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Review

Research Progress on Sesquiterpene Compounds from Artabotrys Plants of Annonaceae

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Abstract: *Artabotrys*, a pivotal genus within the *Annonaceae* family, is renowned for its extensive biological significance and medicinal potential. The genus's sesquiterpene compounds have attracted considerable interest from the scientific community due to their structural complexity and diverse biological activities. These compounds exhibit a range of biological activities, including antimalarial, antibacterial, anti-inflammatory analgesic, and anti-tumor properties, positioning them as promising candidates for medical applications. This review aims to summarize the current knowledge on the variety, species, and structural characteristics of sesquiterpene compounds isolated from *Artabotrys* plants. Furthermore, it delves into their pharmacological activities and underlying mechanisms, offering a comprehensive foundation for future research.

Keywords: *Artabotrys*; *Annonaceae*; sesquiterpene compounds; biological activities

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1. Introduction

Annonaceae, a prominent family within the tropical flora, is classified under the *Ranunculaceae*. It contains approximately 130 genera and over 2100 species, featuring a rich diversity of tropical trees, shrubs, and climbing plants [1]. Many species within *Annonaceae* family have been widely used in ethnobotany to treat a myriad of health conditions [2]. For instance, *Polyalthia*, one of the largest and most famous genera within *Annonaceae*, has been widely used in the treatment of rheumatic fever, peptic ulcer, and systemic pain [3]. The chemical diversity present in *Annonaceae* species is vast, yielding a plethora of natural compounds such as alkenes [4], terpenoids [5], alkaloids [6–10], and phenols [11]. These compounds demonstrate a broad spectrum of pharmacological activities, including anti-mosquito [12], anti-cancer [13–15], antibacterial [16], anti-protozoal [17,18], and anti-fungal [19]. Among them, Annonaceous acetogenins stand out for their potent anti-tumor potential, making them one of the most promising natural product discoveries [20].

Artabotrys, belonging to the *Annonaceae* family, comprises about 110 species of plants around the world, predominantly distributed in tropical and subtropical regions such as Southeast Asia, Indonesia, and Malaysia. The plants of this genus are climbing shrubs. The leaves of these plants are usually compound, the flowers are small and clustered on the raceme, and the fruits are drupe-shaped. There are many traditional uses of this genus, such as the treatment of cholera, malaria, and other diseases [21]. The plants of this genus have a wide range of biological significance and medicinal value. An examination of data from the Plants of the World Online database facilitated a detailed summary of *Artabotrys* species and their distribution (Table 1).

Table 1. Distribution of *Artabotrys* plant resources.

No.	Species	Distribution
1	*Artabotrys aereus* Ast	Vietnam
2	*Artabotrys antunesii* Engl. & Diels	Angola
3	*Artabotrys arachnoides* J.Sinclair	New Guinea
4	*Artabotrys atractocarpus* I.M.Turner	Borneo
5	*Artabotrys aurantiacus* Engl.	Cameroon, Central African Repu, Congo, Gabon, Zaïre
6	*Artabotrys blumei* Hook.f. & Thomson	China South-Central, China Southeast, Hainan, Vietnam
7	*Artabotrys brachypetalus* Benth.	Botswana, Caprivi Strip, Malawi, Mozambique, Northern Provinces, Tanzania, Zambia, Zaïre, Zimbabwe
8	*Artabotrys brevipes* Craib	Laos, Thailand
9	*Artabotrys burmanicus* A.DC.	Assam, Myanmar
10	*Artabotrys byrsophyllus* I.M.Turner & Utteridge	Malaya, Thailand
11	*Artabotrys cagayanensis* Merr.	Philippines
12	*Artabotrys camptopetalus* Diels	New Guinea
13	*Artabotrys carnosipetalus* Jessup	Queensland
14	*Artabotrys caudatus* Wall. ex Hook.f. & Thomson	Assam, Bangladesh, East Himalaya
15	*Artabotrys chitkokoi* K.Z.Hein, Naive & J.Chen	Myanmar
16	*Artabotrys coccineus* Keay	Nigeria
17	*Artabotrys collinus* Hutch.	Tanzania, Zambia
18	*Artabotrys congolensis* De Wild. & T.Durand	Cameroon, Central African Repu, Congo, Gabon, Zaïre
19	*Artabotrys costatus* King	Borneo, Malaya
20	*Artabotrys crassifolius* Hook.f. & Thomson	Malaya, Myanmar, Thailand
21	*Artabotrys crassipetalus* Pellegr.	Gabon
22	*Artabotrys cumingianus* S.Vidal	Philippines
23	*Artabotrys darainensis* Deroin & L.Gaut.	Madagascar
24	*Artabotrys dielsianus* Le Thomas	Cameroon
25	*Artabotrys fragrans* Jovet-Ast	China South-Central, China Southeast, Vietnam
26	*Artabotrys gossweileri* Baker f.	Cabinda
27	*Artabotrys gracilis* King	Borneo, Malaya, Sumatera
28	*Artabotrys grandifolius* King	Malaya, Sumatera
29	*Artabotrys hainanensis* R.E.Fr.	China Southeast, Hainan
30	*Artabotrys harmandii* Finet & Gagnep.	Cambodia, Laos, Thailand, Vietnam
31	*Artabotrys hexapetalus* (L.f.) Bhandari	Comoros, India, Laos, Sri Lanka
32	*Artabotrys hienianus* Bân	Vietnam
33	*Artabotrys hildebrandtii* O.Hoffm.	Madagascar
34	*Artabotrys hirtipes* Ridl.	Borneo
35	*Artabotrys hispidus* Sprague & Hutch.	Guinea, Ivory Coast, Liberia, Sierra Leone
36	*Artabotrys inodorus* Zipp.	New Guinea
37	*Artabotrys insignis* Engl. & Diels	Benin, Cameroon, Congo, Gabon, Ghana, Guinea, Ivory Coast, Liberia, Sierra Leone, Zaïre
38	*Artabotrys insurae* Junhao Chen & Eiadthong	Thailand
39	*Artabotrys jacques-felicis* Pellegr.	Cameroon, Central African Repu, Zaïre
40	*Artabotrys javanicus* I.M.Turner	Jawa
41	*Artabotrys jollyanus* Pierre	Cameroon, Guinea, Ivory Coast, Liberia
42	*Artabotrys kinabaluensis* I.M.Turner	Borneo
43	*Artabotrys kurzii* Hook.f. & Thomson	Myanmar
44	*Artabotrys lanuginosus* Boerl.	Borneo, Sulawesi, Sumatera
45	*Artabotrys lastoursvillensis* Pellegr.	Gabon, Uganda
46	*Artabotrys letestui* Pellegr.	Congo, Gabon
47	*Artabotrys libericus* Diels	Liberia
48	*Artabotrys likimensis* De Wild.	Burundi, Central African Repu, Kenya, Rwanda, Uganda, Zaïre
49	*Artabotrys longipetalus* Junhao Chen & Eiadthong	Thailand
50	*Artabotrys longistigmatus* Nurainas	Sumatera
51	*Artabotrys lowianus* King	Malaya
52	*Artabotrys luteus* Elmer	Philippines
53	*Artabotrys luxurians* Ghesq. ex Cavaco & Keraudr.	Madagascar
54	*Artabotrys macrophyllus* Hook.f.	Gulf of Guinea Is.
55	*Artabotrys macropodus* I.M.Turner	Borneo

Table 1. *Cont.*

No.	Species	Distribution
56	*Artabotrys madagascariensis* Miq.	Madagascar
57	*Artabotrys maingayi* Hook.f. & Thomson	Borneo, Malaya
58	*Artabotrys manoranjanii* M.V.Ramana, J.Swamy & K.C.Mohan	Andaman Is.
59	*Artabotrys modestus* Diels	Tanzania
60	*Artabotrys monteiroae* Oliv.	Angola, Burundi, Ethiopia, Kenya, KwaZulu-Natal, Madagascar, Malawi, Mozambique, Northern Provinces, Rwanda, Sudan, Swaziland, Tanzania, Uganda, Zambia, Zaïre, Zimbabwe
61	*Artabotrys multiflorus* C.E.C.Fisch.	China South-Central, China Southeast, Myanmar, Thailand
62	*Artabotrys nicobarianus* D.Das	Andaman Is., Nicobar Is.
63	*Artabotrys oblanceolatus* Craib	Thailand
64	*Artabotrys oblongus* King	Cambodia, Malaya
65	*Artabotrys ochropetalus* I.M.Turner	Borneo
66	*Artabotrys oliganthus* Engl. & Diels	Cameroon, Central African Repu, Gabon, Guinea, Ivory Coast, Liberia
67	*Artabotrys oxycarpus* King	Malaya, Thailand
68	*Artabotrys pachypetalus* B.Xue & Junhao Chen	China Southeast
69	*Artabotrys pallens* Ast	Vietnam
70	*Artabotrys palustris* Louis ex Boutique	Zaïre
71	*Artabotrys pandanicarpus* I.M.Turner	Borneo
72	*Artabotrys parkinsonii* Chatterjee	Myanmar
73	*Artabotrys petelotii* Merr.	Laos, Vietnam
74	*Artabotrys phuongianus* Bân	Vietnam
75	*Artabotrys pierreanus* Engl. & Diels	Cameroon, Congo, Gabon, Zaïre
76	*Artabotrys pilosus* Merr. & Chun	China Southeast, Hainan
77	*Artabotrys pleurocarpus* Maingay ex Hook.f. & Thomson	Malaya, Thailand
78	*Artabotrys polygynus* Miq.	Borneo
79	*Artabotrys porphyrifolius* Nurainas	Sumatera
80	*Artabotrys punctulatus* C.Y.Wu	China South-Central, Thailand
81	*Artabotrys rhynchocarpus* C.Y.Wu	China South-Central, China Southeast
82	*Artabotrys roseus* Boerl.	Borneo
83	*Artabotrys rufus* De Wild.	Benin, Cameroon, Central African Repu, Congo, Gabon, Nigeria, Togo, Zaïre
84	*Artabotrys rupestris* Diels	Tanzania
85	*Artabotrys sahyadricus* Robi, K.M.P.Kumar & Hareesh	India
86	*Artabotrys sarawakensis* I.M.Turner	Borneo
87	*Artabotrys scortechinii* King	Malaya
88	*Artabotrys scytophyllus* (Diels) Cavaco & Keraudren	Madagascar
89	*Artabotrys sericeus* Sujana & Vadhyar	India
90	*Artabotrys siamensis* Miq.	Myanmar, Thailand
91	*Artabotrys spathulatus* Jun H.Chen, Chalermglin & R.M.K.Saunders	Thailand
92	*Artabotrys speciosus* Kurz ex Hook.f. & Thomson	Andaman Is.
93	*Artabotrys spinosus* Craib	Cambodia, Laos, Thailand, Vietnam
94	*Artabotrys suaveolens* (Blume) Blume	Borneo, Jawa, Lesser Sunda Is., Malaya, Maluku, Myanmar, New Guinea, Nicobar Is., Philippines, Sulawesi, Sumatera, Thailand, Bangladesh
95	*Artabotrys sumatranus* Miq.	Borneo, Jawa, Sumatera
96	*Artabotrys tanaosriensis* Jun H.Chen, Chalermglin & R.M.K.Saunders	Thailand
97	*Artabotrys taynguyenensis* Bân	Vietnam
98	*Artabotrys tetramerus* Bân	Vietnam
99	*Artabotrys thomsonii* Oliv.	Cabinda, Cameroon, Central African Repu, Congo, Gabon, Liberia, Nigeria, Zaïre
100	*Artabotrys tipulifer* I.M.Turner & Utteridge	Malaya, Thailand

Table 1. *Cont.*

No.	Species	Distribution
101	*Artabotrys tomentosus* Nurainas	Sumatera
102	*Artabotrys uniflorus* (Griff.) Craib	Myanmar, Thailand
103	*Artabotrys veldkampii* I.M.Turner	Borneo
104	*Artabotrys velutinus* Scott Elliot	Benin, Cabinda, Cameroon, Central African Repu, Congo, Gabon, Ghana, Guinea, Guinea-Bissau, Ivory Coast, Liberia, Nigeria, Senegal, Sierra Leone, Uganda, Zaïre
105	*Artabotrys venustus* King	Borneo, Malaya, Sumatera, Thailand
106	*Artabotrys vidalianus* Elmer	Philippines
107	*Artabotrys vietnamensis* Bân	Vietnam
108	*Artabotrys vinhensis* Ast	Vietnam
109	*Artabotrys wrayi* King	Malaya
110	*Artabotrys zeylanicus* Hook.f. & Thomson	India, Sri Lanka

The genus *Artabotrys*, within the *Annonaceae* family, is distinguished by its wealth of chemical components [22]. To date, research has identified a diverse array of compounds from these plants, including alkaloids [23,24], volatile oils [25,26], cyclohexenes [27,28], phenylpropanoids [29], flavonoids [30], quinones [31], and sesquiterpenes [32]. Among these, sesquiterpenes stand out as one of the principal active components, heralded for their significant medical value and importance in research. So far, there have been many research articles on the plants of *Artabotrys*; however, the majority have focused on individual compounds or relatively extensive research overviews. Comprehensive reviews specifically addressing the sesquiterpene compounds derived from the plants of the genus are notably scarce. Therefore, this paper aims to fill this gap by reviewing the current research progress of sesquiterpene compounds derived from the plants of *Artabotrys* in *Annonaceae*. It meticulously summarizes the variety, species, and structural characteristics of sesquiterpene compounds identified within these plants and explores their pharmacological activities and underlying mechanisms, offering a comprehensive foundation for future research.

2. Chemical Constitution

Sesquiterpenes, a diverse class of natural organic compounds, are characterized by a basic carbon skeleton comprising 15 carbon atoms arranged in three isoprene units. Based on the number of carbon rings in the structure, sesquiterpenes can be divided into five structural types: acyclic sesquiterpenes [33], monocyclic sesquiterpenes [34], bicyclic sesquiterpenes [35,36], tricyclic sesquiterpenes [37], and tetracyclic sesquiterpenes [38]. Acyclic sesquiterpenes encompass linear sesquiterpenes [39] and unsaturated acyclic sesquiterpenes [40] whereas monocyclic sesquiterpenes include germacrane [41], cyclofarnesane [42], bisabolane [43], and elemane [44]. Bicyclic sesquiterpenes feature structures like eudesmane [45], isodaucane [46], guaiane [47], acorane [48], and eremophilane [49,50]. Tricyclic sesquiterpenes include aristolane [51], and aromadendrane [52]. Tetracyclic sesquiterpenes include camphane, labdane, and ginkgolide [53,54].

Sesquiterpenes represent a distinguished class of natural organic compounds, notable for their widespread natural sources. These compounds are predominantly derived from a range of plants [55,56], especially those known for their aromatic properties, as well as from fungi [57–59], and marine organisms [60,61]. Sesquiterpenes have a variety of biological activities, encompassing antimalarial [62], antioxidant [63], anti-inflammatory [64,65], antibacterial [66,67], and anti-tumor effects [68,69]. Therefore, sesquiterpenes have displayed significant therapeutic potential in the pharmaceutical sector, while their unique properties also make them invaluable to the perfume industry.

Extensive research into the sesquiterpenes extracted from *Artabotrys* plants reveals a remarkable diversity within this genus. To date, investigations have identified over 80 distinct sesquiterpene types isolated from *Artabotrys*, underscoring the genus's rich contribution to the pool of naturally occurring sesquiterpenes. A detailed breakdown

of these sesquiterpenes reveals a wide array of structural types, including 19 bisabolane-type, 15 eudesmane-type, 8 norbisabolane-type, 6 guaiane-type, 4 aromadendrane-type, aristolane-type, and cadinane-type, 3 eremophilane-type, 2 isodaucane-type and acorane-type, 1 germacrane-type, alongside a multitude of other sesquiterpene variants.

These findings further attest to the extraordinary potential of the plant as a 'natural drug bank', such as for the development of innovative anti-tumor and anti-inflammatory drugs. Each sesquiterpene identified offers unique insights into potential pharmacological applications and holds the promise of playing a pivotal role in devising novel therapeutic strategies.

2.1. Bisabolane-Type Sesquiterpenes

Bisabolane-type sesquiterpenes, a subclass of monocyclic sesquiterpenes, are characterized by their six-membered carbon rings and side chains. These compounds boast a plethora of natural sources, including marine invertebrates, terrestrial plants, and microorganisms. Notably, bisabolane-type sesquiterpenes exhibit a wide range of biological activities, such as anti-inflammatory and antibacterial [70,71]. To date, more than 350 kinds of bisabolane-type sesquiterpenes have been isolated from various plant families, including *Compositae* and *Zingiberaceae* [72]. In the context of the *Artabotrys* genus, several bisabolane-type sesquiterpenes have also been successfully extracted (Table 2).

Table 2. Bisabolane-type sesquiterpenes from *Artabotrys*.

No.	Name of Compound	Source	Reference
1	Yingzhaosu A	*A. uncinatus*	[73]
2	Yingzhaosu B	*A. uncinatus*	[74]
3	Yingzhaosu C	*A. uncinatus*	[75]
4	Yingzhaosu D	*A. uncinatus*	[75]
5	(4*R*,10*S*,11*E*)-Yingzhaosu F	*A. hexapetalus*	[76]
6	(4*S*,10*S*,11*E*)-Yingzhaosu F	*A. hexapetalus*	[76]
7	(*1R*,2*S*,3*S*,4*E*)-Yingzhaosu G	*A. hexapetalus*	[76]
8	(*1S*,2*R*,3*R*,4*E*)-Yingzhaosu G	*A. hexapetalus*	[76]
9	(4*R*,8*E*,11*S*,12*S*)-Yingzhaosu H	*A. hexapetalus*	[76]
10	(4*R*,8*E*,11*R*,12*R*)-Yingzhaosu H	*A. hexapetalus*	[76]
11	(4*S*,*8S*,10*S*,11*S*)-Yingzhaosu I	*A. hexapetalus*	[76]
12	(4*R*,8*S*,10*S*,11*S*)-Yingzhaosu I	*A. hexapetalus*	[76]
13	(4*R*,8*E*,11*R*,12*S*)-Yingzhaosu J	*A. hexapetalus*	[76]
14	(4*S*,8*E*,11*S*,12*R*)-Yingzhaosu J	*A. hexapetalus*	[76]
15	(4*R*,*8Z*,11*S*,12*S*)-Yingzhaosu K	*A. hexapetalus*	[76]
16	(*4S*,8*Z*,11*R*,12*R*)-Yingzhaosu K	*A. hexapetalus*	[76]
17	(1*S*,2*R*,4*R*,*8S*,10*E*)-Yingzhaosu L	*A. hexapetalus*	[76]
18	Chlospicate E	*A. pilosus*	[77]
19	Arbisabol-9-en-7,11-diol	*A. pilosus*	[77]

Among the isolated compounds, compounds **1** and **2** were extracted from the roots of *Artabotrys uncinatus* in 1979; their structures were elucidated by spectroscopic methods [73,74]. Compounds **3** and **4** were also derived from *A. uncinatus* [75]. Subsequently, researchers isolated 13 bisabolane-type sesquiterpenes (**5**–**17** in Table 2) from the roots of *A. hexapetalus* in 2017 [76]. Moreover, 25 monomeric compounds, including two bisabolane-type sesquiterpenes chlospicate E (**18**) and arbisabol-9-en-7,11-diol (**19**) [77], were isolated from *Artabotrys pilosus* by a combination of chromatographic separation methods and spec-

tral identification techniques. The structural details of the related compounds are shown in Figure 1.

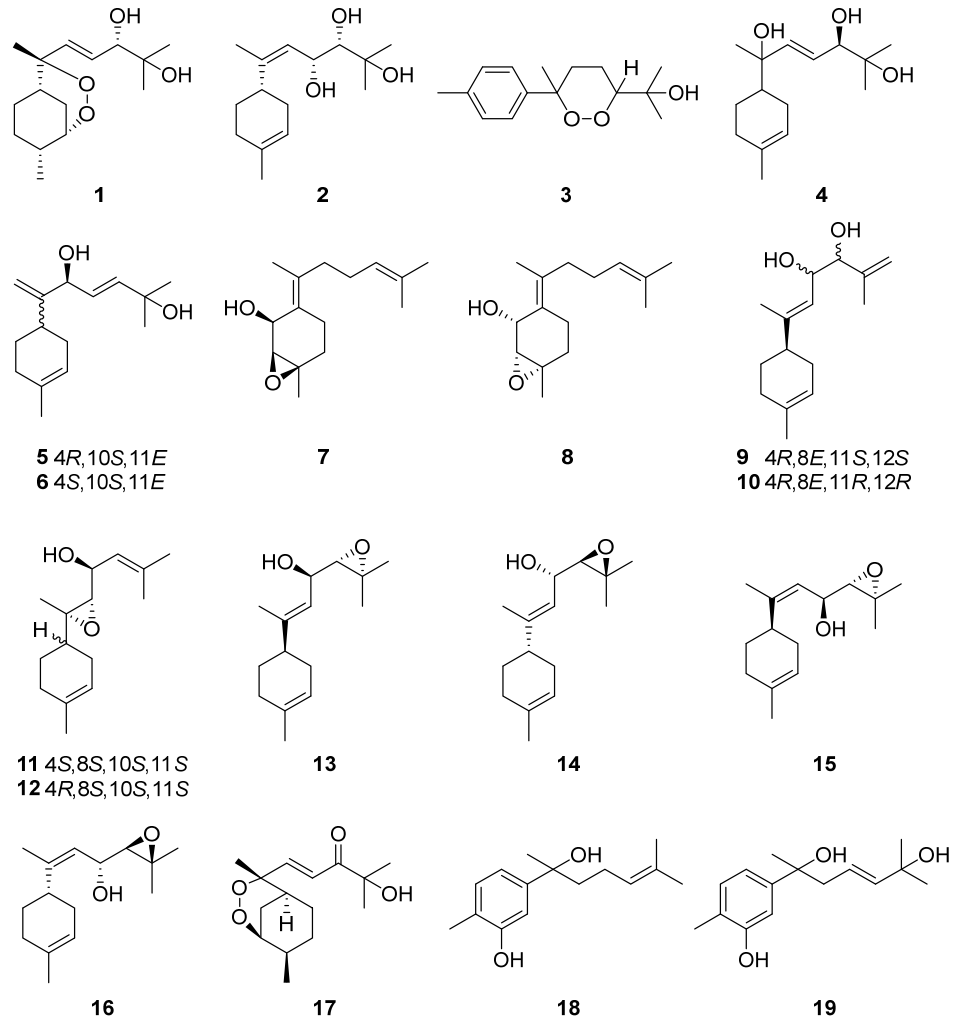


Figure 1. The structures of bisabolane-type sesquiterpenes from *Artabotrys*.

2.2. Norbisabolane-Type Sesquiterpenes

Norbisabolane-type sesquiterpenes, another subset of monocyclic sesquiterpenes, known for their spiroketal structures, have primarily been isolated from *Phyllanthus* spp. within the *Euphorbiaceae* [78]. From the extracts of *Artabotrys* plants, several norbisabolane-type sesquiterpenes (Table 3) were successfully purified by a series of chromatographic techniques, and the structures were elucidated via comprehensive analysis of nuclear magnetic resonance (NMR), mass spectrometry (MS) and other technical means. Among them, compound **20** was isolated from *A. hexapetalus* [76], while compounds **21**–**27** were isolated from the branches and leaves of *A. hongkongensis* in 2017 [79]. The detailed structures of the compounds are shown in Figure 2.

Table 3. Norbisabolane-type sesquiterpenes from *Artabotrys*.

No.	Name of Compound	Source	Reference
20	(1*R*,2*S*,4*R*,8*R*,10*E*)-Yingzhaosu M	*A. hexapetalus*	[77]
21	Blumenol A	*A. hongkongensis*	[79]
22	4,5-Dihydroblumenol A	*A. hongkongensis*	[79]
23	(6*R*,9*S*)-3-Oxo-*α*-ionol	*A. hongkongensis*	[79]
24	3-Hydroxy-*β*-ionone	*A. hongkongensis*	[79]
25	Dehydrovomifoliol	*A. hongkongensis*	[79]
26	(3*R*,6*R*,7*E*)-3-Hydroxy-4,7-Megastigmadien-9-one	*A. hongkongensis*	[79]
27	Sarmentol F	*A. hongkongensis*	[79]

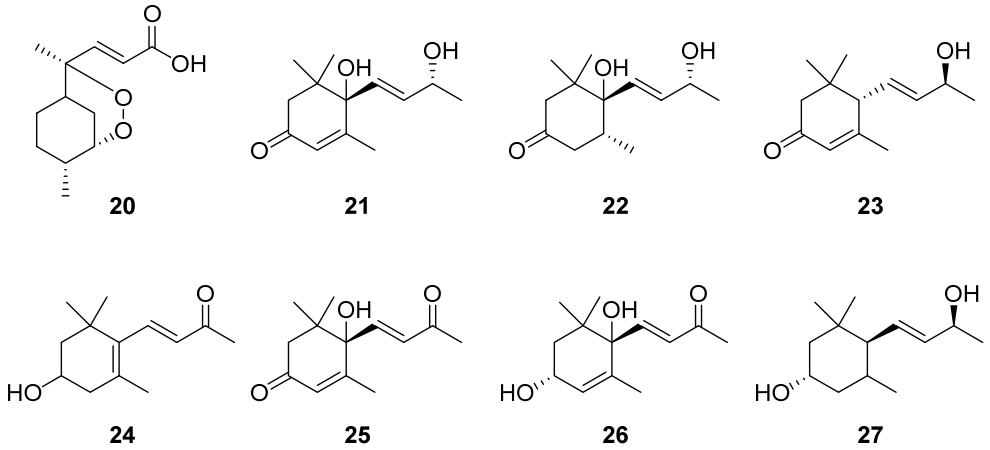


Figure 2. The structures of norbisabolane-type sesquiterpenes from *Artabotrys*.

2.3. Eudesmane-Type Sesquiterpenes

Eudesmane-type sesquiterpenes, classified as bicyclic sesquiterpenes, are notable for their widespread distribution in nature. Eudesmane-type sesquiterpenes are characterized by a core structure comprising two six-membered rings and four substituents with a total of 15 carbon atoms, leading to a considerable structural diversity primarily attributed to variations in the substituents' positioning and the double bonds within the rings. Studies have shown that these compounds displayed anti-inflammatory [80], anti-fungal [81], anti-cancer [82], anti-diabetic nephropathy [83], and the ability to inhibit the proliferation of leukemia cell lines [84].

A significant number of eudesmane-type sesquiterpenes have been isolated from *Artabotrys* (Table 4), with compounds **28**–**42** representing this variety. Among them, compounds **28**–**34**, a series of seven eudesmane-type sesquiterpenes, were isolated from *Artabotrys hongkongensis* Hance in 2020 [85]. The compound 7-trinoreudesma-4(15),8-dien-1*β*-ol-7-one (45) was isolated from the ethyl acetate extract of the 90% ethanol extract of the branches and leaves of *A. pilosus* by various modern chromatographic separation techniques. Its identification as colorless oil soluble in chloroform was identified by structural identification, affirming its classification as an eudesmane-type sesquiterpene [77]. Additionally, the other eight eudesmane-type sesquiterpenes (**35**–**42**) were isolated from *Artabotrys hainanensis* [86], *A. hongkongensis* [79], and *A. pilosus* [77] by various separation techniques. The distinctive structures of eudesmane-type sesquiterpenes from the *Artabotrys* genus plants are depicted in Figure 3.

Table 4. Eudesmane-type sesquiterpenes from *Artabotrys*.

No.	Name of Compound	Source	Reference
28	1α-Hydroxy-5,11-eudesmadiene	*A. hongkongensis*	[85]
29	5-Eudesmene-1β,4α-diol	*A. hongkongensis*	[85]
30	1β,11-Dihydroxy-5-eudesmene	*A. hongkongensis*	[85]
31	1β-Hydroxy-11-methoxy-5-eudesmene	*A. hongkongensis*	[85]
32	2α-Hydroxy pterodontic acid	*A. hongkongensis*	[85]
33	1β,9β-Dihydroxy-4aH-eudesma-5,11(13)-Dien-12-oic acid	*A. hongkongensis*	[85]
34	1β,3α-Dihydroxyeudesma-5,11(13)-Dien-12-oic acid	*A. hongkongensis*	[85]
35	Cryptomeridiol	*A. hainanensis*	[86]
36	4,10-Epi-5β-hydroxydihydroeiidesmol	*A. hainanensis*	[86]
37	Eudesm-4(14)-ene-3α,11-diol	*A. hainanensis*	[86]
38	Oplodiol	*A. hainanensis*	[86]
39	β-Eudesmol	*A. hainanensis* *A. hongkongensis*	[86] [79]
40	Trans-3β-(1-hydroxy-1-methylethyl)-8$\alpha\beta$-methyl-5-methylenedecalin-2-one	*A. hongkongensis*	[79]
41	1β,6α-Dihydroxy-4α (15)-Epoxyeudesmane	*A. pilosus*	[77]
42	7-Trinoreudesma-4(15),8-dien-1β-ol-7-one	*A. pilosus*	[77]

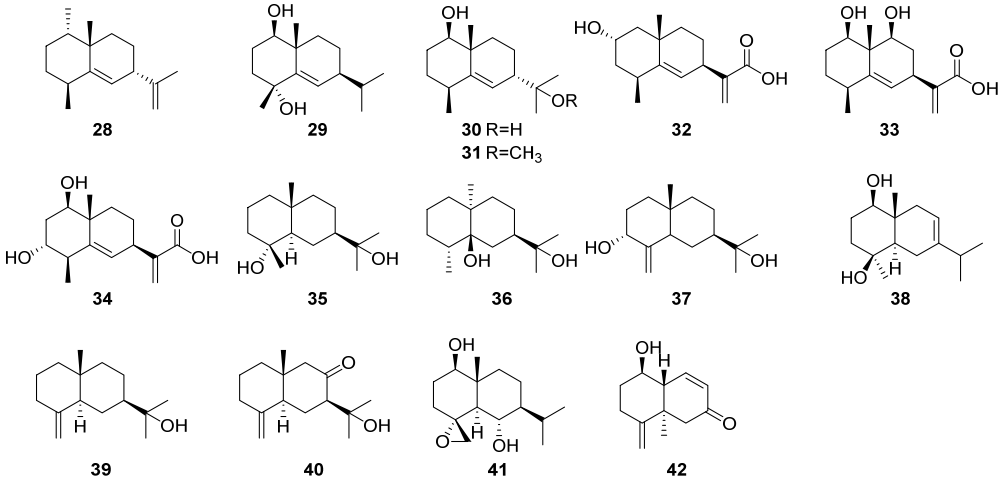


Figure 3. The structures of eudesmane-type sesquiterpenes from *Artabotrys*.

2.4. Guaiane-Type Sesquiterpenes

Guaiane-type sesquiterpenes, a subclass of bicyclic sesquiterpenes, are distinguished by their unique structural framework, which features a seven-membered ring fused with a five-membered lactone ring, augmented by two methyl groups and one isopropyl group. These compounds are prevalent across more than 30 families of plants, demonstrating a broad spectrum of biological activities, including anti-tumor, anti-inflammatory, antibacterial, and antioxidant [87,88]. The genus *Artabotrys* plants, known for its rich chemical diversity, also harbors guaiane-type sesquiterpenes. Compounds **43**–**48** represent guaiane-type sesquiterpenes isolated from various *Artabotrys* species (Table 5). Guaiane pogostol O-methyl ether (**46**) from *Artabotrys stenopetalus* in 1997 marked the beginning of the identification of such compounds within the genus [89]. Compounds **43** and **44** are two

sesquiterpenes isolated from the 90% ethanol extract of the branches and leaves of *A. hainanensis*, both identified as guaiane-type sesquiterpenes [86]. Compound **45**, a colorless oily substance isolated from *A. pilosus* [77], was confirmed as guaianediol through NMR data analysis and comparison with existing literature [90]. Additionally, alismol (**47**) and alismoxide (**48**) were derived from the stem [91] and flower of *A. hainanensis* [86], respectively, with the latter previously identified in *Alisma orientalis* [92]. The structures of these guaiane-type sesquiterpenes are depicted in Figure 4.

Table 5. Guaiane-type sesquiterpenes from *Artabotrys*.

No.	Name of Compound	Source	Reference
43	Liguducin A	*A. hainanensis*	[86]
44	Alpinenone	*A. hainanensis*	[86]
45	Guaianediol	*A. pilosus*	[77]
46	Guaiane pogostol *O*-methyl ether	*A. stenopetalus*	[89]
47	Alismol	*A. hainanensis*	[91]
48	Alismoxide	*A. hainanensis*	[86]

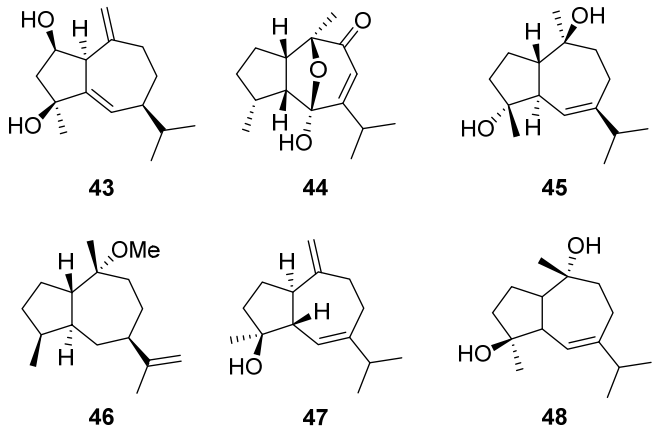


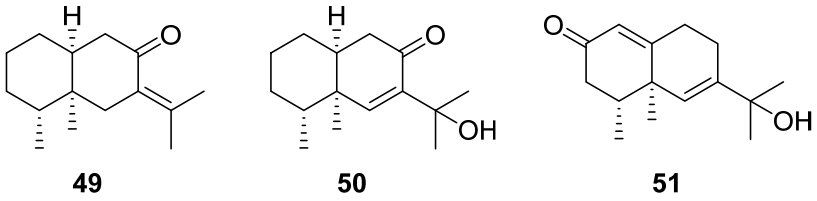
Figure 4. The structures of guaiane-type sesquiterpenes from *Artabotrys*.

2.5. Eremophilane-Type Sesquiterpenes

Eremophilane-type sesquiterpenes, derived from the biosynthetic precursor farnesyl diphosphate (FPP), represent a distinct group within the bicyclic sesquiterpene compound family. These compounds are characterized by their unique irregular bicyclic structures, with structural variations primarily arising from various oxidations on the bicyclic skeleton and the isopropyl side chain [93]. Related studies have shown that these compounds displayed anti-inflammatory effects and can inhibit the NO produced by lipopolysaccharide (LPS)-induced RAW 264.7 macrophages [94]. In studying the chemical constituents of the *Artabotrys* genus, researchers have successfully isolated several eremophilane-type sesquiterpenes (Table 6). Among them, compounds **49** and **50** are two eremophilane-type sesquiterpenes obtained from the branches and leaves of *A. hongkongensis* in the same research process [79], while compound **51** was obtained from the branches and leaves of *A. hainanensis* in another study one year later [86]. The chemical structures of these three eremophilane-type sesquiterpenes with serial numbers **49**–**51** are shown in Figure 5.

Table 6. Eremophilane-type sesquiterpenes from *Artabotrys*.

No.	Name of Compound	Source	Reference
49	Fukinone	*A. hongkongensis*	[79]
50	Petasitolone	*A. hongkongensis*	[79]
51	11-Hydroxy-valenc-1(10)-en-2-one	*A. hainanensis*	[86]



49 **50** **51**

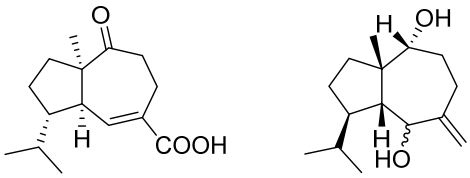
Figure 5. The structures of eremophilane-type sesquiterpenes from *Artabotrys*.

2.6. Isodaucane-Type Sesquiterpenes

Isodaucane-type sesquiterpenes, which belong to bicyclic sesquiterpenes, are distinguished by their distinctive structural configuration, featuring a five-membered ring coupled with a seven-membered ring. Despite their relatively scarce occurrence in nature compared with other common types of sesquiterpenes, dedicated research efforts have led to the successful isolation of two isodaucane-type sesquiterpenes from the *Artabotrys* genus (Table 7). Compounds **52** and **53** were isolated from the branches and leaves of *A. hongkongensis* and the stem bark of *A. stenopetalus*, respectively [79,89]. The structures of the two compounds are shown in Figure 6.

Table 7. Isodaucane-type sesquiterpenes from *Artabotrys*.

No.	Name of Compound	Source	Reference
52	10-Oxo-isodauc-3-en-15-oic acid	*A. hongkongensis*	[79]
53	Artabotrol	*A. stenopetalus*	[89]



52 **53**

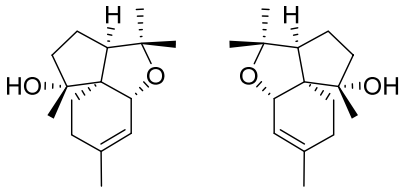
Figure 6. The structures of isodaucane-type sesquiterpenes from *Artabotrys*.

2.7. Acorane-Type Sesquiterpenes

Acorane-type sesquiterpenes are distinguished by their spiro [4.5] decane skeleton, featuring an isopropyl unit at C-1 and a dimethyl substitution at C-4 and C-8 [95]. This unique natural product category falls within the bicyclic sesquiterpene compound, known for its wide range of pharmacological activities, such as antiviral activity [96] and anti-inflammatory activity [97,98]. Despite their notable bioactivity, acorane-type sesquiterpenes are exceedingly rare in both plants and microorganisms. In a significant discovery, two acorane-type sesquiterpenes were successfully isolated from the genus of *Artabotrys* (Table 8). Compounds **54** and **55** were isolated from the roots of *A. hexapetalus* in 2017 alongside 13 bisabolane-type sesquiterpenes (**5**–**17** in Table 2) [76]. The structures of the two compounds are shown in Figure 7.

Table 8. Acorane-type sesquiterpenes from *Artabotrys*.

No.	Name of Compound	Source	Reference
54	(3*R*,4*S*,8*R*,12*R*)-Yingzhaosu E	*A. hexapetalus*	[76]
55	(3*S*,4*R*,8*S*,12*S*)-Yingzhaosu E	*A. hexapetalus*	[76]



54 **55**

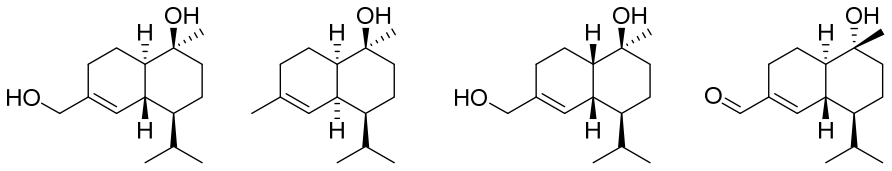
Figure 7. The structures of acorane-type sesquiterpenes from *Artabotrys*.

2.8. Cadinane-Type Sesquiterpenes

Cadinane-type sesquiterpenes, a class of bicyclic sesquiterpenes, are synthesized through the catalytic action of sesquiterpene synthase (STS) on FPP [99]. These compounds have complex stereochemistry and a wide range of pharmacological activities, such as hypoglycemic [100], antifungal [101], and anti-inflammatory [102]. To date, a considerable diversity of cadinane-type sesquiterpenes with diverse structures and biological activities have been isolated and identified from a variety of plants and microorganisms. Furthermore, with the continuous advancement of modern biotechnology, the biosynthetic pathways of representative cadinene-type sesquiterpenes have been substantially elucidated [103]. The following compounds are cadinene-type sesquiterpenes obtained from the genus of *Artabotrys* (Table 9). Notably, 10*β*, 15-hydroxy-*α*-cadinol (**56**) was isolated from both *A. pilosus* [77] and *A. hainanensis* [86]. Additionally, amorph-4-en-10*α*-ol (**57**) was isolated from the branches and leaves of *A. hainanensis* [86]. Compounds **58** and **59**, further enriching the variety of cadinene-type sesquiterpenes, were derived from the branches and leaves of *A. pilosus* [77]. The detailed structures of these compounds are depicted in Figure 8.

Table 9. Cadinane-type sesquiterpenes from *Artabotrys*.

No.	Name of Compound	Source	Reference
56	10*β*,15-Hydroxy-*α*-cadinol	*A. pilosus* *A. hainanensis*	[77] [86]
57	Amorph-4-en-10*α*-ol	*A. hainanensis*	[86]
58	15-Hydroxy-t-muurolol	*A. pilosus*	[77]
59	10*α*-Hydroxycadin-4-en-15-al	*A. pilosus*	[77]



56 **57** **58** **59**

Figure 8. The structures of cadinane-type sesquiterpenes from *Artabotrys*.

2.9. Aristolane-Type Sesquiterpenes

Aristolane-type sesquiterpenes are naturally occurring sesquiterpenes, primarily obtained from *Nardostachys*, *Axinyssa*, and *Russula* [104]. Aristolane-type sesquiterpenes

usually contain a gem-dimethyl cyclopropane structure [105], which belongs to the tricyclic sesquiterpenes. These compounds play a pivotal role in regulating serotonin transporter (SERT) to enhance or inhibit SERT [106], which offers therapeutic potential for the treatment of neuropsychiatric and digestive diseases. Advances in research and technology have enabled the isolation of several aristolane-type sesquiterpenes from *Artabotrys* plants (Table 10). 10-hydroxyaristolan-9-one (**60**), initially isolated from the stems of *A. uncinatus* in 2007, has also been found in the branches and leaves of *A. hongkongensis* in another study a few years later [79,107], alongside compounds **61**–**63** [79]. The structures of aristolane-type sesquiterpenes involved are shown in Figure 9.

Table 10. Aristolane-type sesquiterpenes from *Artabotrys*.

No.	Name of Compound	Source	Reference
60	10-Hydroxyaristolan-9-one	*A. uncinatus* *A. hongkongensis*	[107] [79]
61	Aristol-8-en-1-one	*A. hongkongensis*	[79]
62	Aristolan-9-en-1-one	*A. hongkongensis*	[79]
63	Aristolan-1,9-diene	*A. hongkongensis*	[79]

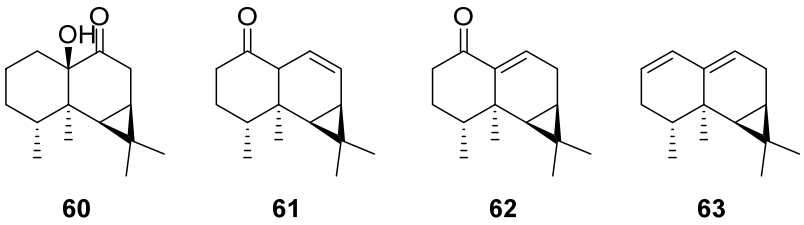


Figure 9. The structures of aristolane-type sesquiterpenes from *Artabotrys*.

2.10. Aromadendrane-Type Sesquiterpenes

Aromadendrane-type sesquiterpenes, akin to the aristolane-type sesquiterpenes mentioned earlier, belong to the tricyclic sesquiterpenes family, noted for their anti-inflammatory [108]. Studies have found that certain aromadendrane-type sesquiterpenes compounds can interact with benzoquinone to form heterodimers, offering cytoprotective effects on glutamate-induced neurological deficits [109]. The following three compounds (**64**–**65**) are classified as aromadendrane-type sesquiterpenes obtained from *Artabotrys* (Table 11). Compound **64** was obtained from branches and leaves of *A. hainanensis* [86]. The remaining compound (-)-ent-4β-hydroxy-10α-methoxyaromadendrane (**65**) was obtained from the stem of *A. uncinatus* by numerous efforts of researchers in 2007 [107]. Compounds **66** and **67** are two sesquiterpenes obtained from the flowers of *A. hexapetalus* [110]. Figure 10 shows the detailed structures of the five aromadendrane-type sesquiterpenes.

Table 11. Aromadendrane-type sesquiterpenes from *Artabotrys*.

No.	Name of Compound	Source	Reference
64	Spathulenol	*A. hainanensis*	[86]
65	(-)-Ent-4β-hydroxy-10α-Methoxyaromadendrane	*A. uncinatus*	[107]
66	Globulol	*A. hexapetalus*	[110]
67	β-Gurjunene	*A. hexapetalus*	[110]

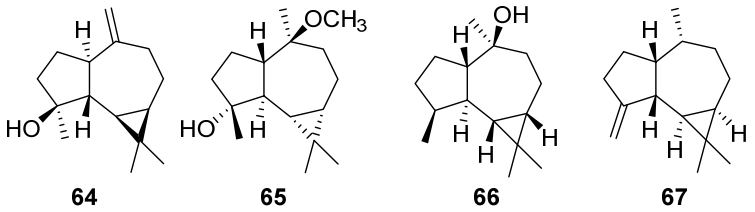


Figure 10. The structures of aromadendrane-type sesquiterpenes from *Artabotrys*.

2.11. Other Types of Sesquiterpenes

Beyond the previously mentioned sesquiterpenes, many other types of sesquiterpenes have also been obtained from the plants of *Artabotrys*, as detailed in Table 12.

Table 12. Other types of sesquiterpenes from *Artabotrys*.

No.	Name of Compound	Source	Reference
68	*β*-Caryophyllene oxide	*A. stenopetalus*	[89]
69	4-Hydroxy-4,7-dimethyl-1-tetralone	*A. pilosus* *A. hainanensis*	[77] [86]
70	Oxyphyllone D	*A. pilosus*	[77]
71	1*β*-Hydroxy-4(15),5*E*,10(14)-germacratriene	*A.hainanensis*	[86]
72	Artahongkongol A	*A. hongkongensis*	[85]
73	Clovane-2*β*,9*α*-diol	*A. hainanensis*	[91]
74	Tricyclohumuladiol	*A. hainanensis*	[91]
75	1-Methoxy-9-caryolanol	*A. uncinatus*	[107]
76	Caryolane-1,9*β*-diol	*A. uncinatus*	[107]
77	Litseachromolaevane A	*A. hainanensis*	[86]
78	Dihydroactinidiolide	*A. hainanensis*	[86]
79	10*β*-Hydroxyisodauc-6-en-14-al	*A. pilosus* *A. hainanensis*	[77] [86]
80	Homalomenol C	*A. hainanensis*	[86]
81	(4*R*,5*R*,7*R*)-1(10)-spirovetiven-11-ol-2-one	*A. hainanensis*	[86]
82	(2*R*,4*S*,8*S*,10*R*)-Artaboterpenoid A	*A. hexapetalus*	[32]
83	(−)-8*R*-Artaboterpenoid B	*A. hexapetalus*	[32]
84	(+)-8*S*-Artaboterpenoid B	*A. hexapetalus*	[32]
85	Junipediol	*A. hainanensis*	[91]

Notably, *β*-caryophyllene oxide (**68**), caryophyllene-type sesquiterpenes with a unique polycyclic structure, were isolated from the stem bark of *A. stenopetalus* [89]. Compounds **74** and **76** in Table 12 also belong to this class of sesquiterpenes. Compounds **69** and **70**, derived by reducing some carbon atoms in cadinane-type sesquiterpenes, represent a class of bicyclic sesquiterpene. 4-hydroxy-4,7-dimethyl-1-tetralone **(69)**, reduced by 3 carbons, and oxyphyllone D (**70**), reduced by 1 carbon, have been isolated from the branches and leaves of *A. pilosus* [77] and *A. hainanensis* [86], respectively. Additionally, 1*β*-hydroxy-4(15),5*E*,10(14)-germacratriene (**71**), a germacrane-type sesquiterpene, was isolated from the branches and leaves of *A. hainanensis* [86] and belongs to monocyclic sesquiterpenes. artahongkongol A (**72**), a unique trinoreudesmane sesquiterpene derived from the corresponding eudesmane-type sesquiterpenes by removing a propyl group, was obtained from the stems and leaves of *A. hongkongensis* [85]. (4*R*,5*R*,7*R*)-1(10)-spirovetiven-11-ol-2-one (**81**), a rare natural

spirovetivane-type sesquiterpene, was first isolated from the flower of *A. hainanensis* [86]. Compounds **82**, **83**, and **84** are three bisabolene-type sesquiterpenes isolated from the roots of *A. hexapetalus*, with compounds **83** and **84** identified as a pair of enantiomers [32]. The remaining compounds listed in Table 12, not described in detail here, represent unique sesquiterpenes with special structural types rare in nature isolated from *Artabotrys* plants. The specific structures of the related compounds are illustrated as follows (Figure 11).

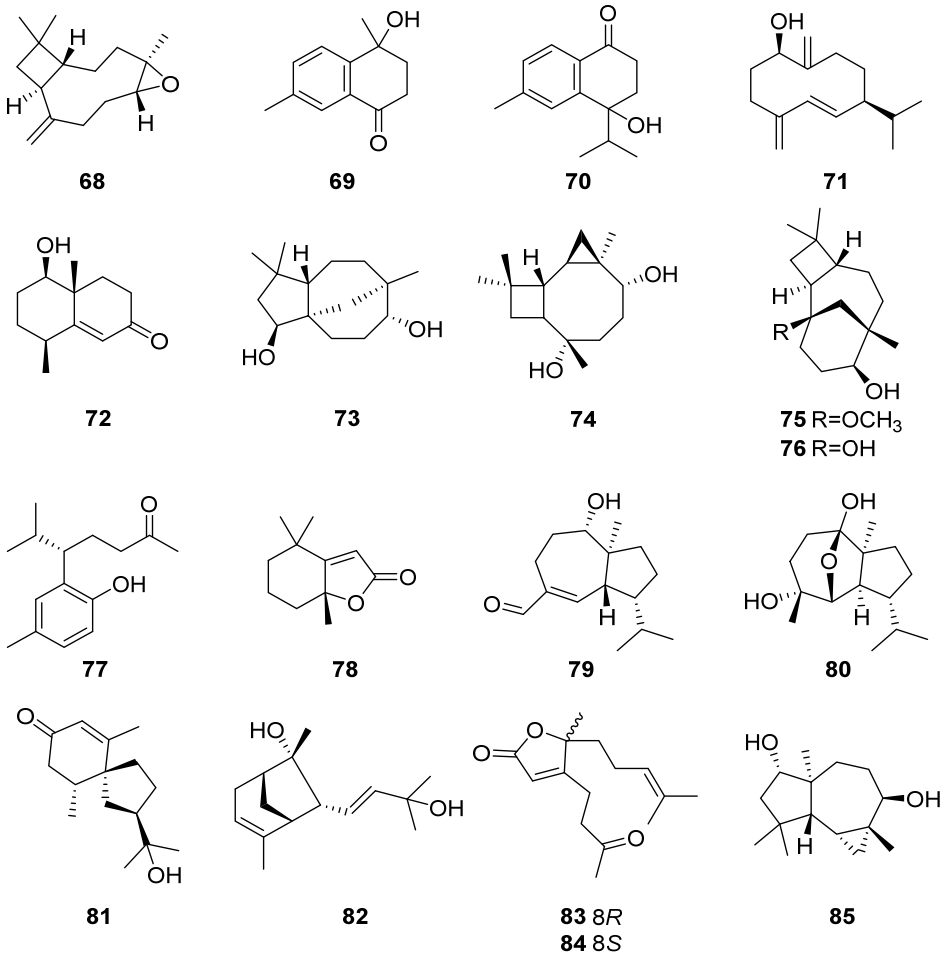


Figure 11. The structures of other types of sesquiterpenes from *Artabotrys*.

3. Pharmacological Activities

Sesquiterpenes, with their distinct carbon skeletons and roles in diverse biochemical processes, play a pivotal role in drug discovery and development. Their unique structures enable a wide array of biological and pharmacological actions, making them invaluable in modern medicinal research. In particular, sesquiterpenes from the plants of the genus *Artabotrys* have shown significant activity across numerous pharmacological studies. The following are some key pharmacological activities attributed to sesquiterpenes isolated from *Artabotrys* plants.

3.1. Antimalarial Activity

Malaria is one of the oldest diseases in humans. It is a disease caused by parasites [111] mainly transmitted to humans through mosquito bites [112]. Malaria is an infectious disease caused by malaria parasites [113–115]. Predominantly prevalent in tropical and subtropical regions, especially in Africa, South Asia, Southeast Asia, and Central America [116], malaria accounts for more than 200 million cases worldwide each year [117]. The development of effective antimalarial drugs can reduce the spread and infection of malaria and accelerate the early recovery of patients [118]. Therefore, it is of great significance

to find more effective antimalarial drugs. In the process of studying antimalarial drugs, researchers have found that some sesquiterpenes and some other natural components derived from *Artabotrys* plants have shown antimalarial activity. Notably, yingzhaosu A (**1**) is the first antimalarial drug with a clear structure containing an endoperoxide structure in history [119]. This discovery has spurred further research and the synthesis of new antimalarial drugs, although the exact mechanism of yingzhaosu A's antimalarial action remains partially understood. Current research suggests that yingzhaosu A's mechanism of action may involve two primary processes. Firstly, in the presence of oxygen and iron (II), yingzhaosu A will undergo a degradation reaction due to the induction of iron (II), forming unsaturated ketones and cyclohexyl radicals, respectively. The active substances produced in this process may be the reason for its antimalarial effect [120].

Secondly, a recent study found that when yingzhaosu A plays a role in the body, it is attacked by heme, which destroys its peroxide structure, produces tertiary oxygen-centered radicals, and rearranges to remove the side chain. Therefore, the yingzhaosu A is split into two parts. Heme is an important marker of malaria parasites. Based on the above findings, a heme-activatable probe has been successfully developed, which will play an important role in the field of antimalarial [121].

Beyond yingzhaosu A (**1**), related compounds such as yingzhaosu B (**2**), yingzhaosu C (**3**), and yingzhaosu C (**4**) have also demonstrated antimalarial effect, expanding the library of potential antimalarial agents derived from natural sources [122–124].

3.2. Antibacterial and Antifungal Activity

Bacterial infections significantly impact global health, causing widespread morbidity and mortality, and placing a significant burden on health care systems [125,126]. At present, many bacteria are resistant to antibiotics, which has become an extremely important public health problem [127–129]. However, due to the increase in global antimicrobial resistance, the efficacy of some treatments for bacterial infections is reduced or even ineffective. Therefore, it is particularly important to find new therapeutic drugs and design new treatment strategies in the field of antibacterial [130,131].

Among the promising candidates, sesquiterpenes derived from *Artabotrys* plants have demonstrated antibacterial effects through different mechanisms, showing potential against a variety of bacterial and fungal pathogens. Notably, isodaucane-type sesquiterpene artabotrol (**53**), isolated from the stem bark of *A. stenopetalus*, a plant belonging to the genus *Artabotrys*, exhibits a specific inhibitory effect on *Cryptococcus neoformans* [132].

Furthermore, globulol (**66**), isolated from the flowers of *A. hexapetalus* and the fruit of *Eucalyptus globulus* Labill, has been shown to inhibit several fungi, including *Alternaria solani*, *Fusarium oxysporum*, *Fusarium graminearum*, *Rhizoctonia solani*, and *Venturia pirina*, with a half maximal inhibitory concentration (IC_{50}) values of 47.1 μM, 114.3 μM, 53.4 μM, 56.9 μM, 32.1 μM, and 21.8 μM, respectively. In addition, the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay results showed that globulol (**66**) also had inhibitory effects on *Xanthomonas vesicatoria* and *Bacillus subtilis*, with IC_{50} values of 158.0 μM and 737.2 μM, respectively [133]. Another compound, dihydroactinidiolide (**78**) showed antibacterial activity against *Bacillus cereus* and *Vibrio parahaemolyticus* in related studies [134].

3.3. Antitumor Activity

Some sesquiterpenoids have been shown to have antitumor activity [135]. A notable example is the sesquiterpene (−)-8*R*-Artaboterpenoids B (**83**) isolated from the root of *A. hexapetalus*, which exhibited cytotoxicity against five tumor cells including HCT-116, Hep G2, A2780, NCI-H1650, and BGC-823 with IC_{50} values of 1.38, 3.30, 6.51, 8.19 and 2.14 μM, indicating its potential as an anticancer agent [32]. Similarly, another study identified seven sesquiterpenoids, chlospicate E (**18**), 1β, 6α-dihydroxy-4α (15)-epoxyeudesmane (**41**), guaianediol (**45**), 10β,15-hydroxy-α-cadinol (**56**), 15-hydroxy-t-muurolol (**58**), 10α-hydroxycadin-4-en-15-al (**59**), and 10β-hydroxyisodauc-6-en-14-al (**79**) from *A. pilosus*

showed significant inhibitory activity against HL-60, SMMC-7721, A-549, MCF-7, and SW480 human tumor cells. These compounds have the potential to develop new anti-tumor drugs as lead compounds. According to the relevant experimental results, the IC_{50} values of chlospicate E (**18**) were 14.25, 21.32, 25.34, 16.23, 10.21 μM, the IC_{50} values of 1β, 6α-dihydroxy-4α (15)-epoxyeudesmane (**41**) were 18.25, 9.65, 8.27, 4.63, 8.64 μM, the IC_{50} values of guaianediol (**45**) were 10.23, 8.64, 9.23, 10.42, 15.22 μM, the IC_{50} values of 10β,15-hydroxy-α-cadinol (**56**) were 10.11, 5.14, 4.38, 6.32, 3.28 μM, the IC_{50} values of 15-hydroxy-t-muurolol (**58**) were 2.36, 4.02, 7.32, 6.41, 5.23 μM, the IC_{50} values of 10α-hydroxycadin-4-en-15-al (**59**) were 5.23, 6.87, 4.96, 5.86, 4.20 μM and the IC_{50} values of 10β-hydroxyisodauc-6-en-14-al (**79**) were 15.23, 6.26, 10.23, 9.32, 5.49 μM, respectively. Among these compounds, 10β, 15-hydroxy-α-cadinol (**56**) had the strongest inhibitory effect on SW480 cells with an IC_{50} value of 3.28 μM, and 1β, 6α-dihydroxy-4α (15)-epoxyeudesmane (**41**) had the strongest inhibitory effect on MCF-7 cells with an IC_{50} value of 4.63 μM [77].

Further research in 2018 unveiled seven eudesmane-type sesquiterpenes (**28**–**34**) and one trinoreudesmane-type sesquiterpene (**72**) from the genus *Artabotrys*, showing cytotoxicity and inhibitory effects on five human tumor cell lines (IC_{50} values of 0.57 to 15.68 μM), with some compounds outperforming the antitumor drug doxorubicin [85]. In addition, yingzhaosu C (**3**) also demonstrated tumor inhibitory effects on HCT-116, HepG 2, and A 2780 cell lines, with IC_{50} values of 3.24, 3.23, and 3.14 μM, respectively [76]. In related studies, compound **24** was found to have a general inhibitory effect on A-549, MCF-7, HT-29, A-498, Pc-3, and PACA-2 human tumor cells, but its effect was not significant, and its IC_{50} values were 11.3, 12.3, 14.5, 16.6, 24.3, and 19.6 μM, respectively [136].

Dihydroactinidiolide (**78**) also has significant anti-tumor activity against four human tumor cell lines, epithelial cell carcinoma (Hela), human prostate cancer (PC-3), breast cancer (MCF-7), and hepatocellular carcinoma (HePG-2) [137]. Additionally, β-caryophyllene oxide (**68**) has been studied for its antitumor mechanism. It is well known that phosphoinositide 3-kinase (PI3K)/protein kinase B (AKT)/mammalian target of rapamycin (mTOR)/ribosomal protein S6 kinase 1 (S6K1) and mitogen-activated protein kinase (MAPK) signaling cascades play an important role in many physiological processes of tumor cells, including cell proliferation, survival, angiogenesis, and metastasis of tumor cells. Through Western blot analysis, MTT assay, and other research methods, it was found that β-caryophyllene oxide (**68**) not only inhibited the constitutive activation of PI3K/AKT/mTOR/S6K1 signaling cascade in human prostate cancer PC-3 and breast cancer MCF-7 cells; it also causes the activation of extracellular signal-regulated kinase (ERK), c-Jun N-terminal kinase (JNK) and p38 MAPK in tumor cells, and down-regulates various gene products related to cell proliferation, anti-apoptosis, and metastasis. In addition, in different tumor cells, β-caryophyllene oxide (**68**) can simultaneously target PI3K/AKT/mTOR/S6K1 and MAPK signaling pathways, inhibit the proliferation of related tumor cells and induce the apoptosis of tumor cells by activating caspase-3 and releasing cytochrome c. These results suggest that β-caryophyllene oxide (**68)** is a potential candidate drug for the prevention and treatment of cancer [138–140].

3.4. Anti-Inflammatory and Analgesic Activity

Inflammation is a complex immune response, which is the body's defense mechanism against injury and infection [141,142]. The five main symptoms of inflammation are pain, fever, redness, swelling, and loss of function. Inflammation can be divided into acute and chronic inflammation [143]. If inflammation is left unchecked, it may lead to autoimmune diseases, neurodegenerative diseases, etc. [144]. At present, there are many effective anti-inflammatory drugs, which are also the most common clinical treatment drugs. However, the commonly used anti-inflammatory drugs will have some side effects during the treatment [145,146]. Therefore, in addition to using traditional non-steroidal anti-inflammatory drugs to treat inflammation, some compounds isolated from natural sources are also considered new options for treating inflammatory diseases [147–150].

Among these, some natural sesquiterpenes obtained from the *Artabotrys* genus have demonstrated promising anti-inflammatory and analgesic activities. For instance, caryolane-1,9β-diol (**76**), which was found in *A.uncinatus* in 2007, exhibits significant anti-inflammatory activity in a dose-dependent manner [107,151]. Similarly, spathulenol (**64**), isolated from the twigs and leaves of *A. hainanensis* and previously found in other species such as *Psidium guineense* Sw. has shown notable inhibitory effect on the related pathological symptoms of the Cg-induced paw edema and pleurisy model in mice established in the experiment [152].

Additionally, alismol (**47**) also has anti-inflammatory effects, reducing the levels of NO and prostaglandin E2 in cells and inhibiting the expression of inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2) stimulated by lipopolysaccharide in the body. It also inhibits the messenger RNA (mRNA) and protein expression of pro-inflammatory cytokines including interleukin and tumor necrosis factor α (TNF-α) [153].

3.5. Antiviral Activity

The ongoing threat of viral infections, such as influenza virus [154], coronavirus disease 2019 (COVID-19) virus [155], and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus [156], underscores the importance of effective antiviral therapies in preventing disease spread, mitigating viral damage, and facilitating patient recovery. Antiviral drugs not only help control outbreaks and improve treatment outcomes but also minimize the risk of viral mutations and drug resistance. In this context, sesquiterpenes, a class of compounds derived from natural products, hold significant promise for antiviral drug development. Their potential for inhibiting viral activity, supporting drug development, and boosting immunity offers valuable insights for future antiviral strategies.

Research indicates that sesquiterpene compounds **3**, **11**, **12**, **17**, **54**, and **55** have inhibitory effects on Coxsackievirus B3 and influenza A virus. Specifically, compounds **3**, **54**, and **55** have moderate antiviral activity against Coxsackievirus B3, with IC_{50} values ranging from 6.41 to 33.33 μM. Meanwhile, compounds **12** and **17** showed weak inhibitory activity against the influenza A virus with IC_{50} values ranging from 19.24 to 33.33 μM [76]. Furthermore, guaianediol (**45**) obtained from *A. pilosus* in 2016 displayed anti-human immunodeficiency virus type 1 (anti-HIV-1) virus activity. In previous related studies, a variety of research methods have been used to explore its anti-HIV-1 activity, such as human immunodeficiency virus type 1 reverse transcriptase (HIV-1 RT) assay, syncytium assay, and other research methods. In addition to its significant anti-HIV-1 activity in syncytium assay, the results suggest that Guaianediol may inhibit HIV-1 RT, though its exact IC_{50} value requires further investigation [157].

3.6. Antioxidant Activity

Studies have shown that some sesquiterpene compounds have significant antioxidant activity [158,159]. These compounds can exhibit antioxidant properties in vivo through a variety of mechanisms, including scavenging free radicals, increasing antioxidant enzyme activity, and regulating oxidation-reduction balance. Among these, spathulenol (**64**) not only exhibits an anti-inflammatory effect but also demonstrates a significant antioxidant effect, with its IC_{50} value ranging from 26.13 to 85.60 μM [152]. Furthermore, studies on the dichloromethane extract of dihydroactinidiolide (**78**) have revealed its free radical scavenging activity, underscoring the antioxidant potential of sesquiterpenes [137].

3.7. Discussion on Structure-Activity Relationships

In general, compounds with the same skeleton structure are often possessed of similar biological activities and pharmacological effects. Through comparison and analysis of some compounds with the same skeleton structure, as well as known activities, the possible structure-activity relationship of some sesquiterpene compounds with the same skeleton structure is discussed.

Compounds **56**, **58**, and **59** are cadinane-type sesquiterpenes, with the same skeleton structure. They are all possessed of anti-tumor activities, but the inhibitory effect on the

same tumor cells is different. The difference in the structure of compounds **56** and **58** structure is only the difference in the hydrogen atom configuration at the C-1 position. The hydrogen atom at the C-1 position of compound **56** is the *R* configuration, and the hydrogen atom at the C-1 position of **58** is the S configuration. It is speculated that it may be the main factor affecting the pharmacological activity of the two. When the hydrogen atom at the C-1 position of the two is the *R* configuration, this may have a better inhibitory effect on the tumor cells of A-549, MCF-7, and SW480.

4. Conclusions

Artabotrys, a prominent genus within the *Annonaceae* family, is renowned for its vast global presence and rich chemical diversity, including flavonoids, alkaloids, and terpenoids. Many of the chemical components have shown good pharmacological activity and have high research value.

This paper presents a comprehensive review of the sesquiterpene compounds identified in plants and their pharmacological activities, aiming to provide a solid scientific foundation for further exploring and utilizing this genus. It also seeks to deepen the understanding of sesquiterpene compounds' pharmacological actions and mechanisms. An extensive review of research literature has cataloged approximately 85 sesquiterpene compounds and their sources from *Artabotrys* plants, categorizing them according to their structural characteristics. In addition to the common types of sesquiterpenes, such as bisabolane-type sesquiterpenes and eudesmane-type sesquiterpenes, which are rich in plant and microbial sources, this genus also harbors sesquiterpenes with special structures that are relatively rare. Pharmacological research reveals that these compounds exhibit a broad spectrum of activities, including antimalarial, anti-inflammatory, antiviral, and antitumor effects, underscoring their significant medicinal potential and positioning them as potential leads for drug development.

Despite the promising pharmacological activity, the mechanism behind the activities of sesquiterpenes from *Artabotrys* plants remains insufficiently explored, posing challenges to their clinical application of the related sesquiterpenes. Furthermore, many sesquiterpene components in the genus of *Artabotrys* remain undiscovered, suggesting vast opportunities for future research. It is anticipated that ongoing studies will uncover new sesquiterpene compounds and elucidate their mechanisms of action, enhancing the therapeutic value of *Artabotrys* sesquiterpenes.

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Abbreviations

NMR	Nuclear magnetic resonance
FPP	Farnesyl diphosphate
LPS	Lipopolysaccharide
STS	Sesquiterpene synthase
SERT	Regulating serotonin transporter
IC_{50}	Half maximal inhibitory concentration
MTT	3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide
PI3K	Phosphoinositide 3-kinase
AKT	Protein kinase B
mTOR	Mammalian target of rapamycin
S6K1	Ribosomal protein S6 kinase 1
MAPK	Mitogen-activated protein kinase
ERK	Extracellular signal-regulated kinase
JNK	c-Jun N-terminal kinase
iNOS	Inducible nitric oxide synthase
COX-2	Cyclooxygenase-2
mRNA	Messenger RNA
TNF-α	Tumor necrosis factor α
COVID-19	Coronavirus disease 2019
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
anti-HIV-1	Anti-human immunodeficiency virus type 1
HIV-1 RT	Human immunodeficiency virus type 1 reverse transcriptase

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