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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Phytochemistry and biological activities of *Cinnamomum*

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).

Spirodiene neolignans 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 spirodiene 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-position 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 compounds 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   | secoisolariresinol | c,o | [25, 28] | 42 | 4-ketopinesolin | c | [28] |
| 2   | methoxysecoisolariresinol | c | [28] | 43 | (7S,8R)-lawsonic | c | [25] |
| 3   | secoisolariresinol differuloyl ester | o | [14] | 44 | urolignoside | z | [29] |
| 4   | 9,9'-Di-O-feruloyl-(+)-5,5'-dimethoxy secoisolariresinol | 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-glucopyranosyl)oxy] lyoniresinol | c | [2] | 47 | samwiside | c | [30] |
| 7   | (6S,7R,8R)-7a-[(β-D-glucopyranosyl)oxy] lyoniresinol (6R,7S,8S)-7a-([β-D-glucopyranosyl]oxy) lyoniresinol | c | [2] | 48 | (+)-leptolepisol C | c | [25] |
| 8   | (7S,8R,8S)-7a-(+)lyoniresinol | c | [25] | 50 | picrasmalignan A | c | [25] |
| 9   | 5-methoxy-isolariresinol | c | [28] | 51 | spicatolignan B | c | [13] |
| 10  | (-)-lyoniresinol | c | [31] | 52 | balanophonin | c | [17] |
| 11  | (7'S,8'R,8R)-Lyoniresinol-9-O-feruloyl ester | o | [14] | 53 | 5-methoxybalanophonin | c | [17] |
| 12  | (7'S,8'R,8R)-Lyoniresinol-9-O-(E)-feruloyl ester | o | [14] | 54 | hierochin B | c | [17] |
| 13  | (7'S,8'R,8S)-lyoniresinol 3a-O-β-D-glucopyranoside | c | [32] | 55 | simulanol | c | [17] |
| 14  | schizandraside | d | [33] | 56 | salvinal | c | [17] |
| 15  | cinnacassin G | c | [17] | 57 | herpetal | c | [17] |
| 16  | cinnacassin H | c | [17] | 58 | cinnacassoside B | c | [13] |
| 17  | (+)-(7'R,8R,8'R)-5,5'-dimethyllariciresinol | c | [25] | 59 | (-)-erythro-(7'R,8S)-guaiaacylglycerol-β-O-4'-sinapyl ether | c | [25] |
| 18  | (+)-(7'S,8'R,8R)-5,5'-dimethyllariciresinol | c | [25] | 60 | (-)-erythro-(7'S,8R)-syringylglycerol-β-O-4'-sinapyl ether | c | [25] |
| 19  | 5'-methyllariciresinol | c | [34] | 61 | cinnacass E | c | [25] |
| 20  | cinnacassin M | c | [17] | 62 | (+)-threo-(7'S,8S)-guaiaacylglycerol-β-coniferyl aldehyde ether | c | [25] |
| 21  | (+)-episesaminone | d | [35] | 63 | (+)-erythro-(7'S,8R)-guaiaacylglycerol-β-coniferyl aldehyde ether | c | [25] |
| 22  | dehydroxycebin | p | [36] | 64 | 1-(4-hydroxy-3-methoxyphenyl)-2-[3-(3-hydroxy-1-propenyl)-5-methoxyphenoxy]-1,3-propanediol | c | [17] |
| 23  | cubinin | p | [36] | 65 | (+)-erythro-(7'R,8S)-guaiaacylglycerol-8-vanillin ether | c | [25] |
| 24  | hinokinin | p | [36] | 66 | 1,2,3-propanetriol, 1-[4-(1R,2R)-2-hydroxy-(4-hydroxy-3-methoxy-phenyle)-1-(hydroxymethyl)phenyl]-3-methoxyphényl | c | [37] |
| 25  | (7'S,8'R,8R)-4,4'-dihydroxy-3,3',5,5'-tetramethoxy-7,9'-epoxy lignan-9'-ol-7-one | c | [17] | 67 | (+)-subvenaminin A | s | [12] |
| 26  | (+)-syringaresinol | b,c,k,m,r,s,t | [38-40] | 68 | (+)-subvenaminin B | s | [12] |
| 27  | (+)-yangamin | b,c | [28, 38] | 69 | (-)-subvenaminin A | s | [12] |
| 28  | clemaphenol A | k | [41] | 70 | (-)-subvenaminin B | s | [12] |
| 29  | cinnacassin F | c | [17] | 71 | Cinnacassin I | c | [17] |
| 30  | (+)-pinoresinol | b,c,d | [28, 31, 42] | 72 | cinnacassin J | c | [17] |
| 31  | (+)-medioresinol | b,c | [28, 43] | 73 | 6-hydroxy-2-(4-hydroxy-3,5-dimethoxy-phenyl)-3,7-dioxabicyclo[3.3.0]octane | c | [13] |
| 32  | pinoresinol methyl ether | d | [42] | 74 | zhebei resinol | c | [17] |
| 33  | sesamin | b,d,j,k,n,s,t | [27, 44-47] | 75 | (-)-(7'R,8S,8'R)-acuminatolide | d | [42] |
| 34  | (+)-diacessamin | d,j,n | [27, 47] | 76 | buddlenol A | c | [17] |
| 35  | (+)-episesamin | d,j | [27, 47] | 77 | erythro-buddlenol B | c | [17] |
| 36  | pluvialloside | k | [41] | 78 | ficusesequillignan A | c | [28] |
| 37  | pipertanol | d | [42] | 79 | buddlenol C | c | [28] |
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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 IC₅₀ 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 IC₅₀ 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 EC₅₀ 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].

| No. | Name                | Substance | Ref. |
|-----|---------------------|-----------|------|
| 39  | 9α-hydroxysemasin   | d         | [48] |
| 40  | 9β-hydroxysemasin   | d         | [48] |
| 41  | l-asarinin          | d         | [48] |
| 80  | hedyotisol A        | c         | [17] |
| 81  | cinnaburmanin A     | b         | [49] |
| 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.
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1. **R₁ R₂ R₃**
   - 1. H H H 8R, 8'R
   - 2. OCH₃ OCH₃ H 8R, 8'R
   - 3. H H feruloyl 8R, 8'R
   - 4. OCH₃ OCH₃ feruloyl 8S, 8'S

2. **R₁ R₂ R₃ R₄**
   - 5. H H H 7R
   - 6. OCH₃ OCH₃ H H Glec 7'R, 8'R, 8'R
   - 7. OCH₃ OCH₃ H H Glec 7'R, 8'R, 8'S
   - 8. OCH₃ OCH₃ H H Glec 7'S, 8'S, 8'R
   - 9. H H H H 7'R, 8'S, 8'S
   - 10. OCH₃ H H H 7'R, 8'S, 8'S
   - 11. OCH₃ OCH₃ H H 7'R, 8'S, 8'S
   - 12. OCH₃ OCH₃ feruloyl H 7'S, 8'R, 8'R
   - 13. OCH₃ OCH₃ feruloyl feruloyl 7'S, 8'R, 8'R
   - 14. OCH₃ OCH₃ H H Glec 7'R, 8'S, 8'S
   - 15. H H H Xyloside

3. **R₁ R₂**
   - 16. 7'S
   - 17. 7'R

4. **R₁ R₂**
   - 18. 7'R
   - 19. 7'S

5. **R₁ R₂**
   - 20. H H

6. **R₁ R₂**
   - 21. H H

7. **R₁ R₂**
   - 22. H H

8. **R₁ R₂**
   - 23. H H
   - 24. OH H
   - 25. =O

9. **R₁ R₂**
   - 26. H H

10. **R₁ R₂**
    - 27. H H

11. **R₁ R₂**
    - 28. H H

12. **R₁ R₂**
    - 29. H H

13. **R₁ R₂**
    - 30. H H

14. **R₁ R₂**
    - 31. H H

15. **R₁ R₂**
    - 32. H H

16. **R₁ R₂**
    - 33. H H

17. **R₁ R₂**
    - 34. H H

18. **R₁ R₂**
    - 35. H H

19. **R₁ R₂**
    - 36. H H

20. **R₁ R₂**
    - 37. H H

21. **R₁ R₂**
    - 38. H H

22. **R₁ R₂**
    - 39. H H

23. **R₁ R₂**
    - 40. H H

24. **R₁ R₂**
    - 41. H H

25. **R₁ R₂**
    - 42. H H

26. **R₁ R₂**
    - 43. H H

27. **R₁ R₂**
    - 44. H H

28. **R₁ R₂**
    - 45. H H

29. **R₁ R₂**
    - 46. H H

30. **R₁ R₂**
    - 47. H H

31. **R₁ R₂**
    - 48. H H

32. **R₁ R₂**
    - 49. R = CHO

33. **R₁ R₂**
    - 50. R = CH–CHCHO
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![Chemical structures]

**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                |        | [37] | 106 | subamolide D                           |        | [50] |
| 84  | 3-hydroxy-4,4-dimethyl-4-             | c      | [57] | 107 | subamolide E                           |        | [50] |
|     | butyrolactone                          |        |      |     |                                        |        |      |
| 85  | cinnamiscin A                          |        | [17] | 108 | Linderanolid B                         |        | [44, 50] |
| 86  | Cinnamiscin A1                         |        | [17] | 109 | Isolinderanolid B                      | k,s     | [51, 53] |
| 87  | Cinnamiscin A2                         |        | [17] | 110 | isoreticularide                        | r       | [58] |
| 88  | Cinnamiscin A3                         |        | [17] | 111 | lincomolide                            | k       | [40] |
| 89  | Cinnamiscin A4                         |        | [17] | 112 | subamolide A                           | s       | [44, 50] |
| 90  | Cinnamiscin A5                         |        | [17] | 113 | subamolide B                           | s       | [44, 50] |
| 91  | Cinnamiscin A6                         |        | [17] | 114 | philippinolide B                       | q       | [52] |
| 92  | Cinnamiscin A7                         |        | [17] | 115 | tubufolinolide B                       | t       | [45] |
| 93  | cinnamomulactone                      |        | [17] | 116 | subamolide C                           | s       | [44, 50] |
| 94  | cinnamomumolide                       |        | [31] | 117 | kotolactone B                         | k       | [41] |
| 95  | 5R-methyl-3-heptatriacontyl-2(5H)      | c      | [34, 59] | 118 | kotomolide                              | k       | [60] |
|     | furanone                               |        |      |     |                                        |        |      |
| 96  | Cinnakotolactone                      | k      | [51] | 119 | 5-dodecanyl-4-hydroxy-4-methyl-2-     | d       | [60] |
|     |                                        |        |      |     | cyclopentenone                         |        |      |
| 97  | isobutusilactone                      |        | [39, 45, 47] | 120 | Kotolactone A                         | k       | [40] |
|     |                                        | d,j,k,n, |      |     |                                        |        |      |
|     |                                        | r,s,t |      |     |                                        |        |      |
| 98  | obtusilactone A                       |        | [39, 45, 47] | 121 | kotolactone B                         | k       | [40] |
|     |                                        | d,j,n,k,|      |     |                                        |        |      |
|     |                                        | r,s,t |      |     |                                        |        |      |
| 99  | isokotomolide A                       | k      | [41] | 122 | 2-acetyl-5-dodecylfururan             | k       | [40] |
| 100 | kotomolide A                          | k      | [41] | 123 | 2-acetyl-5-methylfururan              | k       | [40] |
| 101 | tenufolide A                          | t      | [45] | 124 | secokotomolide A                      | k       | [40] |
| 102 | isotenufolide A                       | t      | [45] | 125 | secokotomolide                        | k       | [40, 60] |
| 103 | isophilippinolide A                   |        | [52] | 126 | secobutenulfolide A                   | t       | [45] |
| 104 | philippinolide A                      |        | [52] | 127 | secosubamolide                        | s       | [44, 50] |
| 105 | isomahubanolide                       |        | [48] | 128 | secosubamolide                        | 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 EC50 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].
Phytochemistry and biological activities of *Cinnamomum*

Figure 2. The structures of butanolides from *Cinnamomum*
2.3. Flavonoids

Leaves are mostly used as a medicinal part in traditional Chinese medicine, which undoubtly 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 EC₅₀ 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* IC₅₀ values against DPPH for tiliroside (158) was found to be 60.40 μg/mL and the ferric ion (Fe³⁺) 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 IC₅₀ 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-carotene-linolate 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 reported 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 IC₅₀ values ranging from 1.6 to 8.4 μg/mL. Both of them show highest inhibition on NCI-H460 cell line, with IC₅₀ values 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 cytoxicity of natural killer cells and increased CD4⁺ and CD8⁺ 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 a-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-rhamnopyranoside | 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-apiofuranosyl-(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-β-D-glucopyranoside | c,d,s | [28, 72] | 170 | phloridzin | s | [72] |
| 138 | kaempferol-3-O-α-L-rhamnopyranoside | d,o,p,s | [1, 71] | 171 | 3′-methoxy-(-)-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 | 5,7,5′-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′,3′-dimethoxy-(-)-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-β-D-glucopyranoside | c,d | [28, 70] | 176 | 4′-methoxy-(+)-catechin | c | [37] |
| 144 | quercetin 3-O-α-L-rhamnopyranoside | c,d,p,z | [1, 28, 29, 71] | 177 | 7,4′-dimethoxy-(+)-catechin | c | [37] |
| 145 | quercetin 3-O-α-D-arabinopyranoside | c | [28] | 178 | 5,7,4′-trimethoxy-(+)-catechin | c | [37] |
| 146 | rutin | d,p,z | [29, 61] | 179 | (+)-catechin | k,s,t | [40, 41, 45] |
| 147 | nicotifolin | 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′-trimethoxyflavan-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′-methylenedioxyflavan-3-ol | d | [42] |
| 151 | quercetin 3-O(2′,4″-di-trans-p-coumaroyl)-α-L-rhamnopyranoside | c | [28] | 184 | (+)-epicatechin-3-0-β-glucoside | c | [37] |
| 152 | 3″-trans-p-coumaroylquercetin | c | [28] | 185 | (+)-epicatechin-6-β-glucoside | c | [37] |
| 153 | 4″-trans-p-coumaroyl-kaempferol-3-O-α-L rhamnose | c | [28] | 186 | (+)-epicatechin-8-β-glucoside | c | [37] |
| 154 | 4″-cis-p-coumaroyl-kaempferol-3-O-α-L rhamnose | 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″,6″-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)-β-D-glucopyranoside | c | [28] | 190 | parameritannin A-1 | c | [69] |
| 158 |tiltioside | c | [28] | 191 | cassiatannin A | c | [69] |
| 159 | kaempferol 3-O(3″,6″-di-trans-p-coumaroyl)-B-D-galactopyranoside | c | [28] | 192 | epicatechin-(4β→8)-epicatechin | c | [34] |
| 160 | kaempferitin | 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] |
Figure 3. The structures of flavonoids from *Cinnamomum*
2.4. Phenylpropanoids

238

239 H H OGlce COOH
240 H H OGlce COOCH3
241 H H OHO COOGlc
242 OH H H COOH
243 H H H CH2OH
244 H H H CHO
245 C2H5 OH H CH3

246

247 H H
248 OH OCH3
249 OCH3 OCH3

250

251

252

253
**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.

| No. | Compounds                        | Plants   | Ref.  | No. | Compounds                        | Plants   | Ref.  |
|-----|----------------------------------|----------|-------|-----|----------------------------------|----------|-------|
| 194 | cinnamaldehyde                   | b,c      | [78, 82] | 232 | erthro-guaiaic lglycerol         | c        | [37]  |
| 195 | 2-methoxy-cinnamaldehyde        | c        | [82]   | 233 | 4-methoxy guaiacl glycerol 7-O-β-D-glucopyranoside | c        | [37]  |
| 196 | 2-hydroxy-cinnamaldehyde        | c        | [82]   | 234 | D-threo-guaiacl glycerol 7-O-β-D-glucopyranoside | s        | [83]  |
| 197 | coniferaldehyde                 | c        | [82]   | 235 | cinnacasside D                | c        | [13]  |
| 198 | cassineraldehyde                | c        | [82]   | 236 | 3-(3,4-methylenedioxyphenyl)-1,2-propenediol                     | d,p      | [73]  |
| 199 | 4-methoxy-cinnamaldehyde        | 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 | dihydrodimeritolside           | c        | [82]  |
| 202 | cinnamyl alcohol                | b,c,j,m  | [43, 75, 84] | 240 | methyl dihydrodimeritolside    | c        | [82]  |
| 203 | cinnamic acid                   | b,c,j,m,n,z | [43, 84-86] | 241 | dihydrocinnamasside            | 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 | benzene-propanol               | c        | [34]  |
| 207 | rosvain                         | c        | [77, 82] | 245 | 2-ethyl-3-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-dimethoxy-coumarin         | b,d,p    | [38, 42, 61] |
| 212 | methoxyphenylacrylaldehyde      | c        | [37]   | 250 | coumacasia                     | c        | [76]  |
| 213 | 3-(3,4-dimethoxyphenyl)-2-propanol | c    | [37]   | 251 | 3,4-methylenedioxy-cinnamaldehyde | s        | [46]  |
| 214 | 3,4-dimethoxy-cinnamaldehyde   | s        | [46]   | 252 | methyl trans-3-(3,4-dimethoxyphenyl)-3-propanoate              | s        | [46]  |
| 215 | 3,4-methylenediol-cinnamyl alcohol | s        | [46]   | 253 | 2-methoxyphenylacetone        | c        | [34]  |
| 216 | isoeugenol                      | k        | [41]   | 254 | phenethyl (E)-3-[4-methoxyphenyl]-2-propanoate                | c        | [37]  |
| 217 | kobusinol B                     | b,z      | [1, 38] | 255 | trans-cinnamyl 3-phenyl pro 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-propenyl)-benzene                        | a        | [15]  |
| 220 | cis-2-methoxy-cinnamic acid     | c        | [34]   | 258 | 1,2-dimethoxy-4-(1-Z-propenyl)benzene                        | a        | [15]  |
| 221 | linocinamarin                   | c        | [13]   | 259 | rosinarin                     | c        | [13]  |
| 222 | E-(3,4-dimethoxyphenyl)-2-propanol | 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-propanol                           | a        | [15]  |
| 224 | trans-ferulaldehyde             | b        | [43]   | 262 | Cinnacassiol                  | c        | [1]   |
| 225 | trans-3,4,5-trimethoxy-cinnamyl alcohol | c      | [28]   | 263 | dimethylmatairesinol        | d        | [48, 70] |
| 226 | 4-allycatechol                  | t        | [45]   | 264 | linocinamarin                 | c        | [13]  |
| 227 | eugenol                         | d,j,m,n,u,s. | [46, 84, 85, 89] | 265 | cinnacassin N                   | c        | [17]  |
| 228 | methyl-eugenol                  | s,t      | [46, 90] | 266 | cinnacassin O             | c        | [17]  |
| 229 | saffrole                        | p        | [36]   | 267 | cinnacassin L                   | c        | [17]  |
| 230 | (7R, 8S)-syringoylglycerol      | c        | [37]   | 268 | cinnamic aldehyde cyclic syringyl glycerol 1,3-acetel        | 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 IC50 values were 43 and 31 μM, respectively [78]. The phenylpropanoid (250) induced cell death in the HL-60 and A-549 cell lines with IC50 values of 8.2 and 11.3 μM, respectively. Compounds 194-197 showed moderate inhibitory effects with IC50 values ranging from 3.3 to 25.8 μM [76].

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. Compound 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'-hydroxy-3'-yl)-acetic acid               | q      | [91] | 280 | cinnabutamine                                  | b      | [93] |
| 271 | corydaline                                     | q      | [91] | 281 | N-cis-feruloyltyramine                         | r      | [88] |
| 272 | Cinnapine                                      | q      | [92] | 282 | (E)-3-(4-hydroxy-3-methoxyphenyl)-N-phenethylacrylamide | c      | [28] |
| 273 | glaziovine                                     | q      | [91] | 283 | N-trans-caffeoyl-5-hydroxytyramine             | b      | [93] |
| 274 | zenerkine                                      | 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] |
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-dimethoxyphenyl alcohol | c | [34] | 337 | 3,4-dihydroxybenzoate | c | [28] |
| 292 | 4-hydroxy-3-methoxyphenethyl butyrate | r | [39] | 338 | 1,2-dimethoxy-4-(2-propenyl)benzen | c | [28] |
| 293 | 4-hydroxy-3-methoxyphenethyl hexylate | r | [39] | 339 | 3,4- dimethoxybenzaldehyde | a | [15] |
| 294 | 4-hydroxy-3-methoxyphenethyl pentadecyrate | r | [39] | 340 | 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 | cinnacасoside 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-acetalt(9,2-trans) | c | [32] | 349 | dihydrosobamabola | s | [72] |
| 304 | cinnamic aldehyde cyclic glycerol 1,3-acetalt(9,2-cis) | c | [32] | 350 | 2,2′,7a,7a′,7b,7b′-hexamethyldiphenyl ether | s | [46] |
| 305 | cinnamic aldehyde cyclic D-galactitol 3R′,4′S-acetal | c | [31] | 351 | 2-hydroxybenzaldehyde | c | [34] |
| 306 | Subunavoside A | s | [72] | 352 | 2,5-dihydroxybenzoic acid | d | [42] |
| 307 | Subunavoside B | s | [72] | 353 | ethyl ester | c | [34] |
| 308 | Subunavoside C | s | [72] | 354 | benzyl benzoate | d | [48] |
| 309 | Subunavoside D | s | [72] | 355 | dibutyl phthalate | c | [96] |
| 310 | Subunavoside E | s | [72] | 356 | 1-hydroxy-3,6-dimethoxy-8-methyl-anthraquinone | d | [42] |
| 311 | Subunavoside F | s | [72] | 357 | 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-dimethylenobenzol[b][1,5]dioxocin-4(6H)-one | t | [65] |
| 313 | 5′-hydroxy-5-hydroxy methyl-4′,5′-methylene dioxy-1,2,3,4-dibenzo-1,3,5-cycloheptatriene | b | [43] | 359 | cinnamopillolin D | q | [97] |
| 314 | Subamol | s | [50, 87] | 360 | cinnamocide 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 | reticulol | b,m,r | [98] | 363 | 3,4,5-trimethoxyphenol-β-D-apiofuranosyl(1→6)-O-β-D-glucopyranoside | c | [2, 13] |
| 318 | vanillin | b,c,d,k,s | [38, 41, 42] | 364 | cinnamocasside C | c | [13] |
| 319 | 4-hydroxybenzaldehyde | c,k,p,r,s,t | [40, 45, 58] | 365 | cinnamocasside E | c | [2] |
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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