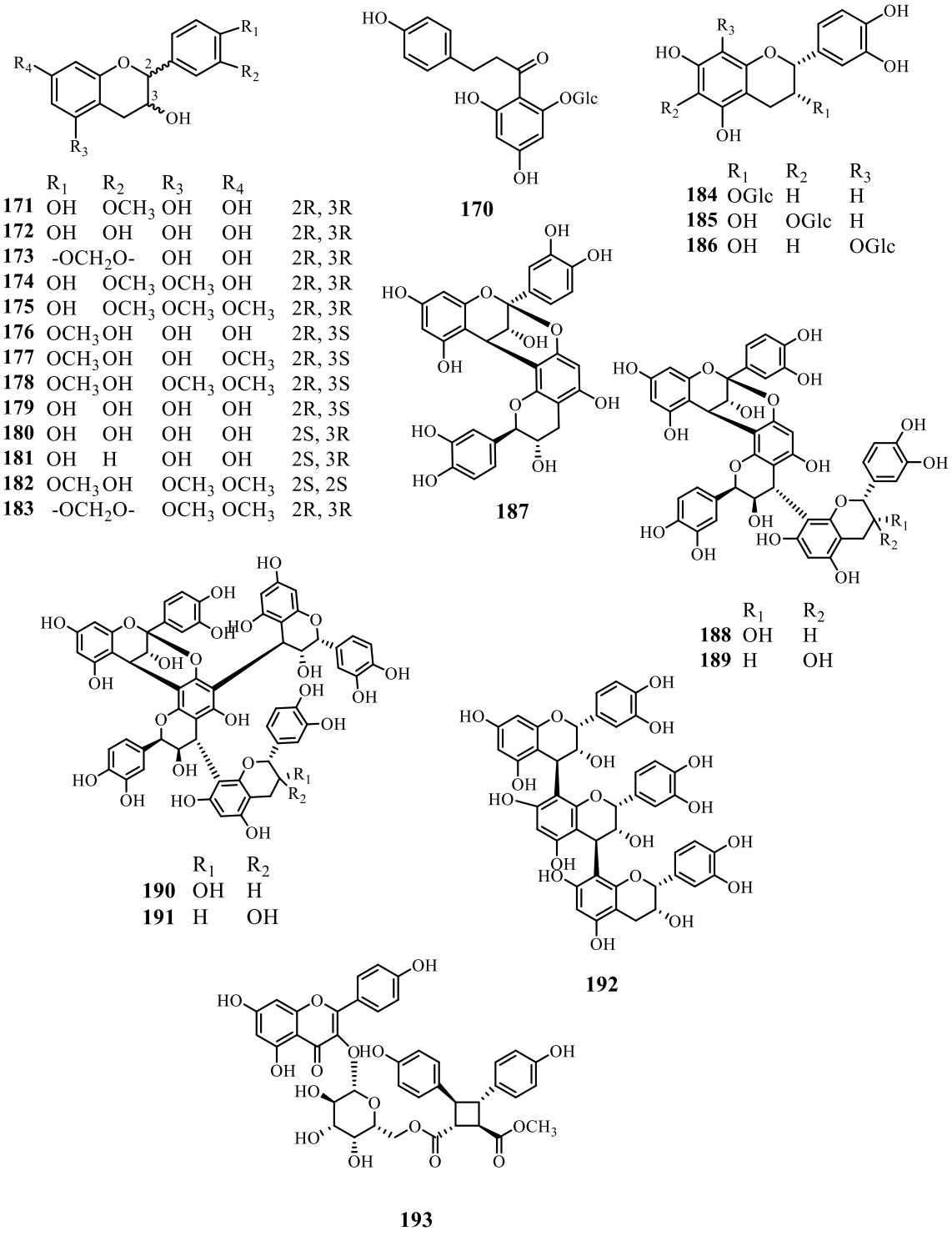
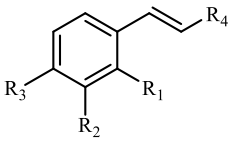
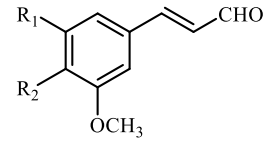


Figure 3. The structures of flavonoids from *Cinnamomum*

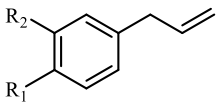
2.4. Phenylpropanoids



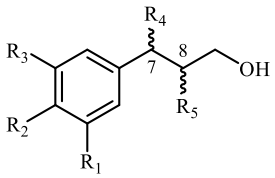
	R_1	R_2	R_3	R_4
194	H	H	H	CHO
195	OCH_3	H	H	CHO
196	OH	H	H	CHO
197	H	OCH_3	OH	CHO
198	OCH_3	OH	H	CHO
199	H	H	OCH_3	CHO
200	H	H	H	CH_2OAc
201	H	H	H	CHO
202	H	H	H	CH_2OH
203	H	H	H	COOH
204	OH	H	H	COOH
205	OH	H	H	CH_2OH
206	OCH_3	H	H	CH_2OH
207	H	H	H	CH_2OGlc_6-Rham
208	$OGlc_6$-Api	H	H	CH_2OH
209	H	OCH_3	OH	COOH
210	H	H	OH	$COOCH_3$
211	H	H	OH	COOH
212	H	OCH_3	H	CHO
213	H	OCH_3	OH	CHO
214	H	OCH_3	OCH_3	CHO
215	H	-OCH_2O-		CH_2OH
216	H	OCH_3	OH	CH_3
217	H	OCH_3	OCH_3	CH_2OH
218	H	OH	OH	COOH
219	H	H	H	$COOCH_3$
220	OCH_3	H	H	COOH
221	H	H	OGlc	$COOCH_3$
222	H	OCH_3	OCH_3	CHO



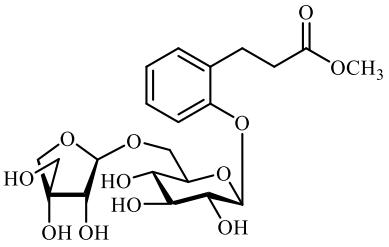
	R_1	R_2	R_3
223	OCH_3	OH	CHO
224	OH	OH	CHO
225	OCH_3	OCH_3	CH_2OH



	R_1	R_2
226	OH	OH
227	OH	OCH_3
228	OCH_3	OCH_3
229	-OCH_2O-	



	R_1	R_2	R_3	R_4	R_5	
230	OCH_3	OH	OCH_3	OH	OH	7R, 8S
231	OCH_3	OH	OCH_3	OH	OH	7S, 8S
232	H	OH	OCH_3	OH	OH	7R, 8R
233	H	OCH_3	OCH_3	OGlc	OH	7S, 8R
234	H	OH	OCH_3	OGlc	OH	7S, 8R
235	H	H	H	OH	OGlc	7S, 8S
236	-OCH_2O-		H	H	OH	
237	-OCH_2O-		H	H	$OGlc_6$-Rham	8S



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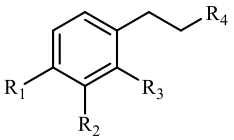
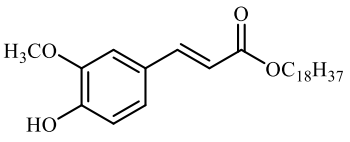


	R_1	R_2	R_3	R_4
239	H	H	OGlc	COOH
240	H	H	OGlc	$COOCH_3$
241	H	H	OH	COOGlc
242	OH	H	H	COOH
243	H	H	H	CH_2OH
244	H	H	H	CHO
245	C_2H_5	OH	H	CH_3



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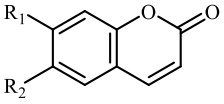
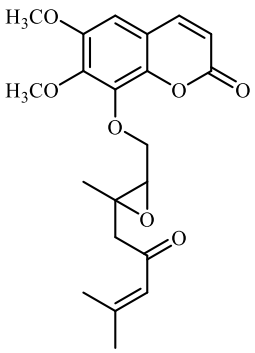


	R_1	R_2
247	H	H
248	OH	OCH_3
249	OCH_3	OCH_3



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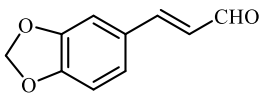

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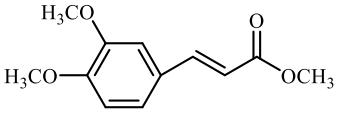

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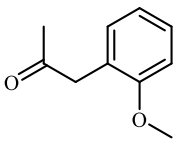

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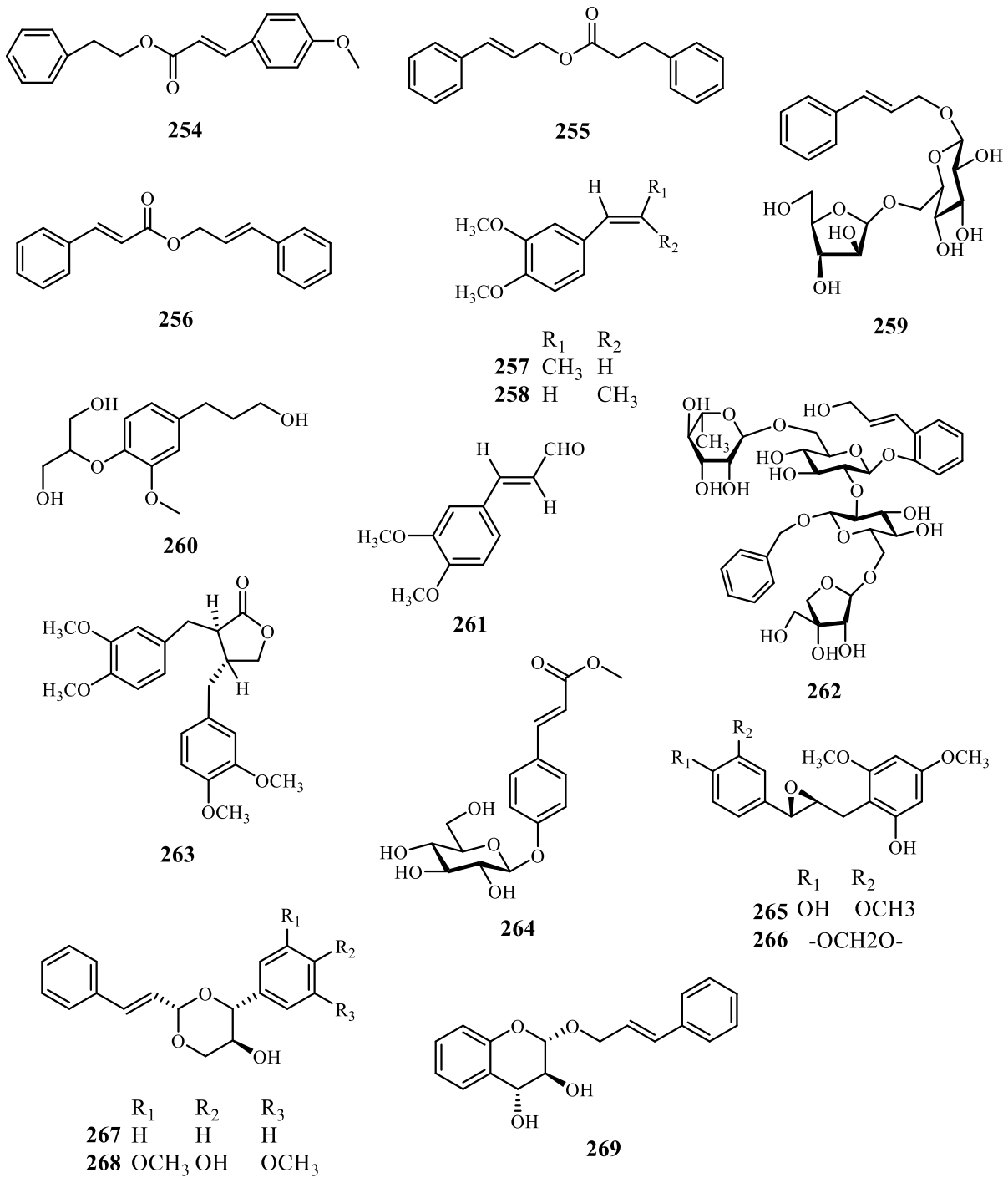

Figure 4. The structures of phenylpropanoids from *Cinnamomum.*

Cinnamomum plants are characterized by the aroma related to phenylpropanoids. Also, phenylpropanoids are common in *Cinnamomum* species with high content, especially in their volatile oils. A total of 76 phenylpropanoids (**194-269**) have been isolated from *Cinnamomum* plants (Table 4 & Figure 4). Only four coumarins (**247-250**) were obtained from *Cinnamomum* but they have shown great biological activities. Compounds **247** and **248** were found in three *Cinnamomum* species respectively and moreover, **248** and **249** have been reported to show potent anti-inflammatory effects. Coumacasia (**250**) was obtained for the first time from *C. cassia* in 2013 and exhibited significant cytotoxic activity [76]. Cinnamaldehyde (**194**) is the main component of essential oil from *C. cassia*. In 2012, Ngoc *et al.* separated cinnacasolide B (**208**) for the first time from in *C. cassia* [77]. Cinnamomdiol A (**237**) is a 3-(3,4-methylenedioxyphenyl)-propane-1,2-diol glycoside which was

isolated for the first time from *C. camphora* [73]. Some phenylpropanoids are common in *Cinnamomum* species, including compounds **202**, **203**, **209** and **227**. This finding supported the chemotaxonomic relationship among *Cinnamomum* species.

Table 4. Phenylpropanoids from *Cinnamomum* genus

No.	Compounds	Plants	Ref.	No.	Compounds	Plants	Ref.
194	cinnamaldehyde	b,c	[78, 82]	**232**	erthro-guaiacy lglycerol	c	[37]
195	2-methoxycinnamaldehyde	c	[82]	**233**	4-methoxy guaiacyl glycerol 7-O-β-D-glucopyranoside	c	[37]
196	2-hydroxycinnamaldehyde	c	[82]	**234**	D-threo-guaiacylglycerol 7-O-β-D-glucopyranoside	s	[83]
197	coniferaldehyde	c	[82]	**235**	cinnacassoside D	c	[13]
198	cassiferaldehyde	c	[82]	**236**	3-(3,4-methylenedioxyphenyl)-1,2-propanediol	d,p	[73]
199	4-methoxycinnamaldehyde	c	[34]	**237**	cinnamomdiol A	d	[36, 73]
200	cinnamyl acetate	b	[43]	**238**	methyl-phenylpropanoate-2-O-β-D-apio-furanosyl-(1→6)-O-β-D-glucopyranoside	c	[2]
201	trans-cinnamaldehyde	b,m	[43, 84]	**239**	dihydomelilotoside	c	[82]
202	cinnamyl alcohol	b,c,j,m	[43, 75, 84]	**240**	methyl dihydromelilotoside	c	[82]
203	cinnamic acid	b,c,j,m,n,z	[43, 84-86]	**241**	dihydrocinnacasside	c	[82]
204	O-coumaric acid	c,s	[82, 87]	**242**	p-dihydrocoumaric acid	r	[88]
205	2-hydroxy-cinnamyl alcohol	c	[37]	**243**	3-phenylpropanol	c	[34]
206	(E)-3-(2-methoxyphenyl)prop-2-en-1-ol	c	[37]	**244**	benzenepropanal	c	[34]
207	rosavin	c	[77, 82]	**245**	2-ethyl-5-propylphenol	c	[34]
208	cinnacasolide B	c	[77]	**246**	stearyl ferulate	d	73
209	ferulic acid	k,r,s,t,z	[44, 45, 58, 88]	**247**	coumarin	b,c,j,m	[38, 43, 47, 84]
210	trans-methyl p-coumarate	r	[88]	**248**	scopoletin	b,d,p	[38, 42, 61]
211	trans-coumaric acid	k	[40]	**249**	6,7-dimethoxycoumarin	d	[42]
212	(E)-3-(3-methoxyphenyl)acrylaldehyde	c	[37]	**250**	coumacasia	c	[76]
213	3-(3,4-dimethoxyphenyl)-2-propenal	c	[37]	**251**	3,4-methylenedioxycinnamaldehyde	s	[46]
214	3,4-dimethoxycinnamaldehyde	s	[46]	**252**	methyl trans-3-(3,4-dimethoxyphenyl)-3-propenoate	s	[46]
215	3,4-methylenedioxycinnamyl alcohol	s	[46]	**253**	2-methoxyphenylacetone	c	[34]
216	isoeugenol	k	[41]	**254**	phenethyl (E)-3-[4-methoxyphenyl]-2-propenoate	c	[37]
217	kobusinol B	b,z	[1, 38]	**255**	trans-cinnamyl 3-phenylpro pionate	b,c	[17, 43]
218	caffeic acid	z	[85]	**256**	(E)-cinnamyl-(E)-cinnamate	c	[17]
219	methyl cinnamate	s	[46]	**257**	1,2-dimethoxy-4-(1-E-propeny1)benzene	a	[15]
220	cis-2-methoxycinnamic acid	c	[34]	**258**	1,2-dimethoxy-4-(l-Z-propenyl)benze	a	[15]
221	linocinnamarin	c	[13]	**259**	rosarin	c	[13]
222	E-(3,4-dimethoxyphenyl)-2-propenal	a	[15]	**260**	2-[4-(3-hydroxypropyl)-2-methoxyphenoxy]-1,3-propanediol	c	[13]
223	sinapaldehyde	b,c	[28, 43]	**261**	E-(3,4-dimethoxyphenyl)-2-propenal	a	[15]
224	trans-ferulaldehyde	b	[43]	**262**	Cinnacassiol	c	[1]
225	trans-3,4,5-trimethoxycinnamic alcohol	c	[28]	**263**	dimethylmatairesinol	d	[48, 70]
226	4-allylcatechol	t	[45]	**264**	linocinnamarin	c	[13]
227	eugenol	d,j,m,n,u,s,z	[46, 84, 85, 89]	**265**	cinnacassin N	c	[17]
228	methyl-eugenol	s,t	[46, 90]	**266**	cinnacassin O	c	[17]
229	safrole	p	[36]	**267**	cinnacassin L	c	[17]
230	(7R, 8S)-syringoylglycerol	c	[37]	**268**	cinnamic aldehyde cyclic syringyl glycerol 1,3-acetal	b	[43]
231	(7S, 8S)-syringoylglycerol	c	[37]	**269**	cinnacassin K	c	[17]

Phenylpropanoids **194** and **195** were found to exhibit potent anti-inflammatory effects by inhibiting transcriptional activity of NF-κB induced by LPS, and their IC_{50} values were 43 and 31 μM, respectively [78]. The phenylpropanoid (**250**) induced cell death in the HL-60 and A-549 cell lines with IC_{50} values of 8.2 and 11.3 μM, respectively. Compounds **194**-**197** showed moderate inhibitory effects with IC_{50} values ranging from 20.5 to 65.6 μM [76]. The anti-proliferation activities of **96** and **109** were evaluated against human HT29 and MCF-7 cancer cell lines, and their IC_{50} values ranged from 3.3 to 25.8 μM [51].

Cinnamaldehyde (**194**) has been demonstrated to show various activities and some *in vivo* experiments have been conducted. It was confirmed to exert *in vivo* anti-inflammatory effects and significantly reduced synovial inflammation in adjuvant arthritis rats due to suppressing IL-1β through modulating succinate/HIF-1α axis and inhibition of NLRP3 [79]. In another *in vivo* experiment, treatment with **194** was demonstrated to exhibit neuroprotective activity against subarachnoid hemorrhage-induced early brain injury through increasing the cross-sectional areas of the basilar artery and reducing the arterial wall thickness in rabbits [80]. Moreover, pretreatment with **194** significantly protected against and ameliorated intestinal ischemia/ reperfusion injuries by synergistic inhibition of NF-κB and p53 in rats [81].

2.5. Alkaloids

Although *Cinnamomum* plants are rich in many types of constituents, alkaloids are not common in the genus and only 19 alkaloids (**270**-**288**) have been isolated up to now (Table 5 & Figure 5). These compounds include five piperidines (**270**-**274**), two pyrrolidines (**275**, **276**), nine amines (**277**-**285**) and three chlorophylls (**286**-**288**). The pyridine alkaloids (**270**-**274**) are all from *C. philippinense. C*ompound **270** was first isolated from this species in 2012 and compound **272** was in 2015 [91, 92]. However, alkaloids from *Cinnamomum* didn't show significant biological activities according to existing activity tests.

Table 5. Alkaloids from *Cinnamomum* genus

No.	Compounds	Plants	Ref.	No.	Compounds	Plants	Ref.
270	2-(4'-hydroxypyridin-3'-yl)-acetic acid	q	[91]	**280**	cinnabutamine	b	[93]
271	corydaldine	q	[91]	**281**	N-cis-feruloyltyramine	r	[88]
272	Cinnapine	q	[92]	**282**	(E)-3-(4-hydroxy-3-methoxyphenyl)-N-phenthy-lacrylamide	c	[28]
273	glaziovine	q	[91]	**283**	N-trans-caffeoyl-5-hydroxytyramine	b	[93]
274	zenkerine	q	[91]	**284**	N-trans-feruloyl-5-methoxytyramine	b,c,r	[28, 39, 94]
275	3-glyceroylindole	c	[28]	**285**	N-trans-feruloyltyramine	b,r	[88, 93]
276	indole-3-carboxaldehyde	c	[28]	**286**	pheophytin b	b	[38]
277	Cinnaretamine	b,q,r	[52, 93, 94]	**287**	pheophytin a	b,s	[38, 53]
278	dihydroferuloyltyramine	r	[58]	**288**	aristophyll C	s	[53]
279	N-cis-feruloyl-5-methoxytyramine	b,r	[93, 94]				

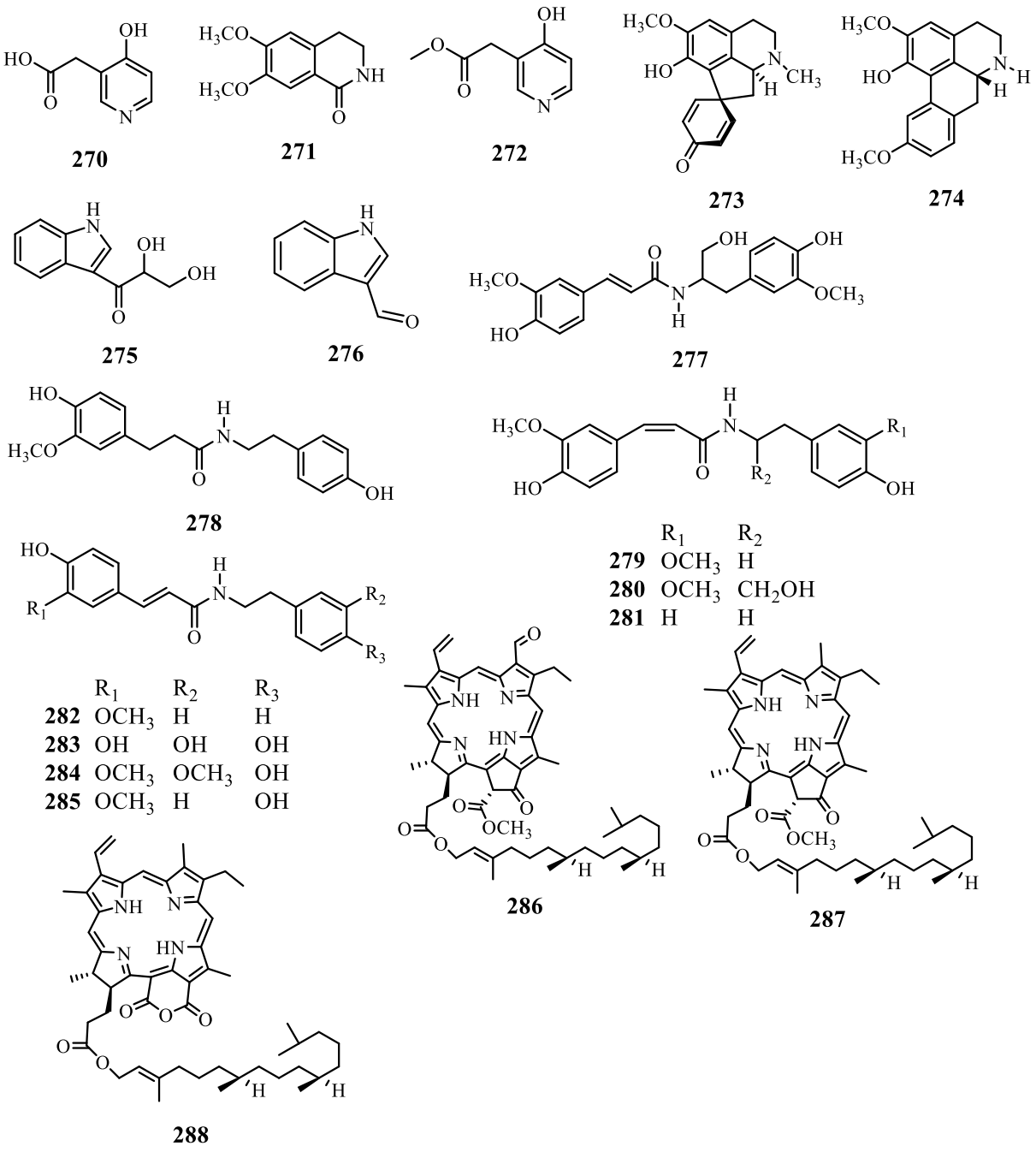

Figure 5. The structures of alkaloids from *Cinnamomum*

2.6. Other Compounds

In addition to lignans, butanolides, flavonoids, phenylpropanoids and alkaloids, other compounds consist of 17 phenylethanols (**289-305**), 69 simple benzenoids (**306-374**) and 6 steroids (**375-380**). Compounds **292-296** are 4-hydroxy-3-methoxyphenethyl derivatives and all were obtained from *C. reticulatum* [39]. phenylethyl glycosides include compounds **300-304** and all are from *C. cassia* [32, 95]. Twelve dibenzocycloheptatrienes (**306-317**) have been obtained from *Cinnamomum* plants. Compounds **306-312** were first isolated from *C. subavenium* in 2012 [72]. Some benzenoids (**318-320**, **322**, **323** and **329**) are common in *Cinnamomum* species. Compounds **375-380** are steroids and **375-379** can be easily found in the genus *Cinnamomum.* These compounds are shown in Table 6.

Table 6. Other compounds from *Cinnamomum* genus

No.	Compounds	Plants	Ref.	No.	Compounds	Plants	Ref.
289	phenylethyl alcohol	c	[34]	**335**	3,4,5-trimethoxyphenyl-1-O-β-D-glucoside	s	[83]
290	hydroxytyrosol	s	[72]	**336**	isovanillin	s	[46]
291	3,4-dimethoxyphenethyl alcohol	c	[34]	**337**	3,4-dihydroxybenzoate	c	[28]
292	4-hydroxy-3-methoxyphenethyl butyrate	r	[39]	**338**	ethyl 3,4-dihydroxybenzoate	c	[28]
293	4-hydroxy-3-methoxyphenethyl hexyrate	r	[39]	**339**	1,2-dimethoxy-4-(2-propenyl)benzen	a	[15]
294	4-hydroxy-3-methoxyphenethyl pentadecyrate	r	[39]	**340**	3,4-dimethoxybenzaldehyde	a	[15]
295	4-hydroxy-3-methoxyphenethyl stearate	r	[39]	**341**	ethyl 3,5-dihydroxy-4-nitrobenzoate	t	[90]
296	4-hydroxy-3-methoxyphenethyl heneicosyrate	r	[39]	**342**	leonuriside	c	[13]
297	4,4'-diacetyl-2,2'-dimethoxydiphenyl ether	n	[86]	**343**	methyl 3-methoxy-4-(β-D-allopyranosyloxy) benzoate	c	[13]
298	cinnamic alcohol	b,c	[43, 82]	**344**	gallic acid	z	[85]
299	icariside DC	c	[82]	**345**	isotachioside	c	[95]
300	cinnacasolide A	c	[77]	**346**	3,4-dimethoxyphenol-β-D-apiofuranosyl(1→6)-b-D-glucopyranoside	c	[13, 96]
301	2-phenylethyl-O-β-D-glucopyranoside	c	[95]	**347**	kelampayoside A	c	[96]
302	2-O-β-D-glucosyl-(1S)-phenylethylene glycol	c	[95]	**348**	glucosyringic acid	c	[31]
303	cinnamic aldehyde cyclic glycerol 1,3-acetal(9,2'-trans)	c	[32]	**349**	dihydrisosubamol	s	[72]
304	cinnamic aldehyde cyclic glycerol 1,3-acetal(9,2'-cis)	c	[32]	**350**	2,2′,7a,7a′,7b,7b′-hexamethyldiphenyl ether	s	[46]
305	cinnamic aldehyde cyclic D-galactitol 3'R,4'S-acetal	c	[31]	**351**	2-hydroxybenzaldehyde	c	[34]
306	Subavenoside A	s	[72]	**352**	2,5-dihydroxybenzoic acid ethyl ester	d	[42]
307	Subavenoside B	s	[72]	**353**	benzyl benzoate	c	[34]
308	Subavenoside C	s	[72]	**354**	dibutyl phthalate	d	[48]
309	Subavenoside D	s	[72]	**355**	(3R,4S,6R)-4,6-dihydroxy-de-O-methyllasiodiplodin	c	[96]
310	Subavenoside E	s	[72]	**356**	1-hydroxy-3,6-dimethoxy-8-methyl-anthraquinone	d	[42]
311	Subavenoside F	s	[72]	**357**	(3R, 4R, 3'R,4'R)-6,6'-dimethoxy-3,4,3',4'-tetrahydro-2H,2'H-[3,3']bichromenyl-4,4'-diol	d,p	[42, 71]
312	9,12-Di-O-methylsubamol	s	[72]	**358**	2,3-dihydro-6,6-dimethylbenzo-[b][1,5]dioxocin-4(6H)-one	t	[65]
313	5′-hydroxy-5-hydroxy methyl-4″,5″-methylenedioxy-1,2,3,4-dibenzo-1,3,5-cycloheptatriene	b	[43]	**359**	cinnamophilin D	q	[97]
314	Subamol	s	[50, 87]	**360**	cinnacasolide C	c	[77]
315	burmanol	b	[38]	**361**	3,4-dimethoxyphenol-β-D-apiofuranosyl(1→6)-β-D-glucopyranoside	c	[34]
316	tenuifolin	r,t	[45, 88]	**362**	3,4,5-trimethoxyphenol-β-D-apiofuranosyl-(1→6)-O-β-D-glucopyranoside	c	[2, 13]
317	reticuol	b,m,r	[98]	**363**	3-trimethoxy-4-hydroxyphenol-β-D-apiofuranosyl (1→6)-β-D-glucopyranoside	c	[2, 13]
318	vanillin	b,c,d,k,s	[38, 41, 42]	**364**	cinnacassoside C	c	[13]
319	4-hydroxybenzaldehyde	c,k,p,r,s,t	[40, 45, 58]	**365**	cinnacasolide E	c	[2]

320	protocatechuic acid	b,c,d,k,r,z	[29, 40, 42, 88]	**366**	phenol-β-D-apiofuranosyl-(1→6)-O-β-D-glucopyranoside	c	[2, 32]
321	benzoic acid	c,k	[40]	**367**	cinnacasolideb	c	[1]
322	p-hydroxybenzoic acid	b,c,d,j,k,p,r,s	[38, 58, 61, 88]	**368**	phenylmethanol O-*α*-L-arabinofuranosyl (1 → 6)-β-D-glucopyranoside	c	[95]
323	vanillic acid	b,c,k,r,s	[38, 58, 61, 88]	**369**	phenylmethanol O-*α*-L-arabinopyranosyl (1→6)-β-D-glucopyranoside	c	[95]
324	benzaldehyde	c	[34]	**370**	cinnacassinol	c	[82]
325	veratraldehyde	s	[46]	**371**	1,4-diphenyl-1,4-butanedione	c	[17]
326	protocatechualdehyde	d	[42]	**372**	evofolin B	c	[13, 17]
327	1,2,4-trihydroxybenzene	p	[71]	**373**	cinncassin B	c	[34]
328	benzene,1,3-dimethyl	c	[34]	**374**	cinncassin C	c	[34]
329	syringaldehyde	b,c,d,k,s	[40, 41, 43, 44]	**375**	β-sitosterol	c,d,j,k,m,n,p,s,t,u	[27, 75, 90, 99]
330	syringic acid	r,s,t	[39, 90, 94]	**376**	stigmasterol	d,k,j,s,t,u	[40, 44, 89, 99]
331	myristicin	s,t	[45, 67, 100]	**377**	daucosterol	d,k,p,s,t	[44, 70, 82]
332	3,4-methylenedioxy-5-methoxycinnamyl alcohol	s	[67, 100]	**378**	stigmasteryl-3-O-β-D-glucoside	d,k,s	[27, 41, 44]
333	myristicic acid	s	[100]	**379**	β-sitostenone	b,j,k,m,n,r,s,t	[39, 45, 46, 86]
334	3-hydroxy-4,5-dinethoxyphenyl-β-D glucopyranoside	s	[83]	**380**	stigmasta-4,22-dien-3-one	k	[40]

3. Conclusion

The medicinal value of the genus *Cinnamomum* has attracted much attention around the world and a great deal of phytochemical and biological investigations have been done. According to the findings, there have been many unique constituents isolated from *Cinnamomum* plants, with various novel skeletons and significant biological activities. The research on *Cinnamomum* species can provide abundant bioactive compounds and promote the further development and utilization of new drugs.

The *Cinnamomum* genes is rich in resources which contains approximately 250 species. However, only a few species have been studied, most of which are only given focus on the investigation of essential oils. Chemical research on the bioactive components from *Cinnamomum* plants have only focused on less than 20 species, such as *C. cassia*, *C. camphora*, *C. kotoense* and *C. subavenium*. Hence, the research range of species of the genus *Cinnamomum* need to be widened and the active ingredients and their pharmacological activities need to be further explored.

The compounds obtained from *Cinnamomum* show various significant activities, especially lignans and butanolides. The lignans from *Cinnamomum* have high content and have shown potent neuroprotective, anti-hyperlipidemic, anti-inflammatory, anticancer and other effects. However, most of the compounds only stays in the study of cell activity *in vitro* except sesamin, which was demonstrated to show various activities *in vivo* and *in vitro* and some clinical experiments have been conducted. Moreover, anti-tumor ingredients are mainly concentrated in butanolides. Nevertheless, though showing significant effects, most of the compounds have only been tested for *in vitro* activities. More *in vivo* experiments are needed to explore the mechanism of action and provide data for clinical trials.

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