Review Article

Terpenoids and Their Biological Activities from *Cinnamomum*: A Review

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Cinnamomum is a genus of the family Lauraceae, which has been recognized worldwide as an important genus due to its beneficial uses. A great deal of research on its phytochemistry and pharmacological effects has been conducted. It is noteworthy that terpenoids are the characteristic of *Cinnamomum* due to the peculiar structures and significant biological effects. For a more in-depth study and the better use of *Cinnamomum* plants in the future, the chemical structures and biological effects of terpenoids obtained from *Cinnamomum* were summarized in the present study. To date, a total of 181 terpenoids with various skeletons have been isolated from *Cinnamomum*. These compounds have been demonstrated to play an important role in immunomodulatory, anti-inflammatory, antimicrobial, antioxidant, and anticancer activities. However, studies on the bioactive components from *Cinnamomum* plants have only focused on a dozen species. Hence, further studies on the potential pharmacological effects need to be conducted in the future.

1. Introduction

Cinnamomum, which is a genus of the family Lauraceae, is represented by evergreen trees and shrubs [1]. Approximately 250 species of this genus have been found around the world and are mainly distributed in tropical and subtropical regions of Southeast Asia, Australia, and North, Central, and South America. There are approximately 46 species in China, and these are mainly in the southern regions. Yunnan province has the most species, followed by Guangdong and Sichuan [2, 3].

Cinnamomum has been recognized worldwide as an important genus due to its beneficial uses. This has been traditionally used in flavoring food and in folk medicine for its sweating, antipyretic, and analgesic effects [4]. Some *Cinnamomum* species, including *C. cassia*, *C. zeylanicum*, *C. tamala*, and *C. wilsonii*, are famous herbs that have a long history of being used as medicine. In addition, the extracted

essential oil from *C. camphora*, with the main ingredients of eucalyptol, linalool, and camphor, is an important raw material for the chemical industry and medicine. Furthermore, the Cinnamomi cortex, which is obtained from some *Cinnamomum* species, has been used for treating cardiovascular, chronic gastrointestinal, and inflammatory diseases [5, 6]. Cinnamaldehyde, which is the main constituent of the volatile oil of *C. cassia* bark, has been mainly used in medicine, foods, and cosmetics and has been proven to exert antifungal and antibacterial activities [7].

To date, many studies on phytochemistry of the genus *Cinnamomum* have been conducted. Over 500 compounds have been obtained from *Cinnamomum* plants, which cover lignans, terpenoids, flavonoids, phenylpropanoids, alkaloids, steroids, and butanolides. Among these compounds, approximately 300 compounds are from *C. Cassia*, which is the most thoroughly studied. This has been reported to show many special contents, particularly terpenoids. Other species

also contain a number of unique terpenoids with rare structures, which can only be found from certain species. More importantly, terpenoids, which are the most abundant and diverse compounds in this genus, have also been proven to show great pharmacological activities, including immunomodulatory, anti-inflammatory, antimicrobial, antioxidant, and anticancer activities. Thus, the present review aimed at summarizing the phytochemistry and pharmacological effects of terpenoids from *Cinnamomum* species and providing a basis for the future in-depth study of the genus *Cinnamomum*.

2. Chemical Constituents and Biological Activities

A number of studies on the phytochemistry of the genus *Cinnamomum* have been conducted, and focus has been given on approximately 14 species. From these studies, the genus has been shown to possess abundant and various terpenoids with unique structures. To date, a total of 181 terpenoids have been isolated from the genus *Cinnamomum*, including 43 monoterpenes, 83 sesquiterpenes, 53 diterpenes, and two triterpenes. Among these compounds, 119 terpenoids were obtained from *C. cassia*, 21 terpenoids were obtained from *C. wilsonii*, 19 terpenoids were obtained from *C. camphora*, 18 terpenoids were obtained from *C. glanduliferum*, 17 terpenoids were obtained from *C. subavenium*, eight terpenoids were obtained from *C. zeylanicum*, eight terpenoids were obtained from *C. osmophloeum*, three terpenoids were obtained from *C. inunctum*, three terpenoids were obtained from *C. philippinense*, two terpenoids were obtained from *C. kotoense*, one terpenoid was obtained from *C. burmannii*, one terpenoid was obtained from *C. parthenoxylon*, one terpenoid was obtained from *C. reticulatum*, and one terpenoid was obtained from *C. tenuifolium*, respectively.

2.1. Monoterpenes. A total of 43 monoterpenes have been reported from *Cinnamomum* (Table 1 and Figure 1), including 24 cyclic monoterpenes (1–17, 37–43) and 19 acyclic monoterpenes (18–36). Among these cyclic monoterpenes, compounds 1–13 are menthane monoterpenes, which are the most abundant types in the genus *Cinnamomum*. In addition, compounds 6–12 are the common constituents in the volatile oils of *Cinnamomum* plants. Compounds 14 and 15 are camphane monoterpenes and camphor (15), along with linalool (29) and eucalyptol (41), is one of the main components of volatile oil in *C. camphora*. Compounds 16 and 17 belong to the pinane-type monoterpenes, which are common in volatile oils. Monoterpenes 18–36 are laurane-type monoterpenes. Among these, compounds 18–24 have a geranylphenylacetate skeleton connected to glucose. Compounds 18–21, 23, and 24 were further cyclized to form a tetrahydrofuran ring. Interestingly, these compounds were only isolated from *C. cassia* and are the characteristic compounds for this species. Extracted from *C. inunctum*, compounds 25–27 were monoterpene lactones. Based on this structure, the original hydroxyl groups at the C-4 and C-7 positions of compound 27 were further cyclized to form

a rare spironolactone structure. Obtained from *C. camphora*, compound 33 is an acyclic monoterpene with one carbon degraded and has shown strong anti-inflammatory activity. Compounds 37 and 38 are normonoterpenes from *C. reticulatum*, with one carbon degraded. Subamone (43), which was obtained from *C. subavenium*, has a cycloheptanone skeleton and has strong antitumor activity.

Some monoterpenes from *Cinnamomum* plants have shown potent antimicrobial activities. Carvacrol (4) showed a broad spectrum of antibacterial activity against both Gram-positive and Gram-negative bacteria [25]. The antimicrobial activity of compound 4 against numerous bacteria was studied and it showed a high inhibitory effect against all these strains, including *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Streptococcus pneumonia*, *Escherichia coli*, *Klebsiella pneumonia*, *Enterobacter* spp., *Serratia* spp., and *Proteus mirabilis* [26]. Furthermore, 4 is also effective against various fungi, such as *Aspergillus niger*, *Aspergillus flavus*, *Alternaria alternata*, *Penicillium rubrum*, *Trichoderma viride*, *Candida* spp., and dermatophytes [27]. The antibacterial activity of compounds 4 and 9 (a precursor of 4) was studied against the foodborne microorganism *V. cholerae*. Compound 4 exerted a good inhibitory effect against *V. cholerae*, while 9 exhibited a weak activity. However, it was interesting to find that the inhibitory effects were enhanced when the two compounds were used together, showing a synergistic effect [28]. According to the findings both 16 and 29 exerted antibacterial activity against *E. faecalis* and *S. aureus*, and 16 showed antifungal activity against *C. albicans*. Similarly, compound 7 was effective against *Ae. aegypti* and *Ae. albopictus* [29], as well as *Culex pipiens molestus* [30].

The antioxidant activities of some monoterpenes were evaluated. The assessment on antioxidant capacity of carvacrol (4) showed that 4 at the doses of 25 (49.79 IU/mg) and 50 mg/kg (52.43 IU/mg) enhanced the level of hippocampal SOD activity in ischemic rats, when compared with the ischemic group (42.9 IU/mg). In the DPPH assay, the percentage of oxidant inhibition was significantly increased in the ischemic group treated with 4 at doses of 25 (41.5%) and 50 mg/kg (36.83%), when compared to the untreated ischemic group (11.29%) [31]. Hakimi et al. confirmed that three doses of compound 4 (25, 50, and 100 mg/kg) could significantly increase the thiol content and improve the activities of both CAT and SOD compared with LPS groups in the hippocampus of rats [32]. In the trolox equivalent antioxidant capacity assay, the antioxidant effects of compounds 4 and 5 were evaluated and compared to that of the synthetic antioxidant trolox. Both compounds have exerted significant antioxidant activity similar to trolox, and the capacity of 4 has been proven to be higher than that of its isomer thymol at the same concentration [25]. Moreover, the antioxidant potential of p-cymene (9) was evaluated in the hippocampus of adult mice. The treatment with 9 at a concentration of 50 mg/kg (0.42 ± 0.03) has produced a significant decrease in lipid peroxidation 65.54%, when compared with the control group. Furthermore, compound 9 at all tested doses (50, 100, and 150 mg/kg) could significantly decrease the nitrite content and produce an increase in SOD and catalase activities [33].

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TABLE 1: Monoterpenes from the genus *Cinnamomum*.

No.	Type	Compound	Molecular formula	Molecular weight	Origin	References
1	Menthane	(3R,4R)-p-Menth-1-ene-3,4-diol 3-O- β -D-glucopyranoside	C ₁₆ H ₂₈ O ₇	332	s	[8]
2		(3R,4S,6R)-p-Menth-1-ene-3,6-diol 3-O- β -D-glucopyranoside	C ₁₆ H ₂₈ O ₇	332	s	[8]
3		(4R)-p-Menthane-1,2 α ,8-triol	C ₁₀ H ₂₀ O ₃	188	s	[8]
4		Carvacrol	C ₁₀ H ₁₄ O	150	s	[9]
5		Thymol	C ₁₀ H ₁₄ O	150	s	[9]
6		α -Terpineol	C ₁₀ H ₁₈ O	154	c, d, g, o	[10–12]
7		α -Phellandrene	C ₁₀ H ₁₆	136	d, g	[10, 13]
8		α -Terpinene	C ₁₀ H ₁₆	136	d, g	[10, 13]
9		p-Cymene	C ₁₀ H ₁₄	134	g	[10]
10		Terpinolene	C ₁₀ H ₁₆	136	d, g	[10, 13]
11		Terpinen-4-ol	C ₁₀ H ₁₈ O	154	g	[10]
12		Limonene	C ₁₀ H ₁₆	136	g, z	[10, 11]
13		(1R,2R,4S,6S)-4-(2-Hydroxypropan-2-yl) -1-methyl-7-oxabicyclo[4.1.0]heptan-2-ol	C ₁₀ H ₁₈ O ₃	186	c	[14]
14	Camphane	Borneol	C ₁₀ H ₁₈ O	154	c, g, z, o	[10–12]
15		Camphor	C ₁₀ H ₁₆ O	152	c, d, g	[10, 13]
16	Pinane	α -Pinene	C ₁₀ H ₁₆	136	d, g, z	[10, 11]
17		β -Pinene	C ₁₀ H ₁₆	136	c, d, g	[10, 11]
18		Cinnacasside A	C ₂₅ H ₃₆ O ₁₁	512	c	[15–17]
19		Cinnacasside B	C ₂₅ H ₃₆ O ₁₁	512	c	[15–17]
20		Cinnacasside C	C ₂₅ H ₃₆ O ₁₁	512	c	[15–17]
21		Cinnacasside D	C ₂₅ H ₃₆ O ₁₁	512	c	[15]
22		Cinnacasside E	C ₂₅ H ₃₈ O ₁₁	514	c	[15]
23		Cinnacasside F	C ₂₆ H ₄₀ O ₁₂	544	c	[17]
24		Cinnacasside G	C ₂₆ H ₄₀ O ₁₂	545	c	[17]
25		5-(2,3-Dihydroxy-3-methylbutyl) -4-hydroxy-4-methyldihydrofuran-2(3H)-one	C ₁₀ H ₁₈ O ₅	218	i	[18]
26		5-(2,3-Dihydroxy-3-methylbutyl) -4-methylfuran-2(5H)-one	C ₁₀ H ₁₆ O ₄	200	i	[18]
27		8-Hydroxy-4,7,7-trimethyl -9-1,6-dioxaspiro[4.4]non-3-en-2-one	C ₁₀ H ₁₄ O ₄	198	i	[18]
28	Laurane	<i>trans</i> -Linalool-3,6-oxide - β -D-glucopyranoside	C ₁₆ H ₂₈ O ₇	332	c	[19]
29		Linalool	C ₁₀ H ₁₈ O	154	c, d	[19, 20]
30		3,7-Dimethyl-1-octene -3,6,7-triol	C ₁₀ H ₂₀ O ₃	188	c	[19]
31		3,7-Dimethyl-oct-1-en-3,6,7 -triol-6-O- β -D-glucopyranoside	C ₁₆ H ₃₀ O ₈	350	c	[19]
32		(6R)-Geraniol-6,7-diol	C ₁₀ H ₂₀ O ₃	188	c	[19]
33		6-Hydroxy-6-methyl-4,7-octadien-2-one	C ₉ H ₁₄ O ₂	154	d	[21]
34		β -Ocimene	C ₁₀ H ₁₆	136	d	[13]
35		β -Myrcene	C ₁₀ H ₁₆	136	g	[10]
36		Geranyl acetate	C ₁₂ H ₂₀ O ₂	196	c	[20]
37		Reticuone	C ₉ H ₁₄ O ₃	170	r	[22]
38	Normoterpenes	(3,3-Dimethylcyclohex-1-ene-1,4-diyl) dimethanol	C ₁₅ H ₂₆ O ₇	318	c	[14]
39	Others	α -Thujene	C ₁₀ H ₁₆	136	d, g	[10]
40		Sabinene	C ₁₀ H ₁₆	136	d, g	[10]
41		Eucalyptol	C ₁₀ H ₁₈ O	154	d, g	[10, 13]
42		Camphene	C ₁₀ H ₁₆	136	c, d, g	[13, 20]
43		Subamone	C ₁₀ H ₁₆ O ₂	168	s	[23, 24]

Note: b: *C. burmannii*; c: *C. cassia*; d: *C. camphora*; g: *C. glanduliferum*; i: *C. inunctum*; k: *C. kotoense*; o: *C. osmophloeum*; p: *C. parthenoxylon*; q: *C. philippinense*; r: *C. reticulatum*; s: *C. subavenium*; t: *C. tenuifolium*; w: *C. wilsonii*; z: *C. zeylanicum*. The same is given in Figure 1.

Some monoterpenes were reported to show significant anti-inflammatory effects. Cyclooxygenase-2 (COX-2) is a rate-limiting enzyme in prostaglandin biosynthesis, which plays a

key role in inflammation. In human macrophage-like U937 cells, compound 4 was shown to suppress the LPS-induced expression of COX-2 and activate the peroxisome proliferator-

FIGURE 1: The structures of monoterpenes from *Cinnamomum*.

activated receptors (PPAR) α and γ [34]. Furthermore, **4** could also inhibit the production and actions of NO [25]. Moreover, NF- κ B has been reported to play an important role in the inflammatory response and LPS/GalN-induced liver injury [35]. The effects of linalool (**29**) on NF- κ B expression were assessed, and it was found that **29** could significantly inhibit LPS-induced p65 NF- κ B translocation into the nucleus and I κ B α degradation. In addition to the NF- κ B inhibition, compound **29** could also induce antioxidant defense via Nrf2 activating and consequently protect against LPS/GalN-induced liver injury [36]. Other than this, another study demonstrated that **29** protected against CS-induced lung inflammation through inhibiting CS-induced NF- κ B activation [37].

The anticancer activity of linalool (**29**) against human prostate cancer (DU145) cells was evaluated by the MTT assay and it was observed that 4.36%, 11.54%, 21.88%, and 15.54% of the cells underwent early apoptosis after treatment with 0, 20, 40, and 80 μ M of **29**, respectively [38]. In addition, Okumura et al. confirmed that terpinolene (**10**) could markedly reduce the expression of protein kinase AKT, which can mediate cell proliferation and survival signals, and contribute to cancer progression [39].

In an immunosuppression assay, Zeng et al. found that monoterpenes **18**, **19**, and **23** exhibited potent immunosuppressive activities against murine lymphocytes. Compound **23** inhibited the proliferation of T cells and B cells with an inhibitory ratio of 36.1% and 20.3%, respectively, at a concentration of 400 μ M [17]. In another assay, the effect of α -terpineol (**6**) on the generation of nitric oxide in macrophages induced by LPS was evaluated. The nitrite production induced by LPS in these cells was reduced at all concentrations of compound **4** tested (1, 10, and 100 μ g/mL) [40]. Rufino et al. reported that α -pinene (**16**) could decrease NO production in a dose-dependent manner in primary human chondrocytes, showing the highest inhibition of NO production at a dose of 200 μ g/mL, with a decrease to 31.5% relative to cells treated with IL-1 β alone [41].

2.2. Sesquiterpenes. A total of 83 sesquiterpenoids (**44**–**126**) were isolated from *Cinnamomum* plants, which contain multiple structural types (Table 2 and Figure 2).

There are 28 ionone sesquiterpenoids (**44**–**71**) among these constituents, which are the most abundant

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TABLE 2: Sesquiterpenes from the genus *Cinnamomum*.

No.	Type	Compound	Molecular formula	Molecular weight	Origin	References
44	Inone	Wilsonol A	C ₁₃ H ₂₄ O ₄	244	w	[42]
45		Wilsonol B	C ₁₃ H ₂₄ O ₄	244	w	[42]
46		Wilsonol C	C ₁₃ H ₂₂ O ₄	242	w	[42]
47		Wilsonol D	C ₁₃ H ₂₄ O ₃	228	w	[42]
48		(3S,4S,5S,6S,9S)-Wilsonol E	C ₁₃ H ₂₆ O ₃	230	w	[42]
49		(3S,4S,5S,6S,9R)-Wilsonol E	C ₁₃ H ₂₆ O ₃	230	w	[42]
50		Wilsonol F	C ₁₃ H ₂₆ O ₃	230	w	[42]
51		Wilsonol G	C ₁₃ H ₂₄ O ₄	244	s, w	[8, 42]
52		(3S,4S,5S,6S,9S)-3,4-Dihydroxy-5,6-dihydro- β -ionol	C ₁₃ H ₂₄ O ₃	228	w	[42]
53		Lasianthionoside A	C ₁₉ H ₃₂ O ₉	404	w	[42]
54		Boscialin	C ₁₃ H ₂₂ O ₃	226	c	[43]
55		(3S,5R,6S,7E)-Megasfigma-7-ene-3,5,6,9-tetrol	C ₁₃ H ₂₄ O ₄	244	s, w	[8, 42]
56		(3S,5S,6S,9R)-3,6-Dihydroxy-5,6-dihydro- β -ionol	C ₁₃ H ₂₄ O ₃	228	w	[42]
57		Wilsonol H	C ₁₃ H ₂₄ O ₅	260	s, w	[8]
58		Wilsonol I	C ₁₃ H ₂₄ O ₃	228	w	[42]
59		Wilsonol J	C ₁₃ H ₂₄ O ₃	228	w	[42]
60		Wilsonol K	C ₁₃ H ₂₂ O ₃	226	w	[42]
61		Wilsonol L	C ₁₃ H ₂₂ O ₃	226	w	[42]
62		(3R,9S)-Megasfigman-5-ene-3,9-diol 3-O- β -D-glucopyranoside	C ₁₉ H ₃₄ O ₇	374	w	[42]
63		(3S,4R,9R)-3,4,9-Trihydroxymegastigman-5-ene	C ₁₃ H ₂₄ O ₃	228	w	[42]
64		Apocynol A	C ₁₃ H ₂₀ O ₃	224	w	[42]
65		Blumenol A	C ₁₃ H ₂₀ O ₃	224	c, p	[43, 44]
66		Dehydrovomifoliol	C ₁₃ H ₁₈ O ₃	222	c	[43]
67		(3S,5R,6S,9S)-3,6,9-Trihydroxymegastigman-7-ene 3-O- β -D-glucopyranoside	C ₁₉ H ₃₄ O ₈	390	c	[19]
68		(1R,2R)-4-[(3S)-3-Hydroxybutyl]-3,3,5-trimethylcyclohex-4-ene-1,2-diol	C ₁₃ H ₂₄ O ₃	228	c	[45]
69		(3S,5R,6S,7E)-3,5,6-Trihydroxy-7-megastigmen-9-one	C ₁₃ H ₂₂ O ₄	242	c	[46]
70		Grasshopper ketone	C ₁₃ H ₂₀ O ₃	224	c	[43]
71		Asicariside B1	C ₁₈ H ₃₀ O ₈	374	s	[8]
72	Caryophyllane	Caryophyllene oxide	C ₁₅ H ₂₄ O	220	o, s	[9, 16]
73		<i>trans</i> -Caryophyllene	C ₁₅ H ₂₄	204	c	[47]
74	Humulane	(2E,9E)-6,7- <i>cis</i> -Dihydroxyhumulan-2,9-diene	C ₁₅ H ₂₆ O ₂	238	c	[46]
75		α -Humulene	C ₁₅ H ₂₄	204	g	[10]
76	Cadinane	Cinnamoid B	C ₁₅ H ₂₄ O ₃	252	c	[48, 49]
77		Cinnamoid C	C ₁₅ H ₂₄ O ₃	252	c	[48, 49]
78		Mustakone	C ₁₅ H ₂₄ O ₃	252	c	[46]
79		Oxyphyllenodiol A	C ₁₄ H ₂₂ O ₃	238	s	[50]
80		Oxyphyllenodiol B	C ₁₄ H ₂₂ O ₃	238	s	[50]
81		(-)-15-Hydroxytmurolol	C ₁₅ H ₂₆ O ₂	238	c	[49]
82		15-Hydroxy- α -cadinol	C ₁₅ H ₂₆ O ₂	238	c	[49]
83		β -Cadinene	C ₁₅ H ₂₄	204	z	[11]
84		δ -Cadinene	C ₁₅ H ₂₄	204	c, d, o, z	[10–13]
85		α -Muurolene	C ₁₅ H ₂₄	204	c, d	[14]
86		α -Cadinol	C ₁₅ H ₂₆ O	222	c, d	[14]
87		α -Calacorene	C ₁₅ H ₂₀	200	c, o, z	[11, 12]
88		Calamenene	C ₁₅ H ₂₂	202	z	[11]

TABLE 2: Continued.

No.	Type	Compound	Molecular formula	Molecular weight	Origin	References
89	Eudesmane	4(15)-Eudesmene-1 β ,7,11-triol	C ₁₅ H ₂₆ O ₃	254	c	[51]
90		1 β ,6 α -Dihydroxyeudesm-4(15)-ene	C ₁₅ H ₂₆ O ₂	238	c	[51]
91		1 α ,6 β -Dihydroxy-5,10-bis-epi-eudesm-15-carboxaldehyde-6-O- β -D-glucopyranoside	C ₂₁ H ₃₆ O ₉	433	s	[8]
92		1 β ,4 β ,11-Trihydroxyl-6 β -gorgonane	C ₁₅ H ₂₈ O ₃	256	c	[51]
93		Cinnamosim B	C ₁₅ H ₂₄ O ₄	270	c	[51]
94		Cinnamosim A	C ₁₅ H ₂₄ O ₃	252	c	[51]
95		1 β ,7-Dihydroxyl opposit-4(15)-ene	C ₁₅ H ₂₆ O ₂	238	c	[51]
96		1 β ,11-Dihydroxyl opposit-4(15)-ene	C ₁₅ H ₂₆ O ₂	238	c	[51]
97		4 α -10 α -Dihydroxy-5 β -H-guaia-6-ene	C ₁₅ H ₂₆ O ₂	238	c	[51]
98	Guaiane	Alpinenone	C ₁₅ H ₂₆ O ₂	238	t	[52]
99		α -Bulnesene	C ₁₅ H ₂₄	204	c	[53]
100		Guaiol	C ₁₅ H ₂₆ O	222	g	[10]
101	Aromadendrane	Aromadendrane-4 β ,10 α -diol	C ₁₅ H ₂₆ O ₂	238	c	[51]
102		Aromadendrane-4 α ,10 α -diol	C ₁₅ H ₂₆ O ₂	238	c	[51]
103		1-Epimeraromadendrane-4 β ,10 α -Diol	C ₁₅ H ₂₆ O ₂	238	c	[51]
104		Espatulanol	C ₁₅ H ₂₄ O	220	c	[14]
105		Spathulanol	C ₁₅ H ₂₄ O	220	o	[12]
106		(-)-Isoledene	C ₁₅ H ₂₄	204	c	[53]
107	Bisabolane	β -Bisabolene	C ₁₅ H ₂₄	204	c	[14]
108		α -Bisabolol	C ₁₅ H ₂₆ O ₂	238	c	[14]
109		Curcumene	C ₁₅ H ₂₂	202	c, o	[14]
110	Germacrane	Germacrene D	C ₁₅ H ₂₈	208	c	[47]
111	Cedrane	Cedrene	C ₁₅ H ₂₄	204	c	[20]
112	Others	3S-(+)-9-Oxonerolidol	C ₁₆ H ₂₆ O	234	d	[21]
113		2,6,11-Trimethyldodeca-2,6,10-triene	C ₁₅ H ₂₆	206	q	[54]
114		(+)-(6S,7E,9Z)-Absciscic ester	C ₁₆ H ₂₂ O ₄	278	w	[42]
115		Gibberodione	C ₁₅ H ₂₄ O ₂	236	s	[55]
116		(+)-Absciscic acid	C ₁₅ H ₂₀ O ₄	264	b, s	[56, 57]
117		Caryolane-1,9 β -diol	C ₁₅ H ₂₆ O ₂	238	c	[46, 51]
118		Vlovane-2 β ,9 α -diol	C ₁₅ H ₂₆ O ₂	238	c	[46]
119		Cinnamoid A	C ₁₅ H ₂₆ O ₂	238	c	[48, 49]
120		Cinnamoid D	C ₁₅ H ₂₄ O ₂	236	c	[48, 49]
121		Cinnamoid E	C ₁₅ H ₂₂ O ₂	234	c	[48, 49]
122		(-)-15-Hydroxy-T-murolol	C ₁₅ H ₂₂ O ₂	218	c	[13]
123		α -Cubebene	C ₁₅ H ₂₄	204	c	[53]
124		α -Copaene	C ₁₅ H ₂₄	204	c, o, z	[11, 12]
125		1-(3-Indolyl)-2,3-dihydroxypropan-1-one	C ₁₅ H ₂₆ O ₂	238	c	[43]
126		Patchouli alcohol	C ₁₅ H ₂₆ O	222	c	[53]

sesquiterpene skeletons from the genus *Cinnamomum*. Although ionone sesquiterpenes are common in natural products, this class of compounds from *Cinnamomum* has its special features, which are demonstrated as follows: (1) C-4 is connected to a hydroxyl group in some compounds, including **44–46**, **48**, **49**, **51–53**, **57**, and **63**. (2) The methyl group attached to C-5 is hydroxylated, such as compounds **47**, **58–61**, and **64**. (3) The hydroxyl group of C-3 was removed in compound **51**. (4) C-2 was connected to a hydroxyl group, such as compounds **51** and **68**.

Compounds **72** and **73** belong to caryophyllane sesquiterpenes. Compounds **74** and **75** belong to humulane sesquiterpenes with an eleven-membered ring. Compounds **97–100** are guaiane sesquiterpenes, among which **98** was further cyclized on the basis of this structure and has exerted potent antitumor activity.

Cadinane sesquiterpenes include compounds **76–88**. The methyl groups attached to the C-9 positions of **79** and **80** were degraded, and both of them are derived from *C. subavenium*. In compounds **81** and **82**, which were isolated from *C. cassia*, the hydrogen at the C-10 position was hydroxylated. In addition, compounds **83–88** are common in the volatile oils of *Cinnamomum* plants.

Eudesmane sesquiterpenes include compounds **89–96**. Compound **92** is a rearranged sesquiterpene, with its isopropanol group migrating from C-7 to C-6. Furthermore, **94–96** are also rearranged sesquiterpenes, with one carbon migrating to form a cyclopentane instead of cyclohexane. Interestingly, the compounds above were all derived from *C. cassia*.

Compounds **101–106** are aromadendrane sesquiterpenes. Furthermore, compounds **107–111** are the common components of the volatile oils in *Cinnamomum* plants.

(a)

FIGURE 2: Continued.

FIGURE 2: The structures of sesquiterpenes from *Cinnamomum*.

Among these, **107–109** are bisabolane sesquiterpenes, while **110** and **111** belong to germacrane and cedrane sesquiterpenes, respectively. Compound **117** is the result of the further cyclization based on the caryophyllane skeleton, and **118** was formed through the migration of one carbon atom based on the structure of **117**.

In 2014, Yan et al. separated cinnamonoid A (**119**) from *C. cassia* with an unprecedented skeleton, which may be derived from cadinane sesquiterpenes. The possible biosynthesis pathway of **119** was carried out by the cleavage of C-5 and C-6, followed by the construction of C-4 with C-6 and C-5 with C-10. Furthermore, compounds **120–122** are rearranged cadinane sesquiterpenes with the cleavage of C-9 and C-4.

Some sesquiterpenoids were reported to show significant anti-inflammatory effects. Tung et al. confirmed that the essential oil of *C. osmophloeum* twig exhibited a potent inhibition on NO production in LPS-stimulated RAW 264.7 macrophage cells. The anti-inflammatory effects of some constituents from essential oils were also evaluated. Compound **72** (54.0%) exhibited stronger inhibition activities than twig essential oil (48.3%) at the concentration of 10 $\mu\text{g/mL}$, while **117** exhibited an activity similar to that of twig essential oil, with inhibition rates of 46.1 and 50.9%, respectively [12]. In addition, Guoruoluo et al. evaluated some sesquiterpenoids for the antimicrobial activities. Compounds including **89**, **90**, **93–95**, **97**, **101**, **102**, and **117** showed significant antimicrobial activities against *Candida albicans* with inhibitory zone diameters ranging from 8 to 11 mm. Moreover, **90**, **101**, and **117** have exhibited moderate inhibitory effects on *Escherichia coli* and *Staphylococcus aureus* with inhibitory zone diameters ranging from 7 to 11 mm [51]. In another antibacterial assay, the activities of **79** and **80** against *Candida glabrata* were also evaluated, and the MIC values were 187.6 and 177.5, respectively [58].

2.3. Diterpenes. A total of 55 diterpenes were isolated from *Cinnamomum* plants (Table 3 and Figure 3). Most of these were derived from *C. cassia* (**127–178**), and **179** was derived from *C.*

kotoense and *C. philippinense*. Nine new diterpene skeletons were found from this species, including ryanodane (cinncassiol B type), 11,12-seco-ryanodane (cinncassiol A type), 7,8-seco-ryanodane (cinncassiol C type), isoryanodane (cinncassiol D type), 10,13-cyclo-12,13-seco-isoryanodane (cinncassiol E type), 12,13-seco-isoryanodane (cinncassiol F type), 11,12-seco-isoryanodane (cinncassiol G type), 6,10-cyclo-12,13-seco-isoryanodane (cinnamomane), and 11,14-cyclo-8,14:12,13-di-seco-isoryanodane (cassiabudane).

Among these nine skeletons, the representative compounds of the cinncassiol A-G types were **127**, **136**, **141**, **143–145**, **148**, **150**, and **164–166**. Furthermore, the typical constituents of cinnamomane-type diterpenes were **173** and **174**, while those of cassiabudane-type diterpenes were **175** and **176**.

The biogenetic relationships of the nine diterpene skeletons were proposed by Zhou et al. (Figure 4) [69]. Cinncassiol B type (**134–140**), that is, renolane-type diterpenes, is a 6/5/5/6/5 pentacyclic skeleton with a ketal structure. The two oxygen atoms connected to C-11 were, respectively, connected to hydrogen and C-6. In addition, cinncassiol A-type diterpenes (**127–133**) have a lactone skeleton produced by the cleavage of the bond between C-11 and C-12, and the formation of the carbon-oxygen double bond at C-11 in cinncassiol B-type diterpenes. The linkage between C-7 and C-8 was cleaved, and two carbonyl groups were formed at the two positions in the cinncassiol B type to produce a diketone skeleton, cinncassiol C type (**141–144**). Cinncassiol D-type diterpenes (**145–163**) are isorinolone diterpenes, which have a pentacyclic ring skeleton produced by the migration of the bond between C-5 and C-6 of cinncassiol B-type diterpenes to the C-1 position. Similarly, cinncassiol G-type diterpenes were formed by the migration of 5,6-bond to C-1 in cinncassiol A-type diterpenes.

The possible biosynthetic pathway of cassiabudane diterpenes was proposed by Zhou et al. [69]. These were formed from 18-hydroxyperseanol (**159**), an isoryanodane diterpenoid, by the cleavage of the 12,13-bond and migration of the 14,8-bond to C-11 through a series of retro-aldol, aldol, and oxidation reactions.

tblBody

TABLE 3: Diterpenes from the genus *Cinnamomum*.

No.	Type	Compound	Molecular formula	Molecular weight	References
127	Cinn cassiol A	Cinn cassiol A	C ₂₀ H ₃₀ O ₇	382	[46, 49]
128		Cinn cassiol A 19-O- β -D-glucopyranoside	C ₂₆ H ₄₀ O ₁₂	544	[59, 60]
129		Anhydrocinnzeylanine	C ₂₂ H ₃₂ O ₇	408	[49]
130		Epianhydrocinnzeylanol	C ₂₀ H ₃₀ O ₆	366	[61]
131		1-Acetylcinn cassiol A	C ₂₂ H ₃₂ O ₈	424	[59]
132		2,3-Dehydroanhydrocinnzeylanine	C ₂₂ H ₃₀ O ₇	406	[59]
133		Cinn cassiol H	C ₂₀ H ₃₀ O ₇	382	[61]
134	Cinn cassiol B	Cinnzeylanol	C ₂₀ H ₃₂ O ₇	384	[61]
135		Cinnzeylanine	C ₂₂ H ₃₄ O ₈	427	[61]
136		Cinn cassiol B	C ₂₀ H ₃₂ O ₈	400	[46]
137		Ryanodol	C ₂₀ H ₃₂ O ₈	400	[46]
138		Ryanodol 14-monoacetate	C ₂₂ H ₃₄ O ₉	442	[46]
139		18-Hydroxycinnzeylanine	C ₂₂ H ₃₄ O ₉	442	[59]
140		Cinnzeylanone	C ₂₀ H ₃₀ O ₇	382	[46]
141	Cinn cassiol C	Cinn cassiol C ₁	C ₂₆ H ₃₈ O ₁₂	542	[62]
142		Cinn cassiol C ₁ -19-O- β -D-glucopyranoside	C ₂₀ H ₂₈ O ₇	380	[63]
143		Cinn cassiol C ₂	C ₂₀ H ₂₈ O ₆	364	[63]
144		Cinn cassiol C ₃	C ₂₀ H ₃₀ O ₇	382	[63]
145	Cinn cassiol D	Cinn cassiol D ₁	C ₂₆ H ₄₂ O ₁₀	515	[64, 65]
146		Cinn cassiol D ₁ glucoside	C ₂₀ H ₃₂ O ₅	352	[64, 65]
147		1-Hydroxycinn cassiol D ₁	C ₂₀ H ₃₂ O ₆	368	[45]
148		Cinn cassiol D ₂	C ₂₀ H ₃₂ O ₆	368	[64]
149		Cinn cassiol D ₂ glucoside	C ₂₆ H ₄₂ O ₁₁	531	[64]
150		Cinn cassiol D ₃	C ₂₀ H ₃₂ O ₅	352	[64]
151		Cinn cassiol D ₃ -2-O-monoacetate	C ₂₄ H ₃₆ O ₈	452	[46]
152		(18S)-3-Dehydroxycinn cassiol D ₃	C ₂₀ H ₃₂ O ₅	352	[45]
153		(18S)-3-Dehydroxycinn cassiol D ₃ glucoside	C ₂₆ H ₄₂ O ₁₀	515	[45]
154		(18S)-3,5-Didehydroxy-1,8-dihydroxycinn cassiol D ₃	C ₂₀ H ₃₂ O ₆	368	[45]
155		(18S)-3-Dehydroxy-8-hydroxycinn cassiol D ₃	C ₂₀ H ₃₂ O ₆	368	[45]
156		Cinn cassiol D ₄	C ₂₀ H ₃₂ O ₅	352	[66]
157		Cinn cassiol D ₄ glucoside	C ₂₆ H ₄₂ O ₁₀	515	[67]
158		Cinn cassiol D ₄ -2-O-monoacetate	C ₂₂ H ₃₄ O ₆	395	[46]
159		18-Hydroxyperseanol	C ₂₀ H ₃₂ O ₈	400	[67, 68]
160		Perseanol	C ₂₀ H ₃₂ O ₇	384	[67, 68]
161		16-O- β -D-Glucopyranosyl-perseanol	C ₂₆ H ₄₂ O ₁₃	563	[45]
162		19-Dehydroxy-13-hydroxycinn cassiol D ₁	C ₂₀ H ₃₂ O ₆	368	[45]
163		(E)-3-Dehydroxy-13(18)-ene-19-O- β -D-glucopyranosyl-cinn cassia D ₃	C ₂₆ H ₄₀ O ₁₀	513	[45]
164	Cinn cassiol E	Cinn cassiol E	C ₂₀ H ₃₀ O ₈	398	[67]
165	Cinn cassiol F	Cinn cassiol F	C ₂₀ H ₃₀ O ₈	398	[67]
166	Cinn cassiol G	Cinn cassiol G	C ₂₀ H ₃₀ O ₇	382	[67]
167		16-O- β -D-Glucopyranosyl-19-deoxycinn cassiol G	C ₂₆ H ₄₀ O ₁₂	545	[67]
168		Cinnamomol C	C ₂₀ H ₃₀ O ₆	366	[45]
169		Cinnamomol D	C ₂₀ H ₃₀ O ₅	350	[45]
170		Cinnamomol E	C ₂₀ H ₃₀ O ₆	366	[45]
171		Cinnamomol F	C ₁₇ H ₂₄ O ₄	292	[45]
172		13-O- β -D-Glucopyranosyl-cinnamomol F	C ₂₃ H ₃₄ O ₉	455	[45]
173	Cinnamomane	Cinnamomol A	C ₂₀ H ₃₀ O ₈	398	[68]
174		Cinnamomol B	C ₂₀ H ₃₀ O ₉	414	[68]
175	Cassiabudane	Cassiabudanol A	C ₂₁ H ₃₂ O ₈	412	[69]
176		Cassiabudanol B	C ₂₀ H ₃₀ O ₈	398	[69]
177	Others	Cinnacasol	C ₂₀ H ₃₀ O ₇	382	[70]
178		Cinnacaside	C ₂₆ H ₄₀ O ₁₂	545	[70]
179		Phytol	C ₂₀ H ₄₀ O	297	[54, 71]

FIGURE 3: The structures of diterpenes from *Cinnamomum*.

According to the research conducted by Zeng et al. [67], isoryanodane diterpenoid perseanol (**160**) is the plausible biosynthetic precursor of cinnassiol F (**165**) and cinnassiol G (**166**), and biosynthetic pathways have been proposed. These were, respectively, formed by the cleavage of the 12,13-bond and 11,12-bond from **160** through a series of reactions under the catalysis of acid. In addition, Zhou et al. [68] proposed that cinnamomane diterpenoids are also generated from perseanol (**160**) through a series of retro-aldol, aldol, and oxidation reactions.

Some diterpenes of *Cinnamomum* have been reported to demonstrate immunomodulatory potency, covering immunostimulative and immunosuppressive activities.

Zhou et al. reported that the cassiabudane diterpenes **175** and **176** showed strong immunostimulative activity. Both of these significantly promoted the expansion of ConA-induced murine T cells with enhancement rates of 10.38 and 19.96%, respectively, at a dose of 0.3906 μM and enhanced the proliferation of LPS-induced murine B cells with enhancement rates of 52.13 and 55.06%, respectively, at the same dose [69]. In another assay conducted by Zhou et al., cinnamomane diterpenes **173** and **174** could promote the proliferation of ConA-induced murine T cells with enhancement rates of 59 and 64%, respectively, at the concentration of 0.3906 μM [68]. By comparing the results, we found that cinnamomane

immunosuppressive activity, which accounts for the stronger inhibition of **166** compared to that of **177** [67]. According to the research by Zhou et al., some diterpenes, including **145**, **152**, **154**, **168–170**, **173**, and **174**, could significantly promote ConA-induced murine T-cell proliferation, with proliferation rates of up to 78% at five different concentrations (0.391 to 100 μM). When the concentration was lower than 25 μM , compounds **168** and **169** appeared to promote proliferation. However, these appeared to inhibit the growth at the concentration of 100 μM [45].

In addition, some diterpenes have been reported to exert anti-inflammatory activities. He et al. reported that compounds **127**, **129**, **130**, **133**, **134**, and **135** had a good performance of inhibiting NO production, with IC_{50} values ranging from 72.3 to 81.8 μM [61].

2.4. Triterpenes. Two triterpenes were obtained from the *Cinnamomum* genus, including squalene (**180**) from *C. kotoense*, *C. philippinense*, and *C. subavenium*, and oleanolic acid (**181**) from *C. camphora* (Table 4 and Figure 5).

3. Conclusion

The medicinal value of the genus *Cinnamomum* has attracted much attention around the world, and many studies have been conducted. Most importantly, terpenes are the most abundant in the genus *Cinnamomum*, with various novel skeletons and significant biological activities, including immunomodulatory, anti-inflammatory, antimicrobial, antioxidant, and anticancer activities. In the present review, the research progress on chemical structures and biological effects of terpenes from *Cinnamomum* has been summarized. This can not only increase the understanding of the genus *Cinnamomum*, but also promote the better use of plants and further development of new drugs. Nevertheless, research on *Cinnamomum* remains incomplete, and more investigations are needed in the future.

First, chemical research on *Cinnamomum* plants has focused on only a few species like *C. cassia* and *C. subavenium*. Some other plants have gradually become research hotspots, but are only limited to the study of volatile oils. *Cinnamomum* plants have great economic and medicinal value and need to be further explored in future studies. Second, the diterpenes from *Cinnamomum* have shown significant immunomodulatory activities according to the findings. However, this only stays in the stage of cell activity *in vitro*. Thus, further pharmaceutical and *in vivo* activity experiments can be performed to promote the development of new drugs.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Authors' Contributions

M.T.W. conceptualized the review and drafted the initial version of the manuscript. L.N. and H.X.L. undertook the

database search for the literature. H.Y.X., S.Q.Z., and X.X.Z. significantly contributed to the gathering of information and discussions of the manuscript. All authors read and approved the final manuscript.

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