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Chemical Constituents and Pharmacological Activities of the Genus *Nageia*

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Abstract: There are seven species in the genus *Nageia*, a member of the Podocarpaceae family; five are found in China. They are primarily found in eastern and southern Asia, close to the equator at the 30th parallel north and south, and in coastal mountainous areas and islands in the western Pacific. These herbs are extremely valuable for medicinal purposes. The three species of *Nageia* that are the subject of most current research on their chemical composition and pharmacological properties are *N. nagi*, *N. fleuryi*, and *N. wallichiana*. There are currently 232 known chemical components, which include steroids, flavonoids, sesquiterpenoids, and diterpenoids. Of these, 86 diterpenoid dilactones comprise most of the chemical components, and only plants of the *Nageia* genus contain C-ring decarbonized diterpenoid dilactones. These plants exhibit promising pharmacological activities such as anti-tumor, antioxidant, antibacterial, and anti-inflammatory properties. For the first time, an in-depth and systematic evaluation of the chemical constituents and pharmacological properties of plants in the *Nageia* genus is presented in the this article. This theoretical framework will help in the future investigation and development of medicinal resources and active ingredients within the genus.

Keywords: *Nageia;* diterpenoids; nagilactones; antitumor; antioxidants; bacteriostatic.

1. Introduction

The *Nageia* genus, a member of the Podocarpaceae family, consists of perennial evergreen trees. Previously, these plants were classified under the *Podocarpus* genus as a separate group [1] (Podocarpus Sect. *Nageia* Endl.). However, De Laubenfels, during the revision of the Podocarpaceae family, separated the *Nageia* genus and reinstated its use as a distinct genus in 1987 [2]. The *Nageia* genus is now classified into two sections: *Nageia* Sect. *Nageia* and *Nageia* Sect. Dammaroideae R. R. Mill, which together consists of seven species [3] (Table 1). *Nageia* genus plants are widely

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distributed in tropical and subtropical humid broadleaf forests in Southeast Asia. They are particularly abundant in China, especially in Fujian, Hunan, Zhejiang, Guangxi, Taiwan, and Hainan regions [4]. The wood of these plants is known for its flexibility, dense structure, and resistance to cracking and deformation after drying, making it suitable for carving, furniture-making, construction, and other high-quality applications. Additionally, the seeds of *Nageia* genus plants have an oil content of up to 30%, which can be processed into high-quality edible oil, thus holding significant economic value [5,6]. Various parts of *Nageia* genus plants, including the roots, stems, leaves, and seeds, are rich in chemical constituents. They are known for their efficacy in promoting blood circulation and treating bruises, rheumatoid arthritis, body odor, eye disorders, and other ailments. Moreover, these plants are highly valued for their appealing tree form, luxuriant green leaves, and the enduring aroma of cloves they release, rendering them both decorative and ecologically advantageous, as they assist in air cleansing, pollution mitigation, and waste decomposition [7,8].

Research on the chemical components of *Nageia* genus plants began with the work of Hayashi Y. and others in 1968 [9]. Their study revealed that these plants are rich in novel and biologically active diterpenoids, which sparked significant interest among researchers worldwide. Currently, a total of 232 compounds have been extracted and characterized from plants belonging to the *Nageia* genus. These compounds encompass 117 diterpenoids, 30 sesquiterpenoids, 31 flavonoids and lignans, 25 steroids and triterpenoids, and 29 miscellaneous chemicals. Significantly, many substances have exhibited exceptional pharmacological actions, including antibacterial, antioxidant, anticancer, antidepressant, insecticidal, and cytotoxic characteristics. This article provides a detailed assessment of the chemical constituents and pharmacological properties of plants belonging to the *Nageia* genus, intending to enhance the comprehension and application of their medicinal resources. This review aims to provide a valuable resource for the extensive exploration and effective application of *Nageia* genus plants for medicinal purposes.

Table 1. Species and Latin Scientific Names of *Nageia* genus plants

Sect Names	**Latin Scientific Names**
Nageia Sect. *Nageia*	*Nageia nagi* (Thunberg) O.Kuntze
	N. nankoensis (Hayata) R. R. Mill
	N. formosensis (Dummer) C. N. Page
	N. fleuryi (Hickel) De Laub.
	N. maxima (De Laub.) De Laub.
Nageia Sect. *Dammaroideae* R. R. Mill	*N. wallichiana* (Presl) O.Kuntze
	N. motleyi (Parl.) DeLaub.

2. Chemical constituents of *Nageia* genus plants

The chemical constituents found in plants of the *Nageia* genus consist primarily of diverse terpenes (such as diterpenes, sesquiterpenes, triterpenes, and monoterpenes), flavonoids, and other chemical compounds.

2.1. Diterpenoids

Diterpenoids are the primary chemical components in *Nageia* genus plants. So far, 117 diterpenes have been isolated and identified from these plants, including diterpenoid dilactones (**1-86**), totarane (**87-93**), abietane (**94-112**), pimarane (**113-116**), and phytane (**117**) diterpenoids [10-42].

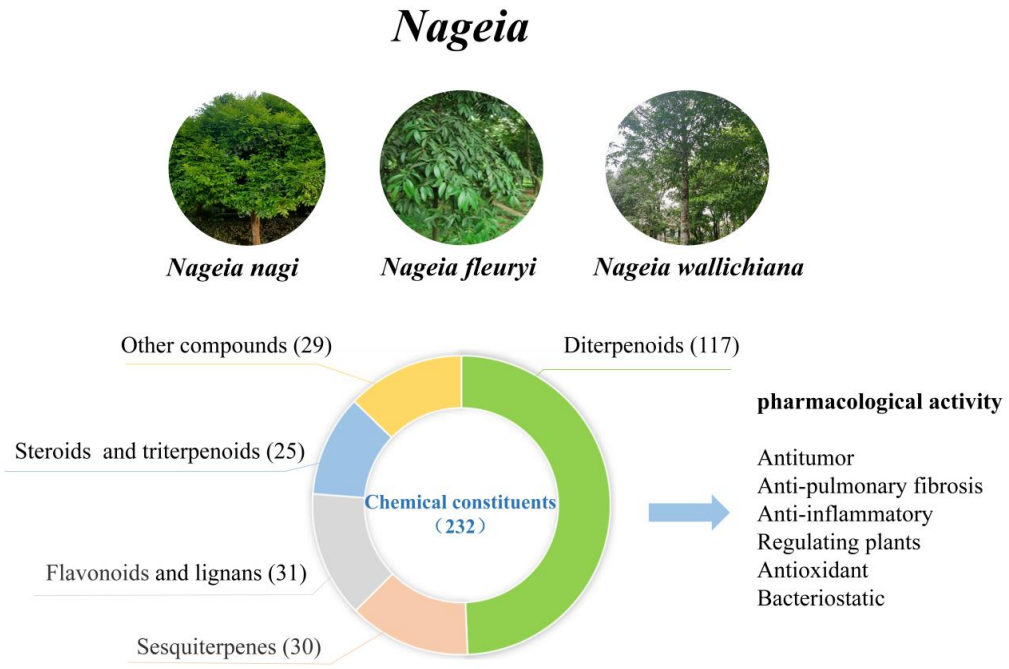


Figure 1. Pharmacological activity and phytochemical constituent map of *Nageia*

2.1.1. Diterpenoid Dilactones

Nageia genus plants are rich in diterpenoid dilactones (**1**-**86**) (Table 2 and Figure 4). These compounds share the following common structural features: 1) Degradation of the C-ring of the abietane skeleton into an unsaturated δ-lactone ring [31]. 2) Presence of C4 *α*-methyl and C10 *β*-methyl groups. 3) Formation of a γ-lactone ring D between the *β*-directed hydroxyl groups at C6 and C19. 4). Furthermore, including hydroxyl, olefinic, and epoxy groups in the A and B rings of most compounds leads to a carbon atom count of 18 or more. The presence of the hydroxyl group in the A ring is crucial for the functionality of diterpenoid dilactones. Based on the nature of the conjugated lactone system between the B and C rings, these diterpenoid dilactones can be categorized into three structural types. Type A compounds feature an *α*-pyrone [8(14),9(11)-dienone] structure (**1**-**56**); type B compounds have a 7*α*,8*α*-epoxy-9(11)-dienone structure (**57**-**74**); and type C compounds possess a 7(8),9(11)-dienone structure (**75**-**84**) [32]. Compounds **85** and **86** are not classified under those three distinct types mentioned above. Unlike common diterpenoid dilactones, these possess a distinct pentacyclic unsaturated lactone ring structure on the C ring. This structure is believed to be produced through further degradation and decarboxylation of the diterpenoid dilactone framework. The unusual structure of this novel C-ring decarbonized diterpenoid dilactone is currently found exclusively in *Nageia* genus plants, specifically *N. nagi* and *N. fleuryi*.

Yuji Hayashi [20] conducted research on the conversion between the A, B, and C structural frameworks of diterpenoid dilactones using compound **12** (type A) isolated from *N. nagi* seeds and compound **57** (type B) isolated from the root bark as starting materials. Conversion of the B-type to the C-type framework is illustrated in Figure 3-1. Compound **57**, which was dehydrated to prepare the compound podolide, was hydrogenated using 10% Pd/C in the presence of two equivalents of hydrogen. Hydrogenation resulted in the formation of the tetrahydro and hexahydro derivatives, P1 and P2, respectively, among which P1 was smoothly converted to compound **81** (type C) in pyridine using methane sulfonyl chloride. The transformation from the A-type to the C-type framework was accomplished by reacting the 7*β*-acetoxy derivative of compound **12** with sodium borohydride (Figure 3-2). The acetoxy derivative P3 of compound **12** yielded the corresponding 14-hydroxy analog P4 upon irradiation in a tetrahydrofuran-water solution. In the presence of cerium chloride, an excess of sodium borohydride was used to reduce P4, yielding P5 and P6. Out of these compounds, the *β*-acetoxy group in P5 underwent hydrolysis in methanol with potassium carbonate, leading to the conversion into compound **78**.

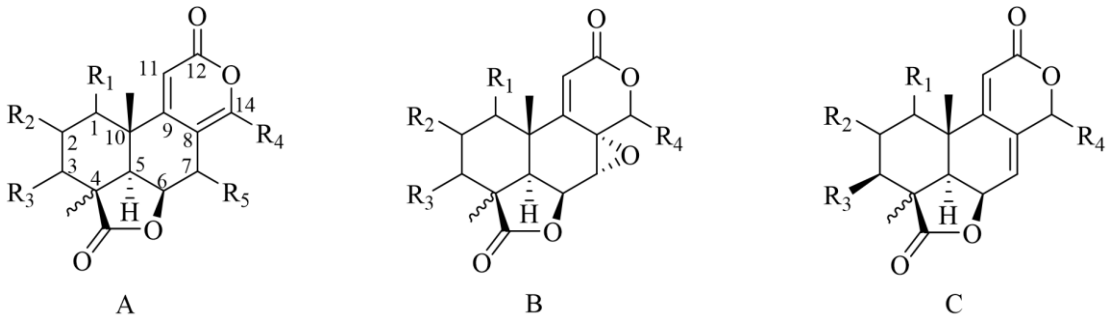


Figure 2. Structures of diterpenoid dilactones

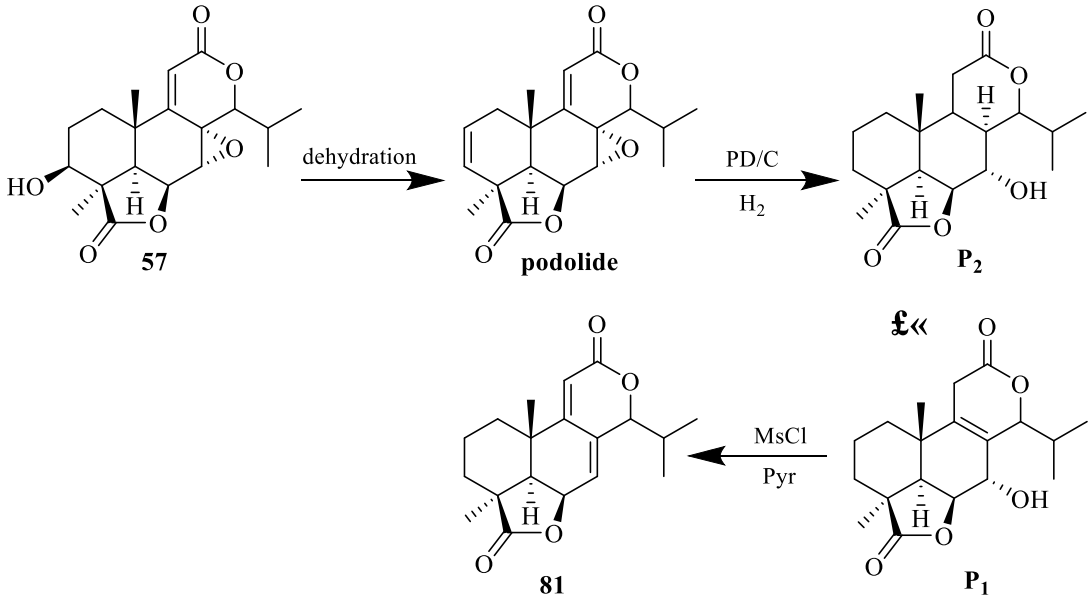


Figure 3.1. Transformation from B-type skeleton to C-type skeleton

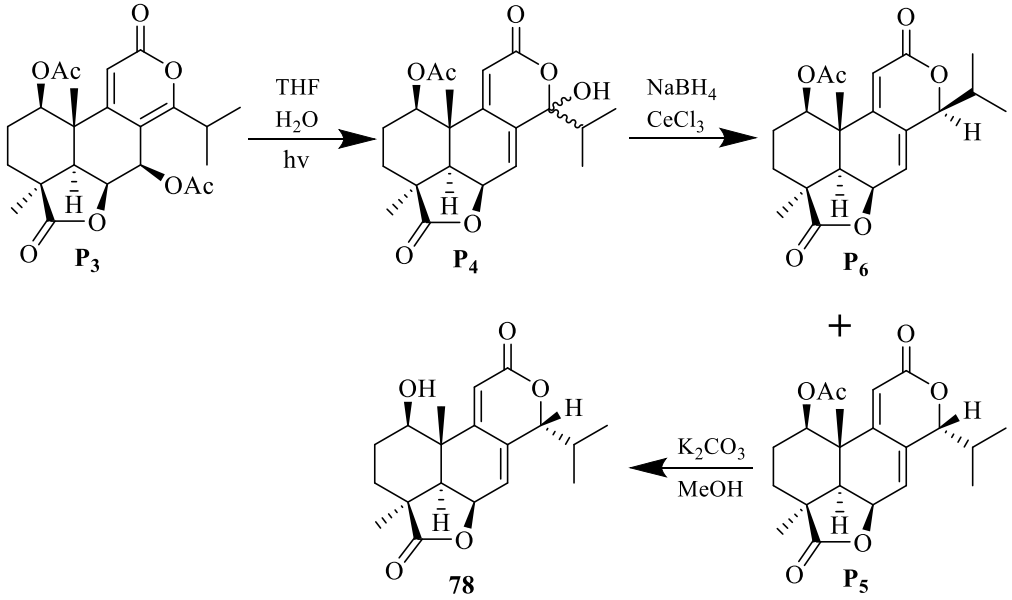


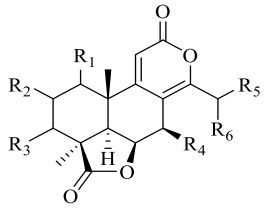
Figure 3.2. Transformation from A-type skeleton to C-type skeleton

Table 2. Diterpenoid dilactones from the *Nageia* genus

No.	Compound name	Molecular formula	Relative molecular mass	Source	Ref.
1	Nagilactone K	$C_{18}H_{22}O_7$	350	N-L, N-Se	[11, 14]
2	1*β*-hydroxy-nagilactone K	$C_{18}H_{22}O_7$	350	N-Se	[10]
3	Nagilactone L	$C_{18}H_{22}O_5$	318	N-L, N-Se	[11, 14]
4	3*β*-hydroxynagilactone L	$C_{18}H_{22}O_6$	334	N-L, N-Se	[11, 14]
5	2*β*-hydroxynagilactone L	$C_{18}H_{22}O_6$	334	N-L, N-Se	[11, 14]
6	2*α*,3*β*,15-trihydroxy-nagilactone L	$C_{18}H_{22}O_8$	366	N-Se	[14]
7	1α-chloro-2*β*,3*β*,15-trihydroxynagilactone L	$C_{18}H_{21}O_7Cl$	384	N-Se	[11]
8	1-chloro-2*β*-hydroxynagilactone D	$C_{18}H_{21}O_5Cl$	352	N-Se	[11]
9	15-hydroxynagilactone L	$C_{18}H_{22}O_6$	334	N-L, N-Se	[11, 14]
10	7*β*-hydroxynagilactone D	$C_{18}H_{20}O_7$	348	N-L, N-Se	[11, 14]
11	3-epi-15-hydroxynagilactone D	$C_{18}H_{20}O_7$	348	N-L, N-Se	[11, 14]
12	Nagilactone A	$C_{19}H_{24}O_6$	348	N-Se, N-L	[14, 15]
13	1-deoxy-2*β*, 3*β*-epoxynagilactone A	$C_{19}H_{22}O_6$	346	N-Se	[13]
14	1-deoxy-2*α*-hydroxynagilactone A	$C_{19}H_{24}O_6$	348	N-Se	[13]
15	1-deoxy-3*α*-hydroxynagilactone A	$C_{19}H_{24}O_6$	348	N-T	[15]
16	1-deoxy-3*α*-O-*β*-D-glucopyranosylnagilactone A	$C_{25}H_{34}O_{11}$	510	N-T	[15]
17	1-deoxy-3*β*-O-*β*-D-glucopyranosylnagilactone A	$C_{25}H_{34}O_{11}$	510	N-FT	[16]
18	1-deoxy-2*β*-O-*β*-D-glucopyranosylnagilactone A	$C_{25}H_{34}O_{11}$	510	N-T	[15]
19	1-deoxy-2*β*-hydroxynagilactone A	$C_{19}H_{24}O_6$	348	N-Se, N-T	[14,15]
20	1, 7-deoxy-2*β*-nagilactone A	$C_{18}H_{20}O_6$	332	N-T	[15]
21	Nagilactoside A	$C_{25}H_{34}O_{11}$	510	N-Se, N-T	[13, 15]
22	3*β*-hydroxynagilactone A	$C_{19}H_{24}O_7$	364	W-L, N-T	[12, 15]
23	Nagilactone B	$C_{19}H_{24}O_7$	364	N-Se	[14]
24	2-epinagilactone B	$C_{19}H_{24}O_7$	364	N-Se	[17]
25	Nagilactoside B	$C_{25}H_{34}O_{12}$	526	N-Se	[17]
26	1-deoxynagilactone A	$C_{19}H_{24}O_5$	332	N-Rb	[18]
27	3-epinagilactone C	$C_{19}H_{22}O_7$	362	N-L	[19]
28	Nagilactone C	$C_{19}H_{22}O_7$	362	N-T	[11]
29	Nagilactoside C	$C_{31}H_{44}O_{16}$	672	N-Se	[21]
30	3-deoxynagilactone C	$C_{19}H_{22}O_6$	346	N-T, N-L	[15, 23]
31	Sellowin C	$C_{19}H_{24}O_6$	348	N-T	[15]
32	Nagilactone D	$C_{18}H_{20}O_6$	332	N-Se, N-T	[14,15]
33	Nagilactoside D	$C_{31}H_{44}O_{16}$	672	N-Se	[21]
34	Nagilactoside E	$C_{31}H_{44}O_{16}$	672	N-Se	[21]
35	3-epinagilactone D	$C_{18}H_{20}O_6$	332	N-T, N-Se	[11, 14]
36	15-hydroxy-nagilactone D	$C_{18}H_{20}O_7$	348	N-Se	[10]
37	15-methoxynagilactone D	$C_{19}H_{22}O_7$	362	N-L	[19]
38	15R-methoxycarbonylnagilactone D	$C_{20}H_{22}O_8$	390	N-Se	[22]
39	15S-methoxycarbonylnagilactone D	$C_{20}H_{22}O_8$	390	N-Se	[22]
40	1*α*-hydroxyurbalactone	$C_{19}H_{24}O_8$	380	N-T	[15]
41	1*β*-hydroxyurbalactone	$C_{19}H_{24}O_8$	380	N-T	[16]
42	3*β*-hydroxy-7-deoxy-17-nor-nagilactone	$C_{18}H_{22}O_7$	350	N-T	[15]
43	Urbalactone	$C_{19}H_{24}O_7$	364	N-T	[15]
44	Nagilactoside F	$C_{37}H_{54}O_{21}$	834	N-FT	[16]
45	Nagilactoside G	$C_{37}H_{54}O_{21}$	834	N-FT	[24]
46	Nagilactone N3 3-O-*β*-D-glucoside	$C_{25}H_{34}O_{13}$	542	N-Se	[17]
47	1-deoxy-2*β*, 16-dihydroxynagilactone A	$C_{19}H_{24}O_7$	364	N-T	[15]
48	1-deoxy-3*β*, 16-dihydroxynagilactone A	$C_{19}H_{24}O_7$	364	N-T	[15]
49	1-deoxy-2,3-dehydronagilactone A	$C_{19}H_{22}O_5$	330	N-Rb	[18]

50	2,3-dehydronagilactone A	$C_{19}H_{22}O_6$	346	N-Rb	[18]
51	Nagilactone Z1	$C_{19}H_{22}O_7$	362	N-T	[15]
52	Nagilactone Z2	$C_{18}H_{18}O_6$	330	N-T	[15]
53	10, 20-isopropylidene-nagilactone B	$C_{22}H_{28}O_7$	404	N-T	[15]
54	2-oxonagilactone A	$C_{19}H_{22}O_7$	362	N-L, N-Se	[11, 14]
55	1-deoxy-1, 2-dehydro-3 *α*-hyrdoxynagilactone A	$C_{19}H_{22}O_6$	346	N-T	[15]
56	1-deoxy-2,3-dehydro-3α-O-*β*-D-glucopyranosylna-gilactone A	$C_{25}H_{32}O_{11}$	508	N-T	[15]
57	Nagilactone E	$C_{19}H_{24}O_6$	348	N-Se, N-T	[14,15]
58	3-deoxy-2*α*-hydroxynagilactone E	$C_{19}H_{24}O_6$	348	N-L	[19]
59	3-deoxy-2*β*-hydroxynagilactone E	$C_{19}H_{24}O_6$	348	N-T	[15]
60	3-deoxy-2*β*,16-dihydroxynagilactone E	$C_{19}H_{24}O_7$	364	N-FT, N-T	[16, 27]
61	16-O-*β*-D-glucopyranosylnagilactone E	$C_{25}H_{35}O_{12}$	527	N-T	[27]
62	16-hydroxynagilactone E	$C_{19}H_{24}O_7$	364	N-T	[27]
63	Nagilactone G	$C_{19}H_{24}O_5$	332	N-L, N-Se	[11, 14]
64	3-O-β-D-glucopyranosyl-16-hydroxynagilactone G	$C_{25}H_{35}O_{12}$	527	N-T	[27]
65	3-O-β-D-glucopyranosylnagilactone G	$C_{25}H_{34}O_{11}$	510	N-T	[27]
66	2,3-*β*-epoxy-16-O-*β*-D-glucopyranosylnagilactone G	$C_{25}H_{33}O_{12}$	525	N-T	[27]
67	Sellowin A	$C_{19}H_{22}O_7$	362	N-T	[27]
68	16-O-*β*-D-glucopyranosylnagilactone G	$C_{25}H_{34}O_{11}$	510	N-T	[27]
69	2,3-*β*-epoxy-podolide	$C_{19}H_{22}O_8$	378	N-T	[10]
70	2,3-dihydro-16-hydroxy-podolide	$C_{19}H_{24}O_6$	348	N-T	[10]
71	2,3-dehydro-16-O-*β*-D-glucopyranosylnagilactone G	$C_{25}H_{32}O_{11}$	508	N-T	[27]
72	16-hydroxypodolide	$C_{19}H_{22}O_6$	346	N-T	[28]
73	Podolactone A	$C_{21}H_{26}O_5$	358	N-T	[10]
74	Podolactone D	$C_{20}H_{24}O_7S$	408	N-T	[10]
75	2,3-dehydro-16-O-*β*-D-glucopyranosylnagilactone F	$C_{25}H_{32}O_{10}$	492	N-T	[15]
76	2,3-dehydro-16-hydroxynagilactone F	$C_{19}H_{22}O_5$	330	N-Rb	[28]
77	2*α*-hydroxynagilactone F	$C_{19}H_{24}O_5$	332	N-Rb	[29]
78	1*β*-hydroxynagilactone F	$C_{19}H_{24}O_5$	332	N-Rb	[20]
79	2*β*-hydroxynagilactone F	$C_{19}H_{24}O_5$	332	N-T	[15]
80	2*β*, 16-dihydroxynagilactone F	$C_{19}H_{24}O_6$	348	N-T	[15]
81	Nagilactone F	$C_{19}H_{24}O_4$	316	W-TL	[30]
82	3-hydroxynagilactone F	$C_{19}H_{24}O_5$	332	N-Rb	[28]
83	Nagilactone I	$C_{20}H_{24}O_7$	376	N-FT	[16]
84	(3aS,5aR,7S,10bS,10cR)-7-[2-(*β*-D-glucopyranosyloxy)-1-methylethyl]-1,2,3,3a,5a,7,10b,10c-octahydro-3a,10b-dimethyl-4H,9H-furo[2',3',4':4,5]naphtho[2,1-c]pyran-4,9-dione	$C_{25}H_{34}O_{10}$	494	N-FT	[16]
85	Nagilactone J	$C_{18}H_{22}O_7$	350	N-Sb	[25]
86	Fleuryilactone	$C_{18}H_{24}O_6$	336	F-TL	[26]

N: *Nageia nagi*, W: *N. wallichiana*, F: *N. fleuryi*, Se: Seed, L: Leaf, Sr: Seed coat, E: Endosperm, T: Twig, TL: Twig and leaf, Rb: Root bark, FT: Fruit-twig mixture, B: Bark, Sb: Stem-bark, A: Aboveground, the same below.



1 R_1=*α*-OH,R_2=*β*-OH,R_3=*β*-OH,R_4=H,R_5=CH_3,R_6=H
2 R_1=*β*-OH,R_2=*β*-OH,R_3=*β*-OH,R_4=H,R_5=CH_3,R_6=H
3 R_1=*β*-OH,R_2=H,R_3=H,R_4=H,R_5=CH_3,R_6=H
4 R_1=*β*-OH,R_2=H,R_3=*β*-OH,R_4=H,R_5=CH_3,R_6=H
5 R_1=*β*-OH,R_2=*β*-OH,R_3=H,R_4=H,R_5=CH_3,R_6=H
6 R_1=*β*-OH,R_2=*α*-OH,R_3=*β*-OH,R_4=H,R_5=CH_3,R_6=OH
7 R_1=*α*-Cl,R_2=*β*-OH,R_3=*β*-OH,R_4=H,R_5=CH_3,R_6=OH
8 R_1=Cl,R_2=*β*-OH,R_3=H,R_4=H,R_5=CH_3,R_6=H
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13 R_1=H,R_2=*β*-epoxide,R_3=*β*-epoxide,R_4=OH,R_5=CH_3,R_6=CH_3
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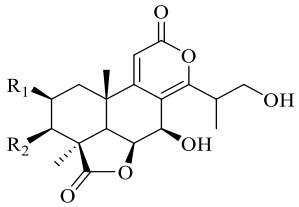
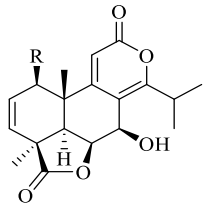
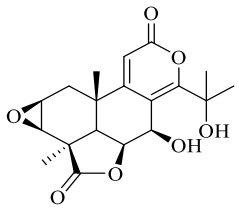
23 R_1=*β*-OH,R_2=*β*-OH,R_3= H,R_4=OH,R_5=CH_3,R_6=CH_3
24 R_1=*β*-OH,R_2=*β*-OH,R_3= H,R_4=OH,R_5=CH_3,R_6=CH_3
25 R_1=*β*-O-*β*-D-Glc,R_2=*β*-OH,R_3= H,R_4=OH,R_5=CH_3,R_6=CH_3
26 R_1=H,R_2=H,R_3=H,R_4=OH,R_5=CH_3,R_6=CH_3
27 R_1=*β*-epoxide,R_2=*β*-epoxide,R_3=*α*-OH,R_4=OH,R_5=CH_3,R_6=CH_3
28 R_1=*β*-epoxide,R_2=*β*-epoxide,R_3=*β*-OH,R_4=OH,R_5=CH_3,R_6=CH_3
29 R_1=H,R_2=*β*-D-glc-(1→3)-*β*-D-glc-,R_3=H,R_4=OH,R_5=CH_3,R_6=CH_3
30 R_1=*β*-epoxide,R_2=*β*-epoxide,R_3= H,R_4=OH,R_5=CH_3,R_6=CH_3
31 R_1=H,R_2=H,R_3=*β*-OH,R_4=OH,R_5=CH_3,R_6=CH_3
32 R_1=*β*-epoxide,R_2=*β*-epoxide,R_3=*β*-OH,R_4=H,R_5=H,R_6=CH_3
33 R_1=H,R_2=*β*-D-glc-(1→6)-*β*-D-glc-,R_3= H,R_4=OH,R_5=CH_3,R_6=CH_3
34 R_1=*β*-D-glc-(1→6)-*β*-D-glc-,R_2=H,R_3=H,R_4=OH,R_5=CH_3,R_6=CH_3
35 R_1=*β*-epoxide,R_2=*β*-epoxide,R_3=*α*-OH,R_4=H,R_5=H,R_6=CH_3
36 R_1=*β*-epoxide,R_2=*β*-epoxide,R_3=*β*-OH,R_4=H,R_5=CH_3,R_6=OH
37 R_1=*β*-epoxide,R_2=*β*-epoxide,R_3=*β*-OH,R_4=H,R_5=CH_3,R_6=OCH_3
38 R_1=*β*-epoxide,R_2=*β*-epoxide,R_3=*β*-OH,R_4=H,R_5=CH_3,R_6=OCH_3(C=O),(15*S*)
39 R_1=*β*-epoxide,R_2=*β*-epoxide,R_3=*β*-OH,R_4=H,R_5=CH_3,R_6=OCH_3(C=O),(15*R*)
40 R_1=*α*-OH,R_2=*β*-OH,R_3=*β*-OH,R_4=OH,R_5=CH_3,R_6=CH_3
41 R_1=*β*-OH,R_2=*β*-OH,R_3=*β*-OH,R_4=OH,R_5=CH_3,R_6=CH_3
42 R_1=*β*-OH,R_2=*β*-OH,R_3=*β*-OH,R_4=H,R_5=CH_3,R_6=H
43 R_1=H,R_2=*β*-OH,R_3=*β*-OH,R_4=OH,R_5=CH_3,R_6=CH_3
44 R_1=H,R_2=*β*-D-glc-(1→3)-*β*-D-glc-(1→6)-*β*-D-glc-,R_3=H,R_4=OH,R_5=CH_3,R_6=CH_3
45 R_1=H,R_2=*β*-D-glc-(1→6)-*β*-D-glc-(1→3)-*β*-D-glc-,R_3=H,R_4=OH,R_5=CH_3,R_6=CH_3
46 R_1=*β*-OH,R_2=*β*-OH,R_3=*β*-O-*β*-D-Glc,,R_4=OH,R_5=CH_3,R_6=CH_3



47 R_1=OH,R_2=H
48 R_1=H,R_2=OH



49 R=H
50 R=OH



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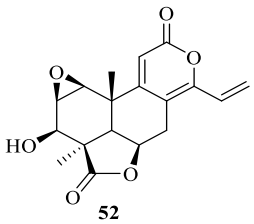

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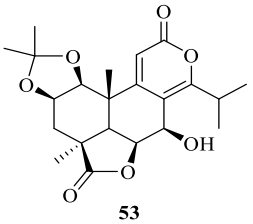

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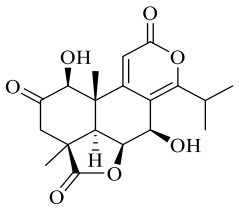

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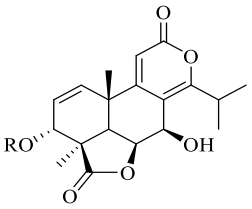


55 R=H
56 R=Glc

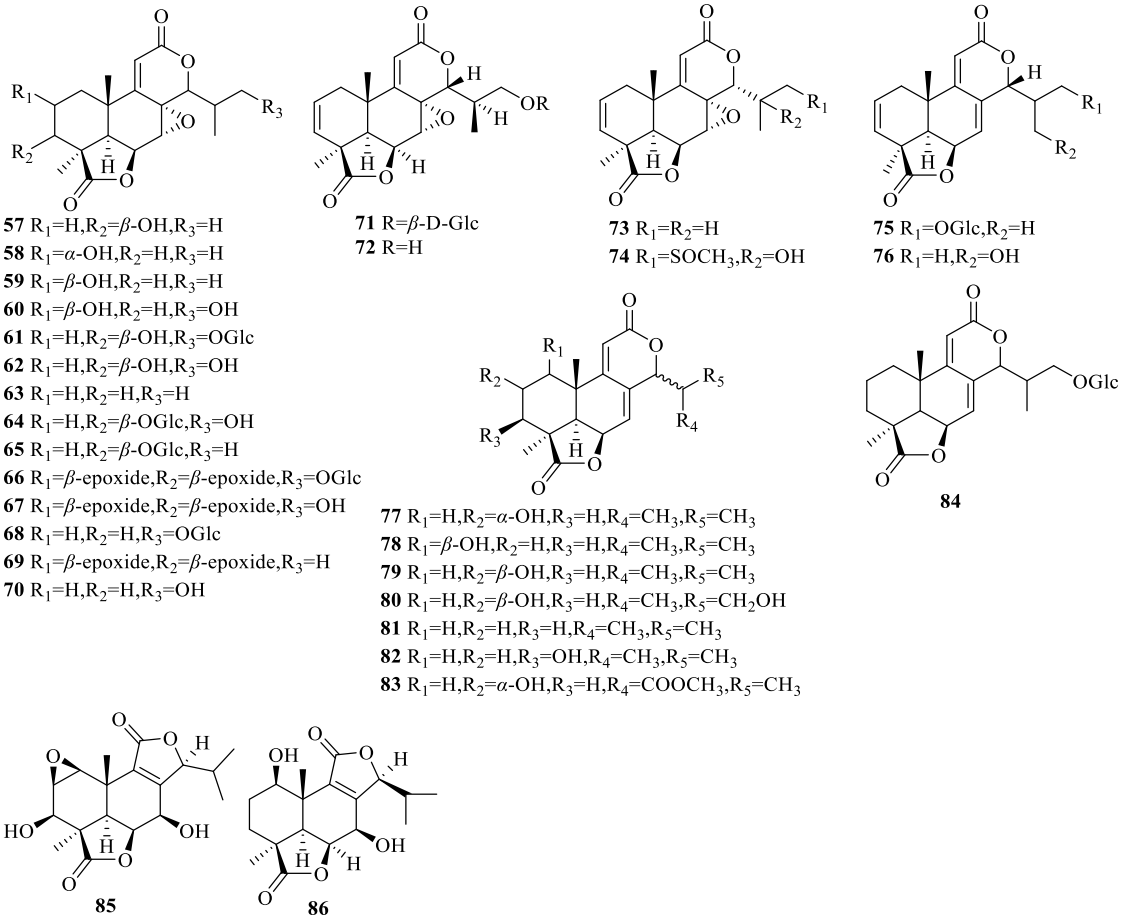


Figure 4. Chemical structures of the diterpenoid dilactones in *Nageia*

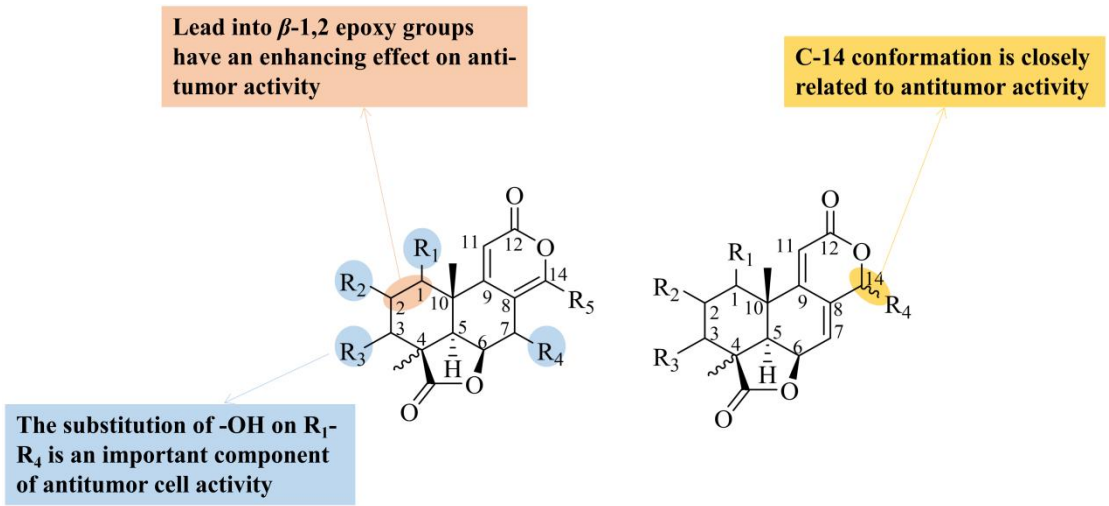


Figure 5. Structure-activity relationship of compounds against tumors

Diterpenoid dilactones have numerous pharmacological activities, including anti-tumor, anti-inflammatory, anti–pulmonary fibrosis, and plant growth–regulation effects. Several diterpenoid dilactones show potent anticancer activity against different cancer cell lines and tumor models. Hayashi [43] studied the cytotoxic activity of diterpenoid dilactones isolated from *N. nagi* against Yoshida sarcoma cells *in vitro*. The 50% inhibitory concentrations (IC_{50}s) of the type A diterpenoid dilactones **32**, **12**, and **2** were 3.32, 32, and 305×10^{-4} mM, respectively. The compounds exhibited hydroxyl substitutions at positions 1, 2, and 3, suggesting an inverse relationship between the amount of hydroxyl substitutions and anti-tumor efficacy. Compound **28**, also a type A diterpenoid dilactone, has two hydroxyl substitutions; introducing of a *β*-1,2-epoxy group slightly enhances the activity with an IC_{50} of 22.5×10^{-4} mM compared to compound **12**. The type C diterpenoid dilactone compound **81**, which lacks hydroxyl substitutions, exhibits the strongest activity with an IC_{50} of 1.7×10^{-4} mM. When its 14-C configuration is changed from *α* to *β*, the activity decreases, indicating a close relationship between the 14-C conformation and activity. Xu Yaming [13] found that compounds **12**-**14** had strong inhibitory effects on P_{388} leukemia cells, with inhibition rates reaching 73%, 88.5%, and 97.4%, respectively, at a dose of 10 μg/mL doses. However, the diterpenoid dilactone glycoside **21** and the acylated derivative of compound **14** showed no inhibitory effect on P_{388}, suggesting that the hydroxyl groups of diterpenoid dilactones lose their activity when glycosylated or acylated. They also evaluated the cytotoxicity of two new diterpenoid dilactones (**25** and **31**) isolated from *N. nagi* seeds [44]. The findings demonstrated that compound **31** effectively suppressed the proliferation of P_{388} leukemia cells *in vitro*, with an inhibition rate of 61.8% at a 10 μg/mL dosage. Conversely, compound **25** did not exhibit any inhibitory effects. Once again, this highlights the importance of hydroxyl substitutions in influencing the effectiveness of diterpenoid dilactones. Hui Shan [45] discovered that compound **60** present in *N. nagi* can inhibit the growth of MDA-MB-231 and MDA-MB-468 breast cancer cells with overactivated STAT3 and induce apoptosis. Le-Le Zhang [46] found that compound **57** could inhibit the proliferation of non-small cell lung cancer A549 and NCI-H1975 cells, with IC_{50}s of 5.18 and 3.57 μmol/L, respectively. Lin Ligen [14] discovered that compound **57** has a significant inhibitory effect on the growth of various cancer cell lines, including human lung cancer (A549), ovarian cancer (A2780), liver cancer (HepG2), breast cancer (MCF-7), gastric cancer (SGC7901), and melanoma (A375), with IC_{50}s ranging from 1.07 to 6.58 μmol/L.

Ao Li [47] conducted SBE luciferase reporter experiments using compound **32** isolated from *N. nag* and found that it inhibited the expression of TβR I and the activation of Smad 2, thereby inhibiting the synthesis of fibrotic markers and the transformation of fibroblasts into myofibroblasts. These findings suggest its potential in treating pulmonary fibrosis. Lu Jinjian [48] found that the extracts from the *Nageia* genus, including the ethyl acetate and n-butanol extracts, and diterpenoid dilactones having A, B, and C structures (**23**, **32**, **53**, **63**, **83**) could effectively improve the morphological changes and marker alterations in a cell model of TGF-β1–induced lung fibrosis. These compounds demonstrated significant anti–pulmonary fibrosis activity. In the context of anti-inflammatory activity, Ye Yang [49] discovered that several diterpenoid dilactones could significantly enhance the uptake of low-density lipoproteins (LDLs) at a concentration of 5 μmol/L, with the highest enhancement reaching 161% to 180%. Compounds **12**, **14**, and **23** also significantly increased LDLR gene expression, with 2-fold, 4.5-fold, and 3-fold increases, respectively, compared with that in the control group. Their effects were superior to the drug pravastatin. Yuzhou Gui [50] discovered that compound **23**, obtained from the root bark, can hinder the development of atherosclerosis in ApoE-deficient mice by enhancing the removal of cholesterol from macrophages. It significantly enhanced cholesterol efflux at concentrations of 0.02, 0.1, and 0.5 μmol/L, with maximum increases of 5.72-fold ($P<0.05$) and 2.34-fold ($P<0.01$). Concerning plant-growth regulation, Isao Kubo [51] assessed the effects of eight nagi lactones isolated from *N. nagi* on the root growth of lettuce seedlings and found that compounds **12**, **13**, **14**, **23**, **28**, and **37** stimulated the development of lettuce seedling roots at concentrations below 10 μg/mL. However, at concentrations of 100 μg/mL and higher, they completely inhibited the germination of lettuce seeds. Compounds **32** and **57** exhibited weak stimulatory effects at low concentrations (5.5 and 3.5 μg/mL, respectively) but showed significant inhibitory effects on root growth with increasing concentrations. Compound **32** was the most potent and completely inhibited the germination of lettuce seeds at 10 μg/mL. Isao Kubo [16] discovered that the combined usage of compounds **57** and **153**, each at doses of 0.1 and 3 μg/mL, resulted in a 48%

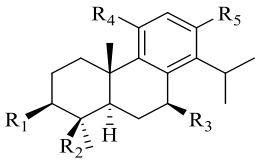
and 52% increase in the length of rice seedlings, respectively. This increase was compared to the individual application of only 0.1 µg/mL and 1 µg/mL of compound **57**.

2.1.2. Totarane Diterpenoids

Compounds **87**-**93** belong to the category of totarane diterpenoids (Table 3 and Figure 6). Compounds **91** and compounds **88**-**92** are generally representative of the compounds described. These compounds demonstrate potent antioxidant activity and protect against oxidative stressors in biological systems. Compound **90** shows significant antibacterial activity against gram-positive bacteria, but its activity decreases significantly when an additional hydroxyl group is added at the C-3 position to transform it into compound **88**.

Table 3. Totarane diterpenoids from the genus *Nageia*

No.	Compound name	Molecular formula	Relative molecular mass	Source	Ref.
87	Inumakiol D	$C_{20}H_{28}O_4$	332	F-A	[33]
88	Totaradiol	$C_{20}H_{30}O_2$	302	F-A, N-Rb	[33, 34]
89	19-hydroxytotarol	$C_{20}H_{30}O_2$	302	F-A, N-Rb	[33, 34]
90	Totarol	$C_{20}H_{30}O$	286	N-Rb	[34]
91	Totaral	$C_{20}H_{28}O_2$	300	N-Rb	[34]
92	4*β*-carboxy-19-nortotarol	$C_{20}H_{28}O_3$	316	N-Rb	[34]
93	Inumakoic acid	$C_{20}H_{28}O_3$	316	F-T	[35]



87 R_1=H,R_2=COOH,R_3=OH,R_4=H,R_5=OH
88 R_1=OH,R_2=CH_3,R_3=H,R_4=H,R_5=OH
89 R_1=H,R_2=CH_2OH,R_3=H,R_4=H,R_5=OH
90 R_1=H,R_2=CH3,R_3=H,R_4=H,R_5=OH
91 R_1=H,R_2=CHO,R_3=H,R_4=H,R_5=OH
92 R_1=H,R_2=COOH,R_3=H,R_4=H,R_5=OH
93 R_1=H,R_2=COOH,R_3=H,R_4=OH,R_5=H

Figure 6. Chemical structures of totarane diterpenoids in *Nageia*

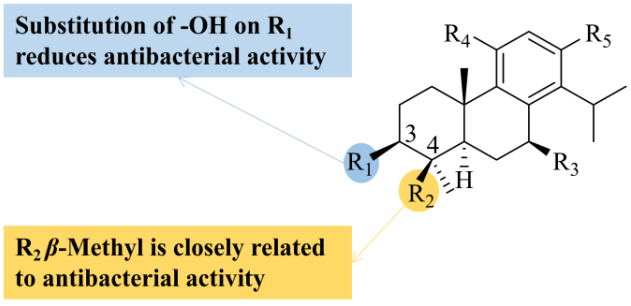


Figure 7. Structure-activity relationship related to antifungal activity

The pharmacological activities of totarane diterpenoids found in the *Nageia* genus, primarily include antibacterial and antioxidant effects. Isao Kubo [52] evaluated the antibacterial activity of totarane diterpenoids (**88**-**92**) isolated from *N. nagi* bark at 400 μg/mL concentration against 12 selected microorganisms. Compound **90** exhibited higher antibacterial activity against all tested gram-positive bacteria, with *Propionibacterium acnes* being the most sensitive and having minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) values of 0.39 and 0.78 μg/mL, respectively. The MIC and MBC values for other gram-positive bacteria ranged from 0.78 to 1.56 μg/mL and 0.78 to 6.25 μg/mL, respectively. In contrast, the structurally similar compound **88** had much lower antibacterial potency with MIC values ranging from 25 to 200 μg/mL, indicating a decrease in activity when a hydroxyl group was added to C-3 to obtain compound **88** from compound **90**. The three other structurally similar compounds **89**, **91**, and **92** showed no antibacterial activity. This suggests that the activity was lost entirely when the β-CH_3 at position C-4 of compound **90** was oxidized at the tested concentration of 400 μg/mL. H. Haraguchi [34] found that totarane diterpenoids from *N. nagi* exhibited strong antioxidant activity. Compounds **88**-**92** could inhibit Fe(III)-ADP/NADPH–induced microsomal lipid peroxidation (IC_{50}s ranging from 4.79 to 31.24 μmol/L), Fe(III)-ADP/NADH–induced mitochondrial lipid peroxidation (IC_{50}s ranging from 0.43 to 2.66 μmol/L), and autoxidation of linoleic acid (IC_{50}s ranging from 6.98 to 24.88 μmol/L).

2.1.3. Abietane Diterpenoids

Abietane diterpenoids, including compounds **94**-**112**, are presented in Table 4 and Figure 8. Compound **94** is derived from compound **98** by oxidation of the methyl group at C-16 to a hydroxymethyl group. Compounds **104**-**107** have a carbonyl carbon substituting the methylene group at C-7. Compound **104** demonstrates excellent antioxidant properties, effectively suppressing the oxidation of lipids in both microsomes and mitochondria, as well as the auto-oxidation of linoleic acid. Compounds **108** and **109** are mono-deacetyl diterpenoids, with the isopropyl group at C-13 that an acetyl group has replaced.

Table 4. Abietane diterpenoids from the genus *Nageia*

No.	Compound name	Molecular formula	Relative molecular mass	Source	Ref.
94	Fleuryinol A	$C_{20}H_{30}O_3$	318	F-TL	[36]
95	Fleuryinol B	$C_{20}H_{30}O_2$	302	F-TL	[36]
96	Fleuryinol C	$C_{20}H_{30}O_3$	318	F-TL	[36]
97	19-hydroxyferruginol	$C_{20}H_{30}O_2$	302	F-TL	[36]
98	Lambertic acid	$C_{20}H_{28}O_3$	316	F-T	[35]
99	16-hydroxylambertic acid	$C_{20}H_{28}O_4$	332	N-Se	[37]
100	Ferruginol	$C_{20}H_{30}O$	286	N-L	[23]
101	2,3-dihydroxyferruginol	$C_{20}H_{30}O_3$	318	N-L	[38]
102	1β,16-dihydroxylambertic acid	$C_{20}H_{28}O_5$	348	N-T	[39]
103	3β,16-dihydroxylambertic acid	$C_{20}H_{28}O_5$	348	N-T	[39]
104	Sugiol	$C_{20}H_{28}O_2$	300	F-TL, N-L, W-L	[53, 38, 40]
105	Demethylcryptojaponol	$C_{20}H_{28}O_3$	316	F-Re	[41]
106	7-oxo-18-hydroxyferruginol	$C_{20}H_{28}O_3$	316	N-Se	[37]
107	Taiwanin F-12-O-β-D-glucopyranoside	$C_{26}H_{38}O_9$	494	F-Re	[41]
108	Nagiditerpenoid A	$C_{19}H_{26}O_4$	318	N-L	[23]
109	Nagiol A	$C_{19}H_{26}O_4$	318	N-L	[38]
110	5α,12-dihydroxy-6-oxa-abieta-8,11,13-trien-7-one	$C_{19}H_{26}O_4$	318	N-Se	[37]
111	12,15-di-O-acetylhypargenin B	$C_{24}H_{32}O_5$	400	F-Re	[41]
112	Liquiditerpenoic acid B	$C_{20}H_{28}O_3$	316	F-Re	[41]

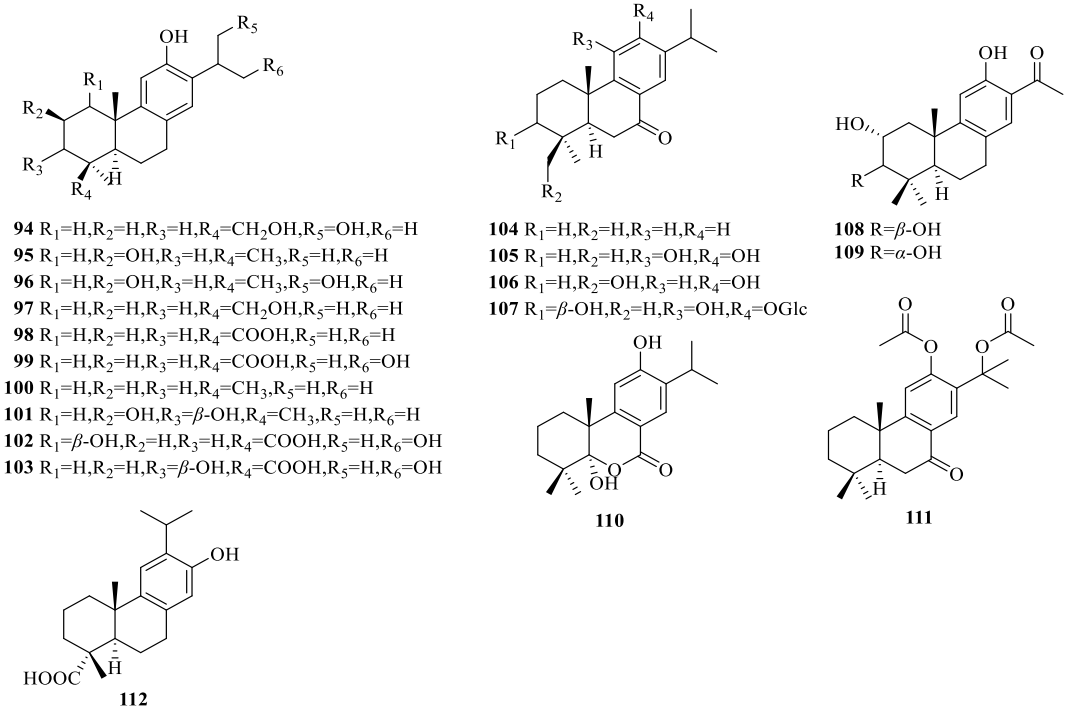


Figure 8. Chemical structures of the abietane diterpenoids in *Nageia*

2.1.4 Pimarane Diterpenoids

Compounds **113**-**116** belong to the group of pimarane diterpenoids (Table 5 and Figure 9). Compounds **113** and **114** are isopimarane diterpenoids. Compound **113** is distinguished from compound **114** by the presence of a ketone group at C-15, substituting the hydroxyl group.

Table 5. Pimarane diterpenoids from the genus *Nageia*

No.	Compound name	Molecular formula	Relative molecular mass	Source	Ref.
113	Ent-2*β*,15,16,18-tetrahydroxypimar-8(14)-ene	$C_{20}H_{34}O_4$	338	N-T	[39]
114	Ent-15-oxo-2*β*,16,18-trihydroxypimar-8(14)-ene	$C_{20}H_{32}O_4$	336	N-T	[39]
115	4*β*-hydroxyl-4(20→5),10(18→9)abeo-pimar-15(16)-ene	$C_{20}H_{34}O$	290	F-T	[35]
116	Rearranged pimarane-type diterpene alcohol	$C_{21}H_{36}O$	304	F-T	[42]

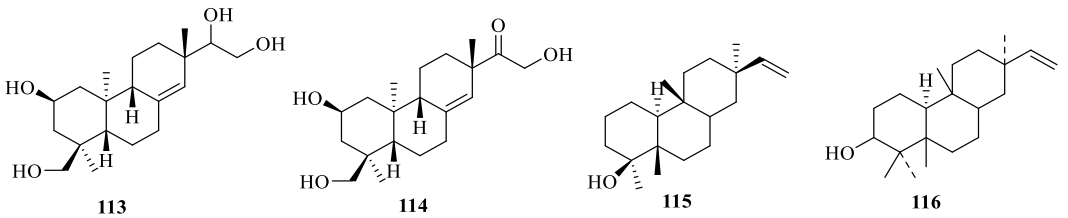


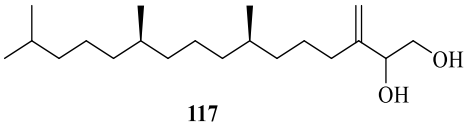
Figure 9. Chemical structures of the pimarane diterpenoids in *Nageia*

2.1.5 Phytane diterpenoids

Compound **117** is a phytane diterpenoid isolated from *N. nagi* leaves.

Table 6. Phytane diterpenoids from the genus *Nageia*

No.	Compound name	Molecular formula	Relative molecular mass	Source	Ref.
117	4,15-dimethyl-2-(1,2-dihydroxy ethyl)-hexadecene	$C_{20}H_{40}O_2$	312	N-L	[23]



117

Figure 10. Chemical structures of the phytane diterpenoid in *Nageia*

2.2. Sesquiterpenoids

A total of 30 sesquiterpenoids have been extracted from plants belonging to the *Nageia* genus. These compounds include various structural types, such as 9 compounds of the aromadendrane type (**118**-**126**), 4 compounds of the eudesmane type (**127**-**130**), 2 compounds of the guaiane type (**131**-**132**), 2 compounds of the maaliane type (**133**-**134**), 2 compounds of the caryolane type (**135**-**136**), 1 compound of the cadinane type (**137**), 8 compounds of the ionone type (**138**-**145**), 1 compound of the spirolaurane type (**146**), and 1 compound of the alloaromadendrane type (**147**) (Table 7 and Figure 11). Among these, aromadendrane-type compounds are the most abundant sesquiterpenoids isolated from *Nageia* genus plants. They possess a basic carbon skeleton consisting of a pentacyclic ring and a tricyclic ring, with four methyl groups attached to the C-4, C-10, and C-11 positions. Compounds **118**-**124** have been isolated from *N. nagi*. Compounds **118**-**123** were first isolated from this species in 2015, whereas compound **124** was first isolated from the same species in 2018.

Table 7. Sesquiterpenes from the genus *Nageia*

No.	Compound name	Molecular formula	Relative molecular mass	Source	Ref.
118	Ent-4*β*-Hydroxy-10*α*-methoxyaromadendrane	$C_{15}H_{28}O$	224	N-L	[23]
119	4*α*-10*β*-alloaromadendramediol-10-methyether	$C_{16}H_{28}O_2$	252	N-L	[23]
120	Alloaromadendrane-4*β*,10*α*-diol	$C_{15}H_{26}O_2$	238	N-L	[23]
121	Aromadendrane-4*β*,10*β*-diol	$C_{15}H_{26}O_2$	238	N-L	[23]
122	D-aromadendrane-4*β*,10*α*-diol	$C_{15}H_{26}O_2$	238	N-L	[23]
123	Aromadend-4*β*-10*β*-diol	$C_{15}H_{26}O_2$	238	N-L	[23]
124	4*β*,10*β*,15-trihydroxy-aromadendrane-10,15-acetonide	$C_{18}H_{30}O_3$	294	N-TL	[55]
125	Aromadendrane-4*β*,10*β*-diol	$C_{15}H_{26}O_2$	238	F-L	[42]
126	(-)-4*α*,7*α*-aromadendranedol	$C_{15}H_{26}O_2$	238	F-A	[33]
127	1*β*-11-dihydroxy-5-eudesmane	$C_{15}H_{26}O_2$	238	N-L	[23]
128	6-eudesmene-1,4-diol	$C_{15}H_{26}O_2$	238	F-A	[33]
129	Arctiol	$C_{15}H_{26}O_2$	238	F-L	[59]
130	1*β*,6*α*-dihydroxy-4(14)-eudesmene	$C_{15}H_{26}O_2$	238	F-L	[42]
131	Guaianediol	$C_{15}H_{26}O_2$	238	N-L	[23]
132	4*β*,10*β*-dihydroxy-1αH,5*β*H-guaia-6-ene	$C_{15}H_{26}O_2$	238	N-L	[23]
133	(1S,4S,5S,6R,7R,10S)-1,4-dihydroxymaaliane	$C_{15}H_{26}O_2$	238	N-L	[23]
134	(+)-Alloaromadendrane-4*β*	$C_{15}H_{26}O_2$	238	N-L	[23]
135	Caryolane-1,9*β*-diol	$C_{15}H_{26}O_2$	238	F-L	[42]
136	9*α*-hydroxy-1*β*-methoxycaryolanol	$C_{16}H_{28}O_2$	252	F-L	[42]
137	1,4-peroxyaurol-ene	$C_{15}H_{24}O_2$	236	N-L	[23]
138	Blumenol B	$C_{13}H_{22}O_3$	226	W-TL	[30]
139	(3R,6R,7E)-3-hydroxymegastigma-4,7-dien-9-one	$C_{13}H_{20}O_2$	208	F-L	[56]

140	Vomifoliol	$C_{13}H_{20}O_3$	224	W-L	[12]
141	Dehydrovomifoliol	$C_{13}H_{18}O_3$	222	F-L	[56]
142	(3R,9R)-3,9-dihydroxymegastigm-5-en-4-one	$C_{13}H_{22}O_3$	226	N-L	[23]
143	4-megastigmen-3,9-dione	$C_{13}H_{20}O_2$	208	F-T	[42]
144	Megastigm-5-en-3,9-diol	$C_{13}H_{24}O_2$	212	N-L	[23]
145	Roseoside	$C_{19}H_{30}O_8$	386	F-T	[42]
146	3,4-dehydrotheaspirone	$C_{13}H_{18}O_2$	206	W-TL	[30]
147	Lochmolin F	$C_{17}H_{28}O_2$	264	N-L	[23]

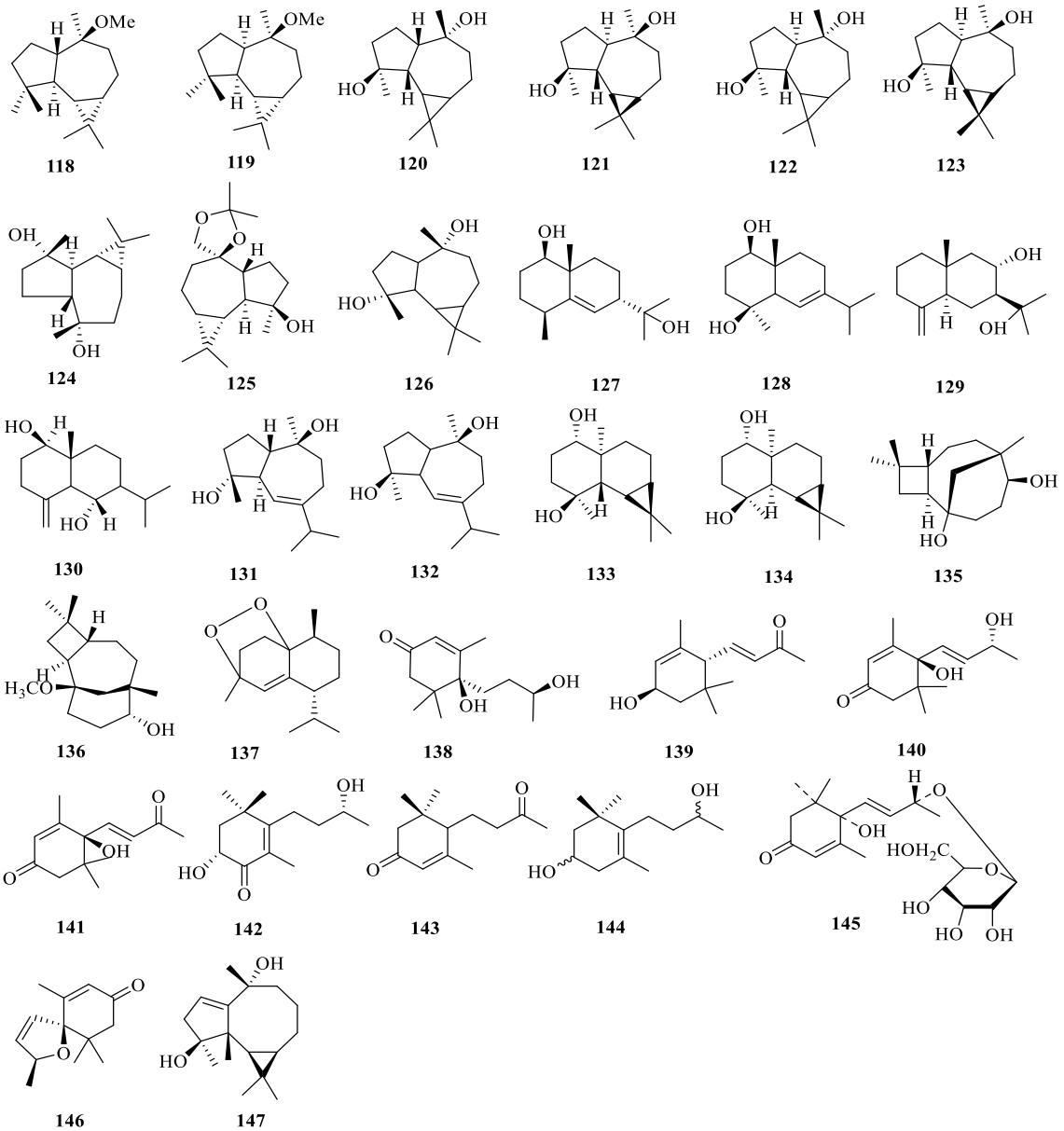


Figure 11. Chemical structures of the sesquiterpenes in *Nageia*

2.3. Flavonoids and Lignans

A total of 22 flavonoids and nine lignans have been isolated from *Nageia* genus plants (Table 8 and Figure 12). The former include biflavones (**148**-**158**), flavanoids (**159**-**162**), flavanones (**163**-**165**), flavonoid glycosides (**166**-**167**), flavonoids (**168**), and flavonols (**169**). *Nageia* genus plants yield the highest concentration of biflavones, the most prevalent flavonoid subgroup. These dimers are produced by polymerizing two identical or distinct types of flavanones and their derivatives. Flavanones exhibit considerable efficacy in treating cardiovascular disorders and possess anti-

neoplastic effects. Currently, 11 biflavones have been isolated and identified from *Nageia* genus plants and are connected by C-C bonds between flavanone molecules. Among them, compound **153** exhibits effective anti-inflammatory and antibacterial activities. The lignans include bis-tetrahydrofuran lignans and bis-epoxydihydrofuran lignans among others (**170**-**178**).

Table 8. Flavonoids and lignans from the genus *Nageia*

No.	Compound name	Molecular formula	Relative molecular mass	Source	Ref.
148	Sciadopitysin	$C_{33}H_{24}O_{10}$	580	F-L	[42]
149	Amentoflavone-4′,4‴,7,7″-tetramethyl ether	$C_{34}H_{26}O_{10}$	594	F-L	[42]
150	Kayaflavone	$C_{33}H_{24}O_{10}$	580	F-L	[42]
151	Robustaflavone-7″-methyl ether	$C_{31}H_{20}O_{10}$	552	F-TL	[57]
152	Isoginkgetin	$C_{32}H_{22}O_{10}$	566	W-L, F-TL	[12, 53]
153	Amentoflavone	$C_{30}H_{18}O_{10}$	538	N-L	[57]
154	Bilobetin	$C_{31}H_{20}O_{10}$	552	N-TL	[55]
155	Podocarpusflavone A	$C_{31}H_{20}O_{10}$	552	F-L, N-TL	[42, 55]
156	Podocarpusflavone B	$C_{32}H_{22}O_{10}$	566	F-L	[42]
157	Heveaflavone	$C_{33}H_{24}O_{10}$	580	F-L	[56]
158	7,4′,7″-trio-methyl amentoflavone	$C_{33}H_{24}O_{10}$	580	F-L	[42]
159	(-)-Catechin	$C_{15}H_{14}O_6$	290	N-TL	[55]
160	Catechin	$C_{15}H_{14}O_6$	290	N-L	[58]
161	Epicatechin	$C_{15}H_{14}O_6$	290	N-L	[58]
162	(-)-Epicatechin	$C_{15}H_{14}O_6$	290	F-T	[42]
163	5,7,3′,4′-tetramethoxyflavanone	$C_{19}H_{20}O_6$	344	F-A	[33]
164	Naringenine	$C_{15}H_{12}O_5$	272	F-A	[33]
165	Apigenin	$C_{15}H_{10}O_5$	270	W-L	[12]
166	Vitexin	$C_{21}H_{20}O_{10}$	432	N-L	[58]
167	Vitexin rhamnoside	$C_{27}H_{30}O_{14}$	578	N-L	[58]
168	Quercetin	$C_{15}H_{10}O_7$	302	N-TL	[55]
169	Chrysoeriol	$C_{16}H_{12}O_6$	300	F-T	[42]
170	(-)-Haplomyfolol	$C_{21}H_{26}O_6$	374	N-L	[23]
171	Anhydroseecoiso lariciresinol	$C_{21}H_{24}O_5$	356	N-L	[23]
172	(-)-Pluviatolide	$C_{20}H_{20}O_6$	356	N-L	[23]
173	Prinsepiol	$C_{20}H_{22}O_8$	390	N-TL	[55]
174	3-acetoxy-methyl-5-[(E)-3-acetoxypropen-1-yl)]-2-(4-hydroxy-3-methoxyphenyl)-7-methoxy-2,3-dihydro benzofuran	$C_{24}H_{26}O_8$	442	F-A	[33]
175	Divanillyltetrahydrofuran	$C_{20}H_{24}O_5$	344	F-A	[33]
176	(+)-Pinoresinol	$C_{20}H_{22}O_6$	358	F-A	[33]
177	Ligballinol	$C_{18}H_{18}O_4$	298	F-A	[33]
178	Secoisolariciresinol-9,9′-acetonide	$C_{23}H_{30}O_6$	402	F-T	[42]

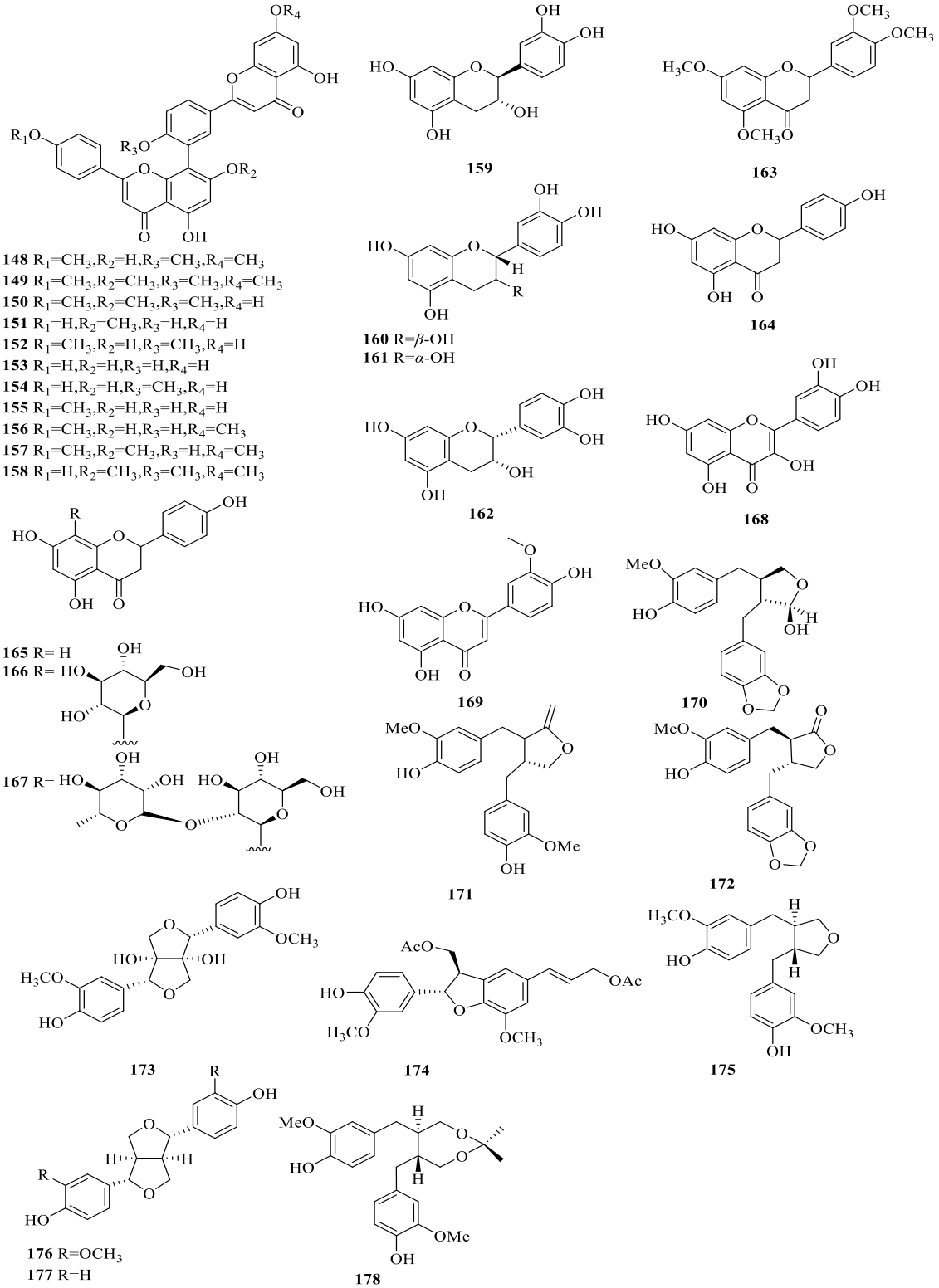


Figure 12. Structures of the flavonoids and lignans from the genus *Nageia*

2.4. Steroids and Triterpenoids

Currently, 21 steroids (**179**-**199**) and four triterpenoids (**200**-**203**) have been isolated from *Nageia* genus plants, (Table 9 and Figure 13). These steroids all share a common structural characteristic, which is the presence of a partly hydrogenated 1,2-cyclopentene phenanthroline steroidal nucleus. Typically, this nucleus has three side chains connected to it. The sterols **188** and **192** were initially extracted from the leaves of *N. nagi*. They possess a comparable structural framework to compound **191** and have significant effectiveness in inhibiting cancer development.

Table 9. Structures of the steroids and triterpenoids from the genus *Nageia*

No.	Compound name	Molecular formula	Relative molecular mass	Source	Ref.
179	5*α*,6*β*-dihydroxysitosterol	$C_{29}H_{52}O_3$	448	N-TL	[55]
180	7*α*-hydroxy sitosterol	$C_{29}H_{50}O_2$	430	W-L	[12]
181	Momordicine IV	$C_{36}H_{58}O_9$	634	N-L	[23]
182	Ergosta-7,22-dien-3*β*,5α,6*β*-triol	$C_{28}H_{48}O_3$	432	F-A	[33]
183	Stigmast-4-ene-3*β*,6*β*-diol	$C_{29}H_{50}O_2$	430	F-A	[33]
184	Sitostenone	$C_{29}H_{48}O$	412	F-T	[35]
185	Stigmast-4-en-3-one	$C_{28}H_{46}O$	398	F-T	[42]
186	Stigmast-5-ene-3*β*,7*α*-diol	$C_{29}H_{50}O_2$	430	F-A	[33]
187	Stigmast-5-ene-7*α*,22α-diol-3*β*-tetradecanoate	$C_{43}H_{76}O_4$	656	F-L	[42]
188	26,27-dinorcholest-5-en-3-*β*-ol	$C_{25}H_{42}O$	358	N-L	[54]
189	*β*-sitosteryl stearate	$C_{48}H_{86}O_2$	694	F-TL	[53]
190	*β*-sitosterol linoleate	$C_{47}H_{81}O_2$	677	F-T	[35]
191	*β*-sitosterol	$C_{29}H_{50}O$	414	N-TL	[55]
192	(24R)-3*β*,5*α*-dihydroxy-24-ethyl-5*α*-cholestan-6-one	$C_{29}H_{50}O_3$	446	N-L	[54]
193	3*β*,5α-dihydroxy-6-stigmastanone	$C_{29}H_{50}O_3$	446	F-TL	[53]
194	5*α*-hydroxy-6-stigmastanone-3*β*-palmitate	$C_{45}H_{80}O_4$	684	F-TL	[53]
195	Ergosterol peroxide	$C_{29}H_{50}O_2$	430	F-A	[33]
196	Podosterol	$C_{29}H_{50}O_3$	446	F-L	[56]
197	Stigmasta-B-nor-formyl-3*β*,5*β*,6-diol	$C_{29}H_{52}O_3$	448	F-T	[42]
198	3*β*,5*β*,6-trihydroxyl-B-norsitostane	$C_{29}H_{52}O_3$	448	F-T	[35]
199	Daucosterol	$C_{35}H_{60}O_6$	576	F-TL	[53]
200	Ursanic acid	$C_{30}H_{48}O_3$	456	F-A	[33]
201	Oleanolic acid	$C_{30}H_{48}O_3$	456	F-A	[33]
202	*α*-onocerin	$C_{30}H_{50}O_2$	442	N-L	[23]
203	*α*-tocopherol quinone	$C_{29}H_{50}O_3$	446	F-L	[56]

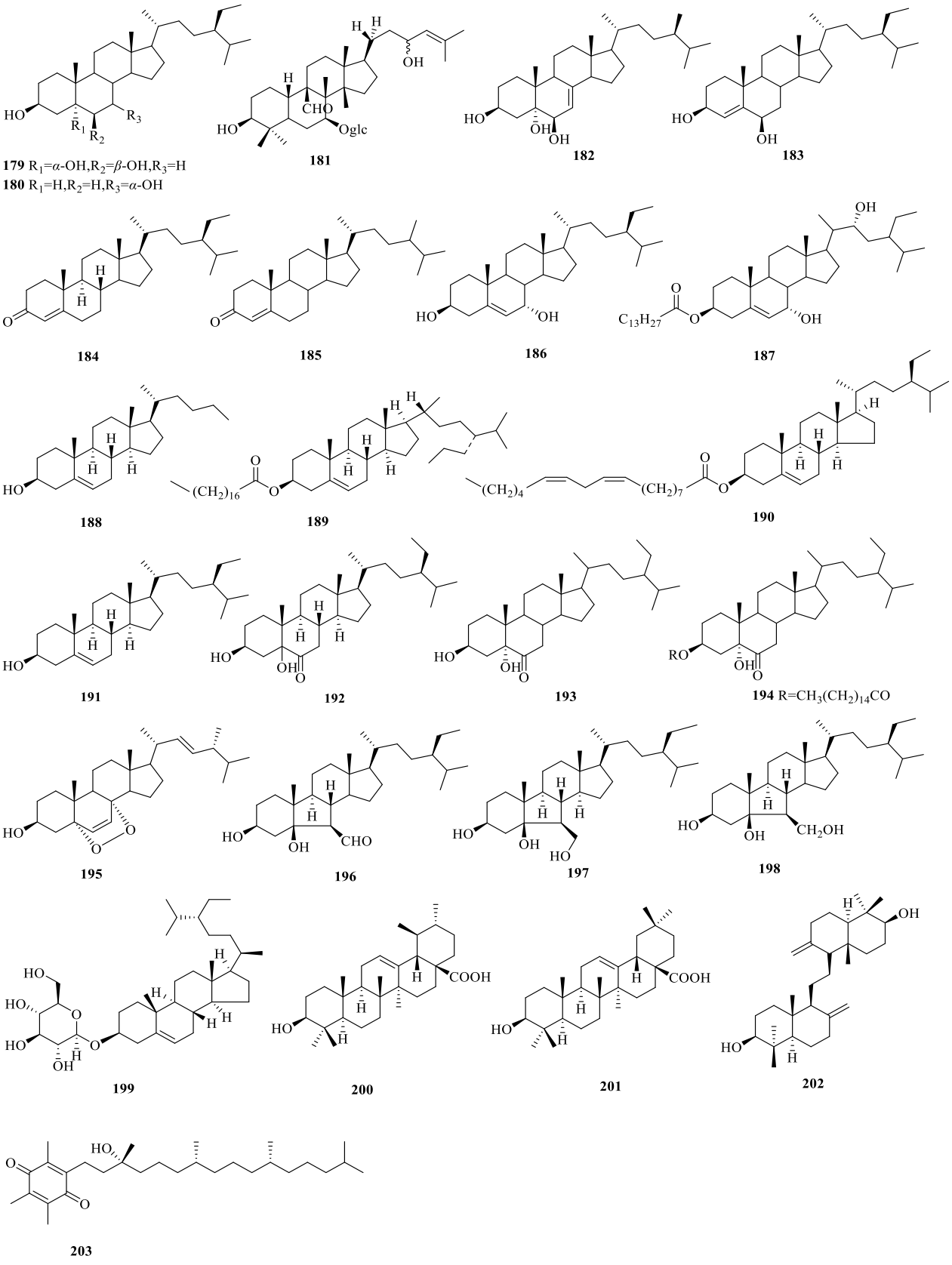


Figure 13. Structures of the steroids and triterpenoids from the genus *Nageia*

2.5. Other Compounds

The other types of compounds primarily consist of monoterpenes, megastigmanes, aromatic compounds, and phenylpropanoids, amounting to a total of 29 substances. The compounds and their structures are listed in Table 10.

Table 10. Structures of other compounds from the genus *Nageia*

No.	Compound name	Molecular formula	Relative molecular mass	Source	Ref.
204	(+)-Isololiolide	$C_{11}H_{16}O_3$	196	N-L	[23]
205	1,2-dihydroxy myrcene	$C_{10}H_{18}O_2$	170	F-TL	[41]
206	Pubinernoid A	$C_{11}H_{16}O_3$	196	F-L	[56]
207	(S)-7-methyl-3-methylene oct-6-ene-1,2-diyldiacetate	$C_{14}H_{22}O_4$	254	F-TL	[41]
208	4-hydroxy-3-methoxy benzaldehyde	$C_8H_8O_3$	152	F-T	[42]
209	(R)-2,3-dihydroxy-1-(4-hydroxyphenyl)propan-1-one	$C_9H_{10}O_4$	182	W-TL	[30]
210	1-(4-hydroxy-3-methoxyphenyl)-3-hydroxypropan-1-one	$C_{10}H_{12}O_4$	196	F-T	[42]
211	C-veratroylglycol	$C_{10}H_{12}O_5$	212	W-TL	[30]
212	*β*-hydroxypropiovanillone	$C_{10}H_{12}O_4$	196	W-TL	[30]
213	Protocatechuic acid	$C_7H_6O_4$	154	W-L	[12]
214	3,4-dimethoxy benzyl alcohol	$C_9H_{12}O_3$	168	F-T	[42]
215	*p*-hydroxy benzyl alcohol	$C_7H_8O_2$	124	F-T	[42]
216	Coniferol alcohol	$C_{10}H_{12}O_3$	180	F-A	[33]
217	3′,4′,5′-trimethoxycinnamyl alcohol	$C_{12}H_{16}O_4$	224	F-T	[42]
218	1-(1,3-dihydro-4-hydroxy-1-isobenzofuranyl)-3-hydroxy-2-butanone	$C_{12}H_{14}O_4$	222	F-T	[42]
219	*p*-hydroxybenzoic acid	$C_7H_6O_3$	138	N-L	[23]
220	methyl 3,4-dihydroxy-benzoate	$C_8H_8O_4$	168	N-L	[23]
221	Vanillin	$C_8H_8O_3$	152	F-L	[56]
222	Vanillic acid	$C_8H_8O_4$	168	N-L	[23]
223	3-hydroxy-4-methoxy benzoic acid	$C_8H_8O_4$	168	F-L	[56]
224	Glyceroylmonopalmitate	$C_{19}H_{39}O_4$	331	N-L	[23]
225	Tridecyl docosanoate	$C_{35}H_{69}O_3$	537	N-L	[23]
226	Chrysophanol	$C_{15}H_{10}O_4$	254	F-T	[42]
227	Ethyl-*β*-D-pyranoglucoside	$C_8H_{16}O_6$	208	N-Se	[20]
228	Nagitide A	$C_{34}H_{41}N_4O_5$	585	N-Sb	[59]
229	Nagitide B	$C_{36}H_{48}N_5O_5$	630	N-Sb	[59]
230	Syringin	$C_{17}H_{24}O_9$	372	F-TL	[53]
231	(4S*,6R*)-4-hydroxy-4,8,8-trimethyl-9-oxabicyclo[4.2.1]-non-1-en-3-one	$C_{11}H_{18}O_3$	194	F-T	[42]
232	hydroxydihydroborolide	$C_{11}H_{16}O_3$	196	N-L	[23]

3. Conclusions

In conclusion, the genus *Nageia* comprises seven plant species, with *N. nagi* and *N. fleuryi* being the most widely distributed. Presently, the primary focus of study on *Nageia* species revolves around the chemical composition and pharmacological effects of *N. nagi* and *N. fleuryi*. However, research on other species within the same genus remains limited and necessitates additional attention. *Nageia* plants are rich in chemical compounds, with diterpenoid dilactones being the characteristic compounds. These compounds are characterized by their wide range and high quantity, demonstrating

multiple pharmacological properties, including anti-tumor, anti-inflammatory, antioxidant, and anti-pulmonary fibrosis effects.

Furthermore, they exhibit substantial potential in treating disorders associated with the TGF-β/Smad signaling system. Nevertheless, information is scarce on how these diterpenoid dilactones work, their safety, how easily the body absorbs them, and their pharmacokinetic properties. Therefore, further comprehensive studies are required.

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