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Ailanthus triphysa: a review of phytochemistry and pharmacology

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Abstract. This article summarizes recent research reports on the chemical composition and biological activities of *Ailanthus triphysa* (Dennstedt) Alston. About 92 compounds have been found from this species, including 11 alkaloids, 48 triterpenoids, 4 quassinoids, 5 steroids and diterpenoids, 2 flavonoids, 6 benzopyranoids, 10 fatty aldehydes, acids, and 6 other compounds. Many of the compounds have unique structures and exhibit potential biological activities including antibacterial, antioxidant, antifungal, anti-inflammatory, anticancer, and cytotoxic activities. This review aims to systematically provide research results on the botany, phytochemistry and pharmacology of *Ailanthus triphysa*.

Keywords: Simaroubaceae, *Ailanthus triphysa*, *Ailanthus malabarica*, phytochemistry, pharmacology.

Classification numbers: 1.1, 1.2, 1.4

1. INTRODUCTION

Ailanthus triphysa (Dennstedt) Alston (family Simaroubaceae) (abbreviation as *A. triphysa*) is a deciduous tree with a tall cylindrical trunk reaching about 30 m in height, with noticeably light and soft wood. It is widely distributed in tropical and subtropical regions, such as China, India, Australia, Thailand, Viet Nam, Cambodia, Laos, Myanmar, and Bangladesh [1]. The species *A. triphysa* was first scientifically described by (Dennstedt) Alston in 1818. Plants of the World Online (2024) has arranged and listed 13 other synonyms of this species [2], including *Adenanthera triphysa* Dennst., *Ailanthus fauveliana* Pierre ex Laness., *Ailanthus imberbiflora* F. Muell., *Ailanthus imberbiflora* var. *macartneyi* F. M. Bailey., *Ailanthus kurzii* Prain., *Ailanthus malabarica* DC., *Ailanthus philippinensis* Merr., *Hebonga mollis* Radlk., *Hebonga obliqua* Radlk., *Hebonga siamensis* Radlk., *Pongelion fauvelianum* (Pierre ex Laness.) Pierre.,

Pongelion imberbiflorum (F. Muell.) Pierre. and *Pongelion malabaricum* Pierre. The oleoresin exuded from the wounded trunk of *A. triphysa* is aromatic and is used in the manufacture of incense and is a commercial commodity in India. *A. triphysa* is considered an important medicinal plant for the treatment of dysentery, indigestion, fever, and bronchitis [3, 4]. The bark of *A. triphysa* is considered a valuable tonic, antipyretic, and antiflatulent [5, 6]. The bark of *A. triphysa* contains a reddish-brown, water-soluble wax containing a bitter principle, called ailantic acid. It is used as a tonic and alternative for indigestion and constipation [7]. The root bark of *Ailanthus malabarica (A. malabarica)* is also used in snakebites; it is pounded and soaked in ginger oil and taken orally as an antidote, especially in cases of cobra bites [8]. In addition, this plant is also used to treat dysentery and vaginal discharge, and to treat fever in folk medicine [9, 10].

Currently, 92 compounds have been isolated and identified from *A. triphysa*, including alkaloids, triterpenoids, quassinoids, steroids, flavonoids, benzopyranoids, and fatty aldehydes, acids [3, 4, 11 - 21]. Modern pharmacological studies have shown that the isolated components and crude extracts of *A. triphysa* have antioxidant, antibacterial, antifungal, anti-inflammatory, antimalarial, and cytotoxic activities [4, 14, 16, 22 - 25]. However, the full relationship between these pharmacological effects and the traditional uses of *A. triphysa* has not been established, and the biological activities of only a few components have been explored. Therefore, more *in vitro* and *in vivo* experiments are needed to critically evaluate the clinical efficacy and safety of *A. triphysa*. To our knowledge, there is still a lack of comprehensive and valuable knowledge regarding *A. triphysa*. Therefore, in this review, we summarize and analyze the botany, phytochemistry, and pharmacology properties of *A. triphysa*. It is expected that the information presented in this review will provide an overview of *A. triphysa* for researchers to identify further research directions.

2. BOTANY

2.1. Botanical characteristics

Ailanthus triphysa is a lofty tree, usually 15-20 m tall. Leaves are odd-pinnate, 40-60 cm long, growing concentrated near the top of the branches; the leaflets grow alternately, the leaf blade is slightly curved like a sickle, with 6 - 17 pairs of leaves; the leaf stalks are hairy, 5 - 7 mm long, the old leaves are red. The inflorescences grow in cymes, arranged in panicles at the leaf axils, about 20 - 25 cm long. The fruit is oval, surrounded by wings, measuring 4.5 - 8 cm in length and 1.5 - 2.5 cm in width, with both ends slightly blunt. The fruit shell is cut to obtain a reddish-brown resin with a fragrant smell. In India, it is called matipaula. When burned, the resin gives off a pleasant aroma. The seeds are round and flat [1, 10, 26, 27].

2.2. Distribution

A. triphysa is distributed mainly in Asia. The official website, Plants of the World Online, states that the main production areas of *A. triphysa* are in Andaman Is., Borneo, Cambodia, South Central China, Southeast China, India, Java, Laos, Malaya, Maluku, Myanmar, Philippines, Queensland, Sri Lanka, Sulawesi, Thailand, Viet Nam (https://powo.science.kew.org) (Figure 1).

3. CHEMICAL COMPONENTS

To date, 92 compounds have been isolated from *A. triphysa*, of which 82 compounds were isolated and characterized by high-performance liquid chromatography (HPLC), Sephadex LH-

20 column chromatography, thin-layer chromatography, silica gel column chromatography, nuclear magnetic resonance, ultraviolet-visible, and infrared spectroscopy. The remaining compounds were found by GC-MS analysis (fatty acids and their derivatives). Most of these compounds are alkaloids, triterpenoids, steroids, flavonoids, and benzopyranoids (Table 1 and Figure 2). Their structures are shown in Figures 3 - 5. In addition, their names, the respective botanical sources, the structural framework, and the chronology of the publications are listed in Table 1.

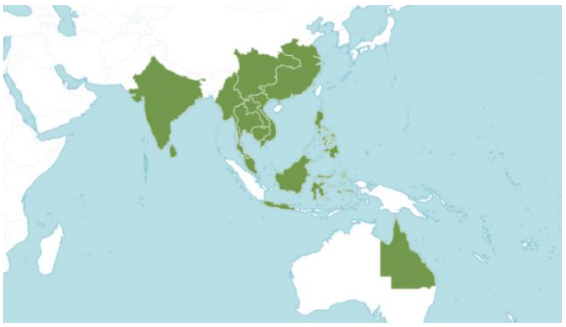

Figure 1. Worldwide distribution of *Ailanthus triphysa* (Dennstedt) Alston.

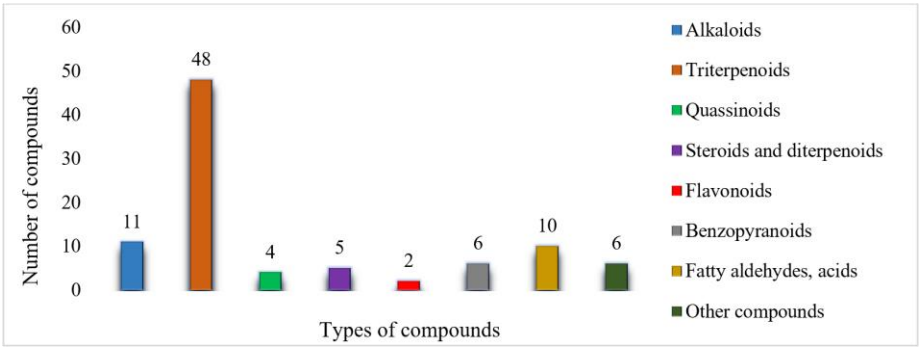

Figure 2. Types and numbers of isolated compounds from *A. triphysa*.

Table 1. Isolated compounds from *A. triphysa*.

Comp.	Name	Bioactivity	Parts Used*
	Alkaloids		
1	1-Ethyl-*β*-carboline	Antihypertensive effect [28]	SW [11]
2	1-Ethyl-4-methoxy-*β*-carboline	Antibacterial [29], antimalarial activity [30]	SW [11]
3	1-Ethyl-4,8-dimethoxy-*β*-carboline		RB [12]
4	4,8-Dimethoxy-1-vinyl-*β*-carboline	Anti-inflammatory [31-33]	RB [12]
5	*β*-Carboline-1-propionic acid	Antileishmanial [34]	SW [11]
6	1-Acetyl-*β*-carboline	Anti-MRSA [35] (methicillin-resistant *Staphylococcus aureus*), antifungal [36], melanogenic stimulating activity [37]	RB [12]
7	1-Carbamoyl-*β*-carboline	Antifungal activity [38]	RB [12]
8	Canthine-6-one	Anti-inflammatory activity [39]	SW [11]
9	1-Hydroxycanthine-6-one		SW [11]
10	Canthine-6-one-3-*N*-oxide	Cytotoxic [40], antiparasitic,	SW [11]

Comp.	Name	Bioactivity	Parts Used*
		antifungal activity [41]	
11	Ailanindole		SW [11]
	Triterpenoids		
	Malabaricanes		
12	(14*S*,17*S*,20*S*)-14,17,20-Trihydroxy-24-malabaricen-3-one	Antibacterial activity [4]	O [4]
13	(14*S*,17*S*,20*S*,24*S*)-14,17,20,24,25-Pentahydroxy-malabarican-3-one		O [4]
14	(17*R*,20*R*,24*R*)-17,20,24,25-Tetrahydroxy-14(18)-malabaricen-3-one	Antibacterial activity [4]	O [4]
15	(17*R*,20*R*,24*R*)-17,20,24,25-Tetrahydroxy-14(18)-malabaricen-3β-ol		O [4]
16	(14*S*,17*R*,20*S*)-20-Hydroxy-14,17-epoxy-24-malabaricen-3-one (malabaricol)	Antibacterial [4], antifungal activity [42]	O, B [4, 13-15]
17	(14*S*,17*R*,20*S*)-14,17-Epoxy-24-malabaricen-3β,20-diol	Antibacterial activity [4]	O [4]
18	(14*S*,17*R*,20*S*)-14,17-Epoxy-23-malabaricen-3β,20,25-triol (ailanthusin F)		S, SB [14]
19	(14*S*,17*R*,20*S*)-20,24-Dihydroxy-14,17-epoxy-25(26)-malabaricen-3-one (ailanthusin G)		S, SB [14]
20	(14*S*,17*R*,20*S*,24*R*)-25-Hydroxy-14,17:20,24-diepoxymalabarican-3-one (epoxymalabaricol)	Antibacterial [4], antifungal activity [42]	O [4]
21	(14*S*,17*S*,20*S*,24*R*)-20,24,25-Trihydroxy-14,17-cyclomalabarican-3-one	Antibacterial activity [4]	O [4]
22	(14*S*,17*S*,20*S*,24*R*)-25-Hydroxy-14,17-cyclo-20,24-epoxy-malabarican-3-one	Antibacterial activity [4]	O [4]
23	(17*S*,20*R*,24*R*)-17,25-Dihydroxy-20,24-epoxy-14(18)-malabaricen-3-one	Antibacterial activity [4]	O [4]
	Dammaranes		
24	Hydroxydammarenone I and II	Antiviral [43], antioxidant, anti-human acyl-CoA:cholesterol acyl*trans*ferase [44]	S, SB [14]
25	Altissimanin C		S, SB [14]
26	Gardaubryone C		S, SB [14]
27	Ocotillone	Antifungal [42], antibacterial activity [45]	S,SB [14]
	Tirucallanes		
28	3-Oxotirucalla-7,24-dien-23-ol		S, SB [14]
29	(23*Z*)-25-Hydroxy-tirucalla-7,23-dien-3-one		S, SB [14]
30	(-)-Leucophyllone	Antidiabetic activity [46]	S, SB [14]
31	24*S*,25-Dihydroxytirucall-7-en-3-one	Cytotoxic activity [47]	L [16]
32	25-methoxy-24α-hydroxytirucallane-7-en-3-one (ailantriphysa C)		L [16]
33	25-Methoxy-24β-hydroxytirucallane-7-en-3-one (ailantriphysa D)		L [16]
34	Phellochin		L [16]
35	Hispidol B 25-methyl ether		L [16]
36	meliasenin G		L [16]
37	21α,25-Dimethylmelianodiol	Antibacterial activity [48]	S, SB [14]

Comp.	Name	Bioactivity	Parts Used*
38	25-Methoxy-7*α*,23*α*,24*β*-trihydroxytirucallane-8-en-3-one (ailantriphysa A)	Anti-inflammatory activity [16]	L [16]
39	25-Methoxy-7*α*,24*α*-dihydroxytirucallane-8-en-3-one (ailantriphysa B)	Anti-inflammatory activity [16]	L [16]
	Apotirucallanes		
40	21-*O*-Methyltoosendanpentol	Cytotoxic activity [49]	L [16]
41	Agladupol A		L [16]
	Cycloapotirucallanes		
42	Ailanthol	Cytotoxic activity [3]	R, B [3, 17]
43	7*α*,25-Dihydroxy-3-oxo-14,18-cycloapotirucalla-1,20(22),23(*Z*)-trien-21,23-olide (ailanthusin A)		S, SB [14]
44	7*α*,25-Dihydroxy-3-oxo-14,18-cycloapotirucalla-1,20(22),23(*E*)-trien-21,23-olide (ailanthusin B)		S, SB [14]
45	7*α*,25-Dihydroxy-3-oxo-14,18-cycloapotirucalla-20(22),23(*E*)-dien-21,23-olide (ailanthusin C)		S, SB [14]
46	7*α*,23,24-Trihydroxy-3-oxo-14,18-cycloapotirucalla-1,20(22),25(26)-trien-21-oic acid (ailanthusin D)		S, SB [14]
47	7*α*-Hydroxy-20,21,22,23,24,25,26,27-octanor-14,18-cycloapotirucalla-3,17-dione (ailanthusin E)		S, SB [14]
48	Malabanone A	Cytotoxic activity [3]	B [3, 14]
49	Malabanone B	Cytotoxic activity [3]	B [3]
	Lupanes		
50	29-Norlup-1-ene-3,20-dione		S, SB [14]
51	Glochidone	Antibacterial, antifungal, anti-inflammatory, anticancer, antidiabetic, antioxidant, cytotoxic activity [50-52]	S, SB [14]
52	Glochidonol	Antibacterial activity [53]	S, SB [14]
53	Lupenone	Cytotoxic activity [51]	S, SB [14]
54	Glochidiol	Cytotoxic, anticancer activity [51]	S, SB [14]
55	3-*Epi*-lupeol	Cytotoxic activity [52]	S, SB [14]
56	Lupeol	Antioxidant, anti-inflammatory, antiarthritic, antimutagenic, antimalarial and anticancer activity [54-56]	S, SB [14]
57	Lup-20(29)-ene-1*β*,3*β*-diol		S, SB [14]
	Oleananes		
58	Olean-12-ene-3,11-dione		T [18]
59	*β*-Amyrin	Anti-inflammatory, antioxidant [57], Antibacterial activity [58]	T [18]
	Quassinoids		
60	Ailanquassin A		SW [11]
61	Ailanquassin B		SW [11]

Comp.	Name	Bioactivity	Parts Used*
62	Chaparrinone	Antitumor, antiviral, antileukemic, antimalarial, phytotoxic, antifeedant [59]	SW [11]
63	13,18-Dehydroexcelsin		B [19]
	Steroids and diterpenoids		
64	*β*-Sitosterol	Analgesic, antimutagenic activity [60, 61]	T [18]
65	Sitosterol-3-*O*-*β*-D-glucoside	Antibacterial activity [62]	T [18]
66	6*α*,7*β*-dihydroxy-17(20)-*cis*-5*α*-pregna-16-one		L [20]
67	8(14),15-Isopimaradiene-2*α*,3*α*,19-triol		L [20]
68	Phyllocladan-16*α*,19-diol	Cytotoxic activity [63]	L [20]
	Flavonoids		
69	Kaempferol-3-*O*-*β*-D-galactopyranoside (trifolin)	Antiproliferative [64], anticancer activity [65]	L [20]
70	Kaempferol-3-*O*-*α*-L-rhamnopyranoside (afzelin)	Antitumor [66, 67], antioxidant activity [68]	L [20]
	Benzopyranoids		
71	Scopoletin	Antibacterial, antioxidant, antifungal, anti-inflammatory, anticancer, and cytotoxic activities [69]	L [20]
72	6-Methoxy-7-prenyloxycoumarin		T [14]
73	Scopolin	Acetylcholinesterase inhibitory activity [70]	T [18]
74	4,7-Dimethoxy-5-methylcoumarin	Metabolite of *Aspergillus variecolor* [71]	T [18]
75	4,6,7-Trimethoxy-5-methylcoumarin	Antiangiogenic activity [72]	T [18]
76	2-Isopropyl-5-methylcyclohexyl-3-(1-(4-chlorophenyl)-3-oxobutyl)-coumarin-4-yl cacbonate	Anti-inflammatory [73], Antibacterial activity [74]	L [21]
	Fatty aldehyde, **acid compounds**		
77	Dodecanal	Antibacterial activity [75, 76]	L [21]
78	Hexadecanal		L [21]
79	Pentadecanoic acid	Anti-inflammatory activity [77]	L [21]
80	Stearic acid	Antitumor activity [78]	T [18]
81	(9*R*,10*E*,12*Z*)-9-Hydroxyoctadecadienoic acid		S, SB [14]
82	14-Methyl-pentadecanoic acid methyl ester	Antitumor activity, analgesic [79]	L [21]
83	(*Z*)-9-Octadecenoic acid methyl ester	Antifungal activity [80]	L [21]
84	Heptacosanoic acid methyl ester		L [21]
85	Gheddic acid		T [18]
86	Glycerol 2-lacceroate		T [18]
	Other compounds		
87	(-)-Pyrocatechuic acid	Anti-nephrotoxic activity [81]	T [18]
88	Protocatechuic acid methyl ester	Antifungal [82], neurological effects [83], modulates fluoride induced pulmonary toxicity in rats [84], antibacterial activity [85]	T [18]

Comp.	Name	Bioactivity	Parts Used*
89	(-)-Pyrocatechuic acid (4α→6)-pyrocatechuic acid		T [18]
90	Iodobis(*n*,*n*-diisobutyldithio-carbamato)arsine		L [21]
91	2,4-Dimetyl-7-oxo-4,7-dihydro-triazolo(3,2-*c*)triazine		L [21]
92	Squalene	Antioxidant, antitumor activity [86]	L [21]

**SW: Stem wood; RB: Root bark; O: Oleoresin; SB: stem bark; L: Leaves;S: Stem; B: Bark; T: Twigs; R: Roots*

3.1. Alkaloids

A total of eleven indole alkaloids have been reported from *A. triphysa*, of which the majority are relatively simple naturally occurring β-carboline derivatives (Figure 3). The β-carboline derivatives include 1-ethyl-β-carboline (**1**), 1-ethyl-4-methoxy-β-carboline (**2**), 1-ethyl-4,8-dimethoxy-β-carboline (**3**), 4,8-dimethoxy-1-vinyl-β-carboline (**4**), β-carboline-1-propionic acid (**5**), 1-acetyl-β-carboline (**6**), and 1-carbamoyl-β-carboline (**7**). In addition, two alkaloids with canthine-6-one structure, including canthine-6-one (**8**) and 1-hydroxycanthine-6-one (**9**), and two other alkaloids, including canthine-6-one-3-*N*-oxide (**10**) and especiallyailanindole (**11**) is a new compound isolated for the first time from *A. triphysa*.

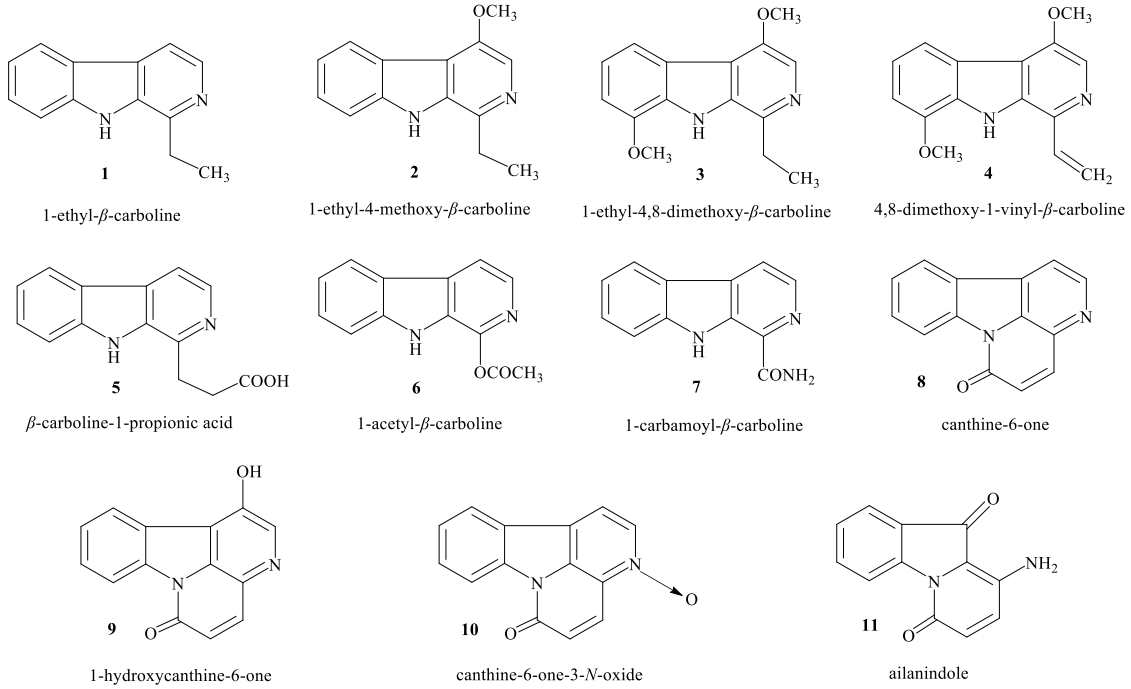

Figure 3. Alkaloids from *A. triphysa*.

3.2. Triterpenoids

To date, 48 triterpenoid compounds have been isolated and their structures determined from different parts of *A. triphysa*, arranged in decreasing order of the number of isolated compounds, including malabaricane (12 compounds), tirucallanes (12 compounds), cycloapotirucallanes (8

compounds), lupanes (8 compounds), dammaranes (4 compounds), apotirucallanes (2 compounds), and oleananes (2 compounds) (Figures 4 and 5).

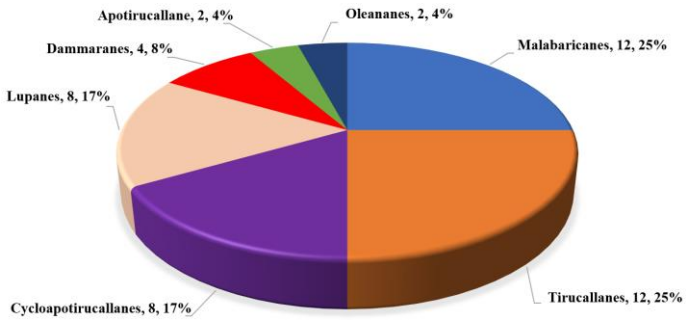

Figure 4. Classes of triterpenoids isolated from the bark of *A. triphysa*.

The first new malabaricane derivative to be discovered and isolated from the oleoresin of *A. triphysa* was (14*S*,17*R*,20*S*)-20-hydroxy-14,17-epoxy-24-malabaricen-3-one (**16**), commonly known as malabaricol. Later, other studies also reported the isolation and identification of eight new malabaricane derivatives from the oleoresin of *A. triphysa*, including (14*S*,17*S*,20*S*)-14,17,20-trihydroxy-24-malabaricen-3-one (**12**), (14*S*,17*S*,20*S*,24*S*)-14,17,20,24,25-pentahydroxy-malabarican-3-one (**13**), (17*R*,20*R*,24*R*)-17,20,24,25-tetrahydroxy-14(18)-malabaricen-3-one (**14**), (17*R*,20*R*,24*R*)-17,20,24,25-tetrahydroxy-14(18)-malabaricen-3*β*-ol (**15**), (14*S*,17*R*,20*S*)-14,17-epoxy-23-malabaricen-3*β*,20,25-triol (**18**), (14*S*,17*R*,20*S*)-20,24-dihydroxy-14,17-epoxy-25(26)-malabaricen-3-one (**19**), (14*S*,17*S*,20*S*,24*R*)-20,24,25-trihydroxy-14,17-cyclomalabarican-3-one (**21**) and (14*S*,17*S*,20*S*,24*R*)-25-hydroxy-14,17-cyclo-20,24-epoxy-malabarican-3-one (**22**). Three known malabaricane derivatives were isolated from this species, including (14*S*,17*R*,20*S*)-14,17-epoxy-24-malabaricen-3*β*,20-diol (**17**), (14*S*,17*R*,20*S*,24*R*)-25-hydroxy-14,17,20,24-diepoxymalabarican-3-one (**20**), and (17*S*,20*R*,24*R*)-17,25-dihydroxy-20,24-epoxy-14(18)-malabaricen-3-one (**23**). In a study on the stem and bark of *A. triphysa*, Thongnest *et al.* [14] identified four dammarane-type triterpenoid derivatives, including hydroxydammarenone I and II (**24**), altissimanin C (**25**), gardaubryone C (**26**), and ocotillone (**27**). In the same study on the stem and bark of *A. triphysa*, Thongnest *et al.* [14] also identified four known compounds belonging to the triterpenoid tirucallane derivatives, including 3-oxotirucalla-7,24-dien-23-ol (**28**), (23*Z*)-25-hydroxy-tirucalla-7,23-dien-3-one (**29**), (-)-leucophyllone (**30**), and 21*α*,25-dimethylmelianodiol (**37**). In another study, from the leaves of *A. triphysa*, Duy *et al.* [16] isolated and determined the structures of eight compounds belonging to tirucallane derivatives, four new compounds, including 25-methoxy-24*α*-hydroxytirucallane-7-en-3-one (**32**), 25-methoxy-24*β*-hydroxytirucallane-7-en-3-one (**33**), 25-methoxy-7*α*,23*α*,24*β*-trihydroxytirucallane-8-en-3-one (**38**) and 25-methoxy-7*α*,24*α*-dihydroxytirucallane-8-en-3-one (**39**), and four other known compounds, including 24*S*,25-dihydroxytirucall-7-en-3-one (**31**), phellochin (**34**), hispidol B 25-methyl ether (**35**) and meliasenin G (**36**).

In addition, in the same study from the leaves of *A. triphysa*, Duy *et al* [16] also found two apotirucallane derivatives, including 21-*O*-methyltoosendanpentol (**40**) and agladupol A (**41**). However, in a previous study of the roots and bark of *A. triphysa*, the authors discovered a cycloapotirucallanes derivative, ailanthol (**42**), a new compound with a tricyclo[4.3.1.0]decane structure. Another study from the bark of this species isolated and determined the structures of two new compounds, malabanone A (**48**) and malabanone B (**49**).

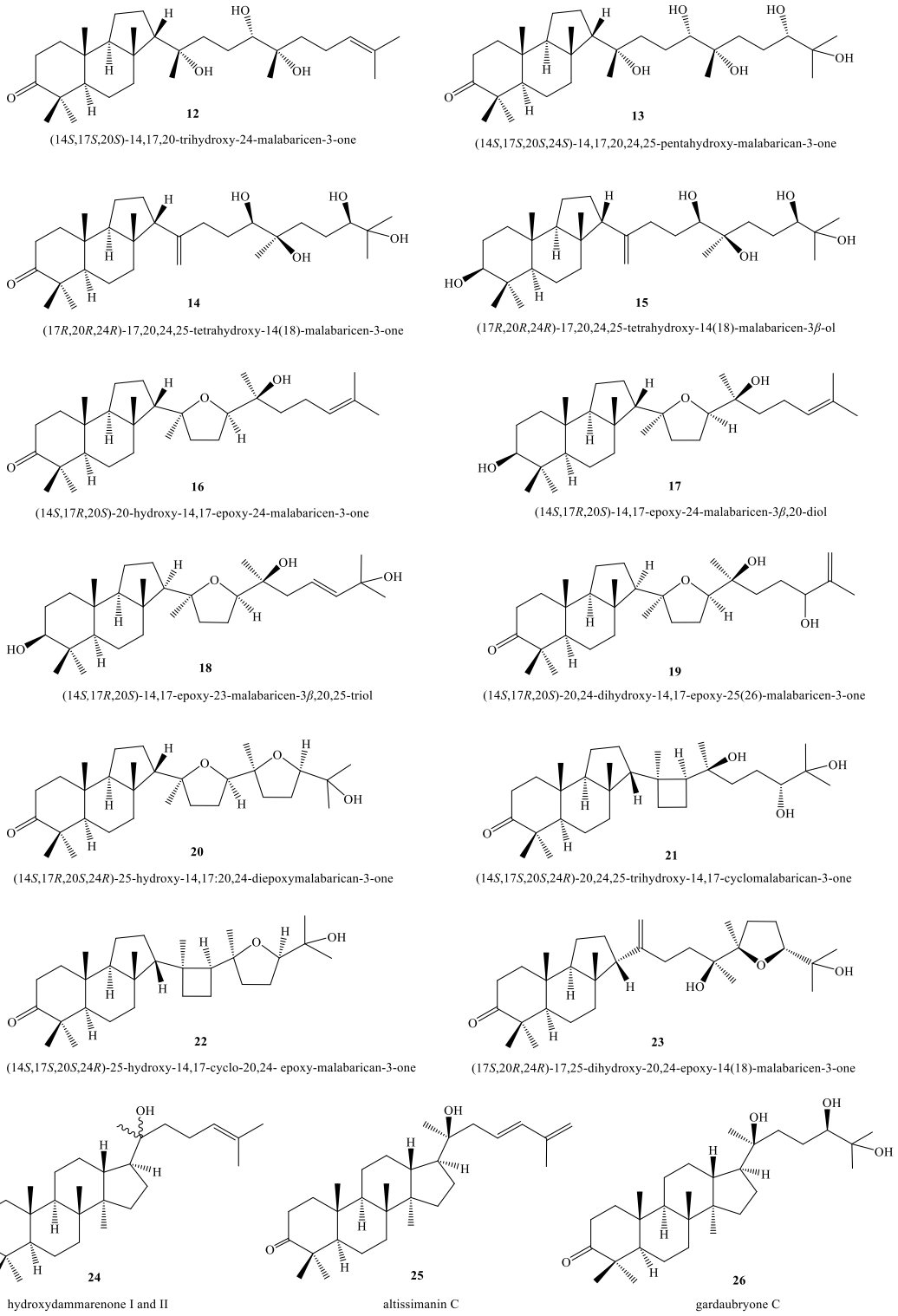

Figure 5. Triterpenoids from *A. triphysa.*

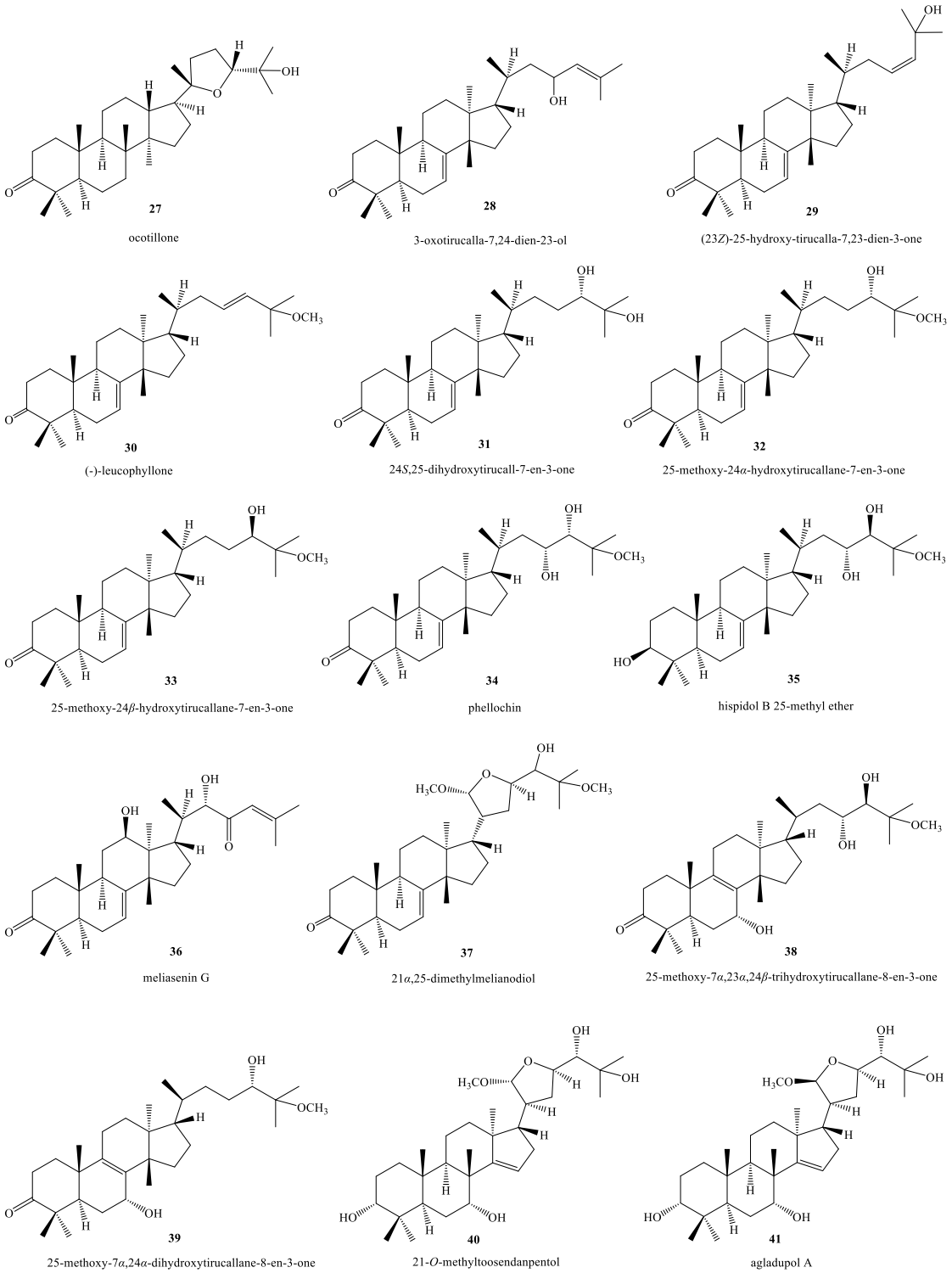

Figure 5. Triterpenoids from *A. triphysa* (*continued*).

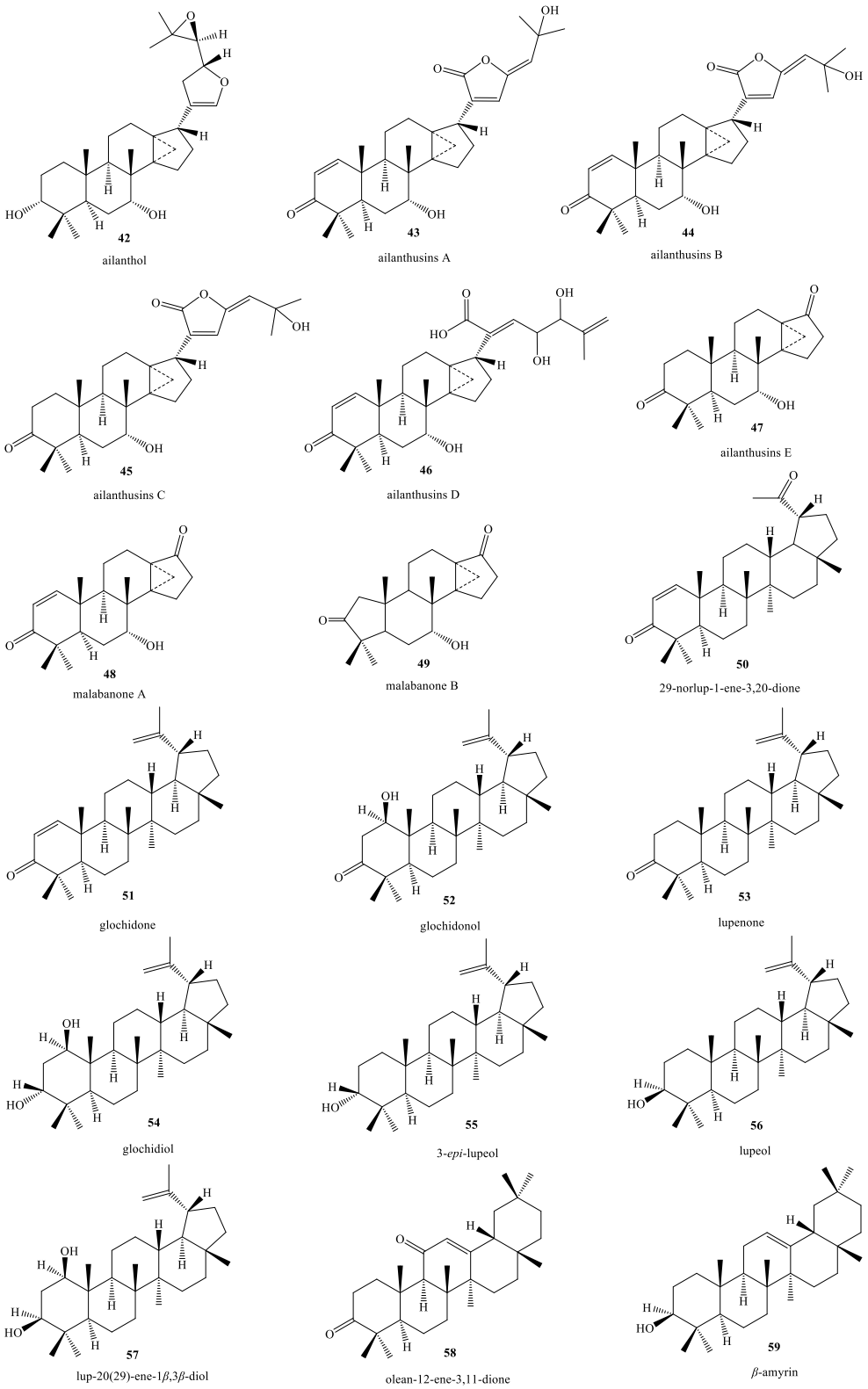

Figure 5. Triterpenoids from *A. triphysa* (*continued*).

This report also suggested that these two compounds were considered to be biosynthesized from ailanthol (**42**). Up to now, an investigation of the stem and bark of *A. triphysa* has isolated and determined five other new compounds belonging to the cycloapotirucallane derivatives, including ailanthusins A-D (**43-47**). Eight lupane triterpenoid derivatives were isolated from the stem and bark of *A. triphysa*, including a new compound 29-norlup-1-ene-3,20-dione (**50**) and seven other known compounds, including glochidone (**51**), glochidonol (**52**), lupenone (**53**), glochidiol (**54**), lupeol (**56**), and lup-20(29)-ene-1*β*,3*β*-diol (**57**). Two known oleanane triterpenoid derivatives were also isolated from the twigs of *A. triphysa*, olean-12-ene-3,11-dione (**58**) and *β*-amyrin (**59**).

3.3. Quassinoids

In a study on the woody stem of *A. triphysa*, Aono *et al*. found three triterpenoid quassinoid derivatives isolated, of which ailanquassin A (**60**) and ailanquassin B (**61**) were two new compounds, and one known compound was chaparrinone (**62**). In addition, another study on the bark of this species also isolated another derivative, 13,18-dehydroexcelsin (**63**) (Figure 6).

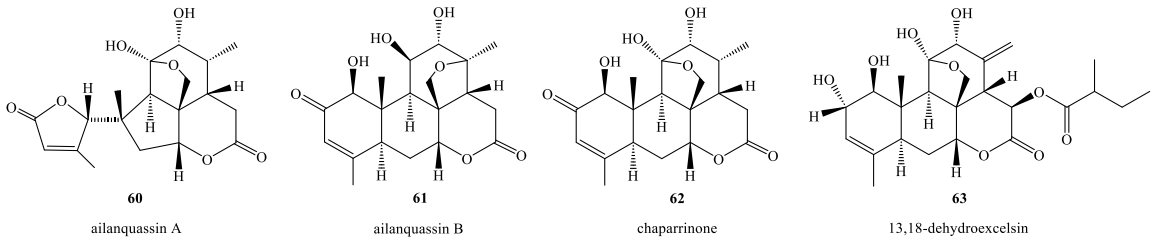

Figure 6. Quassinoids from *A. triphysa*.

3.4. Steroids and diterpenoids

Three steroids (**64**-**66**) and two diterpenoids (**67** and **68**) were isolated from the branches and leaves of *A. triphysa*. Of which, two compounds were isolated and structurally characterized from the leaves of this species, including two news, 6*α*,7*β*-dihydroxy-17(20)-*cis*-5*α*-pregna-16-one (**66**) and 8(14),15-isopimaradiene-2*α*,3*α*,19-triol (**67**), and three other known compounds, *β*-sitosterol (**64**), sitosterol-3-*O*-*β*-D-glucoside (**65**), and phyllocladan-16*α*,19-diol (**68**) (Figure 7).

3.5. Flavonoids

To date, only two flavonoid derivatives have been isolated from the leaves of *A. triphysa*, including kaempferol-3-*O*-*β*-D-galactopyranoside (**69**) and kaempferol-3-*O*-*α*-L-rhamnopyranoside (**70**) (Figure 8*)*.

3.6. Benzopyranoids

Six coumarin-type benzopyranoid derivatives have been reported from *A. triphysa*. Among them, four compounds, scopoletin (**71**), scopolin (**73**), 4,7-dimethoxy-5-methylcoumarin (**74**) and 4,6,7-trimethoxy-5-methylcoumarin (**75**), were isolated and structurally elucidated by the same research group from the leaves and branches of the species. Recently, 6-methoxy-7-prenyloxycoumarin (**72**) was also isolated. In contrast, 2-isopropyl-5-methylcyclohexyl-3-(1-(4-chlorophenyl)-3-oxobutyl)-coumarin-4-yl carbonate (**76**) was identified solely by GC-MS analysis of the ultrasonic ethyl acetate extract of *A. triphysa* (Figure 9).

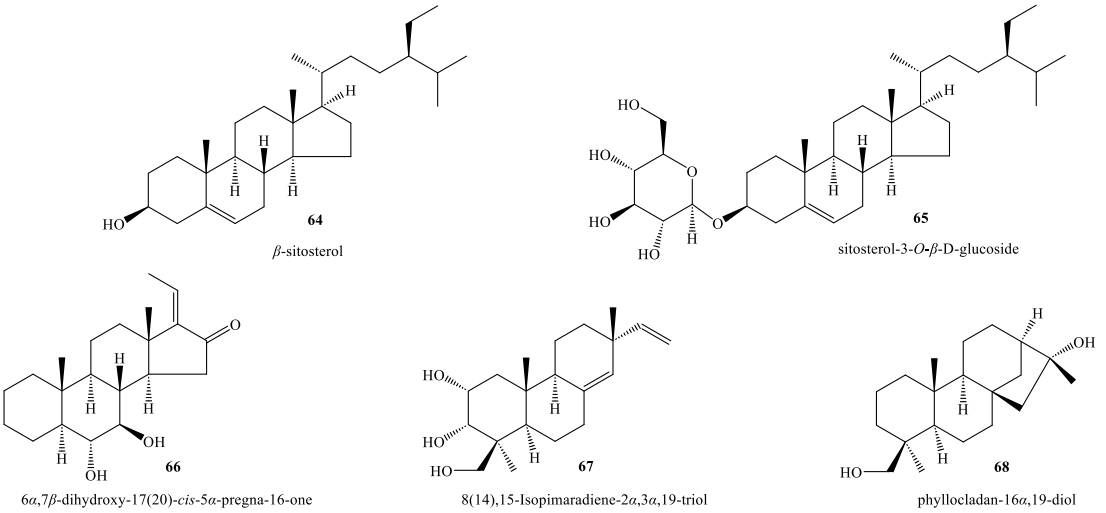

Figure 7. Steroids and diterpenoids from *A. triphysa*.

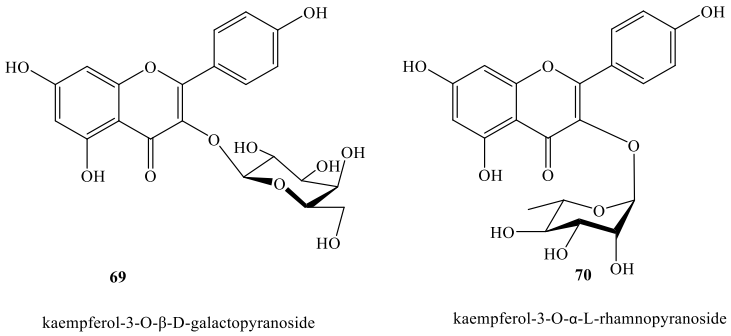

Figure 8. Flavonoids from *A. triphysa*.

3.7. Fatty aldehyde, acid compounds

A total of ten compounds belonging to the lipid group were found in the leaves and branches of *A. triphysa* (Figure 10). Two fatty aldehydes, dodecanal (**77**) and hexadecanal (**78**), were isolated from the leaves and branches of *A. triphysa* by GC-MS analysis of the ultrasonic ethyl acetate extract of the leaves of *A. triphysa*. In the same study, Yadav *et al*. [21] also found one fatty acid, pentadecanoic acid (**79**), and three other fatty acid methyl esters, 14-methyl-pentadecanoic acid methyl ester (**82**), (*Z*)-9-octadecenoic acid methyl ester (**83**), and heptacosanoic acid methyl ester (**84**). In another study, Shu-Hua *et al*. [18] isolated two fatty acids, stearic acid (**80**), gheddic acid (**85**), and one fatty acid methyl ester glycerol 2-lacceroate (**86**) from the branches of *A. triphysa*. Recently, a research report also isolated a fatty acid (9*R*,10*E*,12*Z*)-9-hydroxyoctadecadienoic acid (**81**) from the stem and bark of this species.

3.8. Other compounds

Six other compounds have been reported to be isolated and detected from the branches and leaves of *A. triphysa*, including three natural benzoic acid derivatives isolated from the branches of *A. triphysa*, including (-)-pyrocatechuic acid (**87**), protocatechuic acid methyl ester (**88**) and (-)-pyrocatechuic acid (4α→6)-pyrocatechuic acid (**89**), and three other compounds found by GC-

MS analysis from the ultrasonic ethyl acetate extract of *A. triphysa* leaves, iodobis(n,n-diisobutyldithiocarbamato)arsine (**90**), 2,4-dimethyl-7-oxo-4,7-dihydro-triazolo(3,2-c)triazine (**91**) and squalene (**92**) (Figure 11).

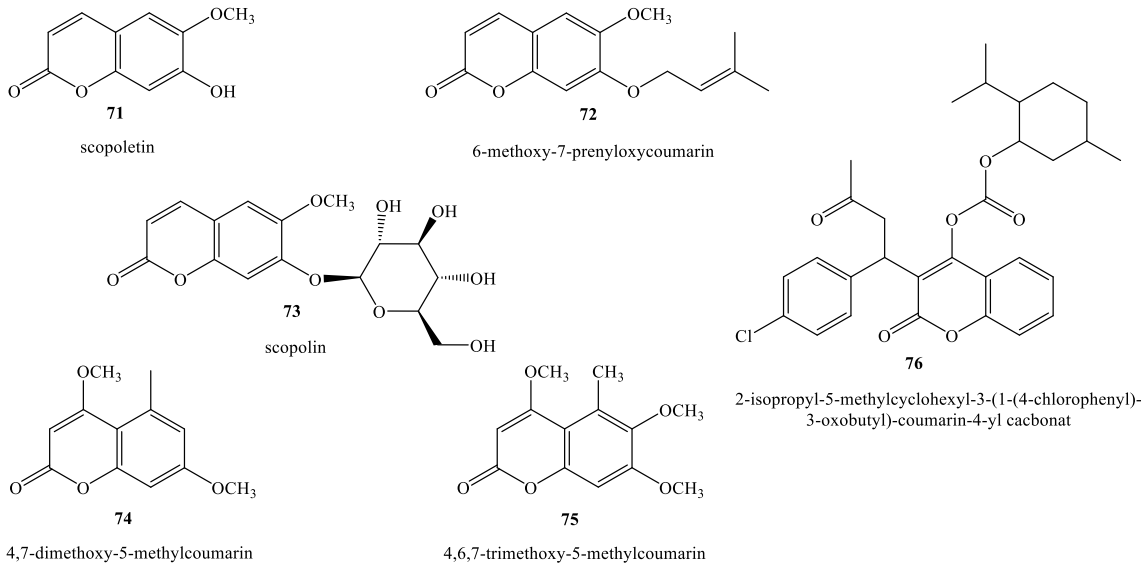

Figure 9. Benzopyranoids from *A. triphysa.*

4. PHARMACOLOGICAL PROPERTIES

Up to now, when comparing with research reports evaluating the biological activities of two species, *Ailanthus altissima* (Mill.) Swingle and *Ailanthus excelsa* Roxb., it shows that although both belong to the genus *Ailanthus*, studies evaluating the biological activities of *A. triphysa* have not been widely implemented, although *A. triphysa* is quite commonly used as a medicine in folk medicine. In addition to reports evaluating part of the biological activities of this species, *A. triphysa*, there have been many other studies evaluating the biological activities of compounds (Table 1) showing diverse and rich pharmacological effects. Therefore, *A. triphysa* can be seen as a species with potential to be used as medicine for disease prevention and treatment, and needs to be further studied to evaluate its overall biological activities. In this report, the authors summarize some reports related to the evaluation of some prominent bioactivities from this species.

4.1. Anti-inflammatory activity

In a study of the anti-inflammatory activity of *A. triphysa*, the authors evaluated the firstly evaluated compounds **31-36** and **38-41** for their production inhibitory activity in LPS-stimulated RAW 264.7 cells. These compounds did not show significant cytotoxic activity and were further screened for their NO production effects in LPS-stimulated RAW 264.7 cells. The results showed that compounds **31-36** and **38-41** exhibited inhibitory activity with IC_{50} values ranging from 8.1-65.5 μM. Compound **38** with the lowest IC_{50} value was then selected for further study on its effects on other inflammatory markers, including IL-6, TNF-α, and PGE-2. Our results indicated that compound **38** (at concentrations of 4, 8, and 16 μM) significantly reduced

secretion of both IL-6 and TNF-α cytokines but did not affect the PGE-2 level in LPS-activated RAW264.7 cells [16].

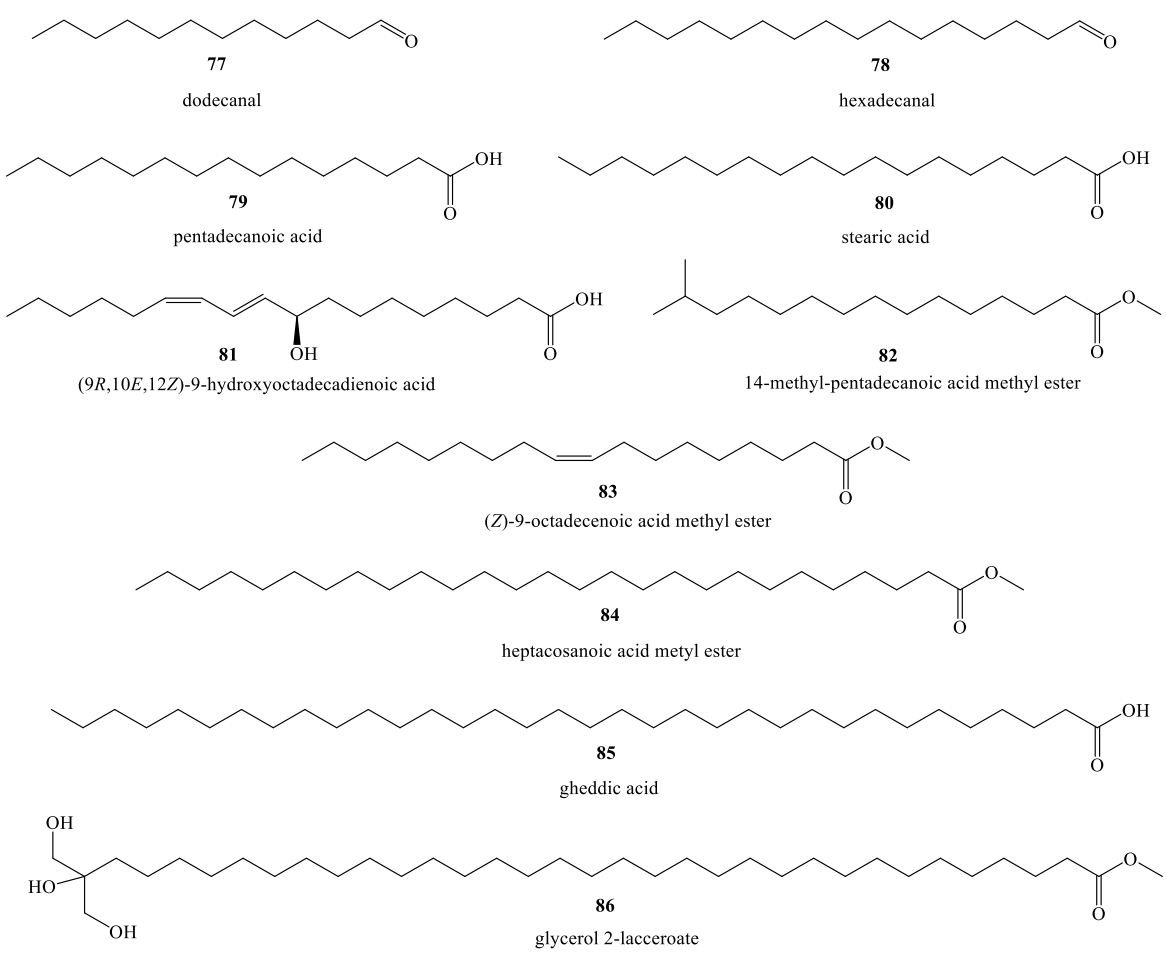

Figure 10. Fatty aldehyde, acid compounds from *A. triphysa*.

4.2. Antibacterial activity

A study evaluating the antibacterial activity of the oleoresin of *A. malabarica* and compounds **12**, **14**, **16**, **17**, and **20–23** isolated from it against *Pseudomonas aeruginosa, Klebsiella pneumoniae*, *Escherichia coli*, and *Candida albicans* revealed that none of the samples exhibited significant activity at the tested concentrations (100 and 250 μg/mL). The compounds were also tested for their toxicity towards red blood cells (RBCs), and all the compounds (except **23**) were considerably less toxic compared to the reference standards, polymyxin (4.99 %), and ampicillin (4.46 %) at 100 μg/ml. Compound **23** was found to be more toxic (4.92 %) and equivalent to polymyxin. Interestingly, compound **14** is structurally related to **23** (opening of epoxy ring in **23** results in **14**), which was found to be the least toxic (1.84 %).

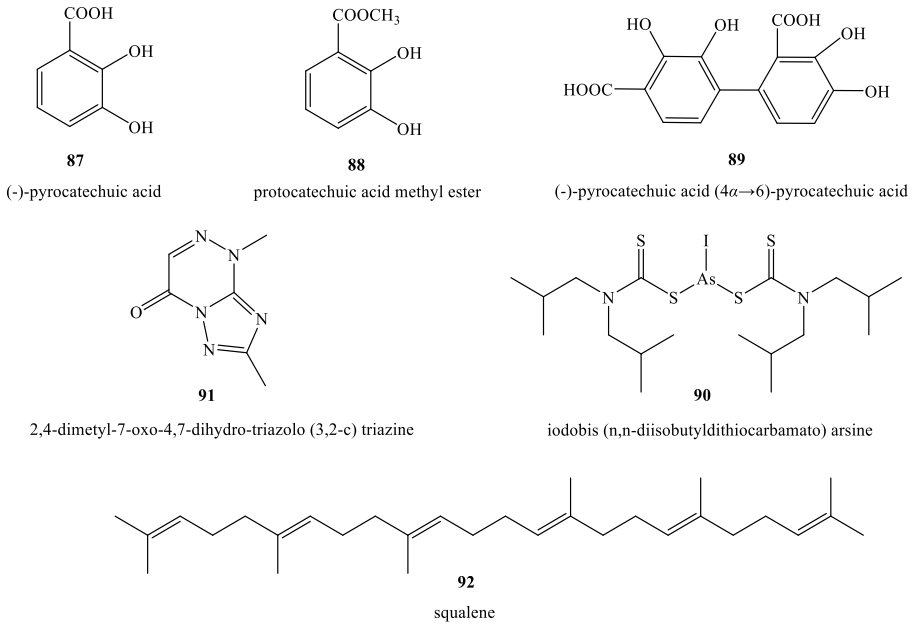

Figure 11. Other compounds from *A. triphysa*.

The authors concluded that the oleoresin and some of the isolates had no antibacterial activity and did not lyse hemocytes [4]. In another report on the antibacterial effect of *A. triphysa*, its ethanol extract was tested against bacterial strains of *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Streptococcus pyogenes*, and *Escherichia coli* by using the broth dilution method. The results showed that this extract at a concentration of 125 μg/ml showed a higher level of inhibitory activity on *P. aeruginosa* (OD-0.250 ± 0.011). The extract at 500 µg/ml showed remarkable activity against *S. aureus* (0.254 ± 0.006). The least effect was observed against *E. coli* and *S. pyogenes* (0.343 ± 0.011 & 0.675 ± 0.026). The authors suggested that *A. triphysa* can be used as an effective antibacterial agent against *S. aureus* and *P. aeruginosa* [23]. In a report, the antibacterial activity of different extracts of *A. triphysa* against Gram-positive bacteria, including *Bacillus cereus* and *Staphylococcus aureus*, and Gram-negative bacteria, including *Acinetobacter baumannii*, *Escherichia coli*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa*, was evaluated. The results were compared with chloramphenicol, a bacterial protein synthesis inhibitor (used as a positive control, and the MIC ranges recorded for Gram-positive and Gram-negative bacteria in the assay were 2-16 and 2-64 μg/ml, respectively). The plant extract showed weak antibacterial and antifungal activity. The lowest minimum inhibitory concentration (MIC) value was exhibited by the ethyl acetate extract against *P. aeruginosa* with a value of 310 μg/ml. The lowest minimum bactericidal concentration (MBC) value recorded in this study was 1250 μg/ml, which was given by the ethyl acetate extract (against *S. aureus*), ethanol, and methanol extracts (against *P. aeruginosa*). Among these six extracts, only the ethyl acetate, methanol, and ethanol extracts showed bactericidal activity (MBC 1250 μg/ml) [25].

4.3. Antioxidant activity

In cellular oxidation reactions, superoxide radicals are usually formed first, and their effects can be amplified because they generate other free radicals and oxidants. In addition, xanthine

oxidase is one of the major enzymatic sources of these reactive oxygen species *in vivo*. A report evaluating the antioxidant activity of *A. malabarica* showed that the maximum inhibitory concentration of the extract was approximately 25 μg/ml, which is much lower than that of other plant-derived active ingredients such as (+)-catechin (100 μg/ml) and ascorbic acid (200 μg/ml) obtained from green tea extract and commonly used in cosmetics. The IC_{50} value of *A. malabarica* leaves extracted by 70% methanol-water extract was 5 μg/ml, which was lower than that of the positive control, α-tocopherol (IC_{50} 12μg/ml). The IC_{50} value of *A. malabarica* leaves extracted by methanol (100%) showed an IC_{50} value of 10 μg/ml, a value close to that of the positive control. It can be seen that the IC_{50} value of *A. malabarica* was much lower than that of *Camellia sinensis* Linn., both green tea (IC_{50} 6.5 μg/ml) and black tea (IC_{50} 9.7 μg/ml), and *Curcuma aromatica* (IC_{50} 12 μg/ml). These results showed that the extracts all had very good superoxide radical scavenging activities. Based on research, the extract of *A. malabarica* shows potential to be used in sun protection and antiaging cosmetic formulations [22].

4.4. Antifungal activity

A report evaluated the antifungal activity of different extracts of *A. triphysa* against six fungi, including four strains of yeasts *Candida albicans*, *Candida parapsilosis*, *Candida krusei* and *Cryptococcus neoformans*, and two strains of filamentous fungi *Aspergillus fumigatus* and *Trichophyton interdigitale*. The ethanol extract of *A. triphysa* exhibited significantly fungistatic activity against *C. krusei* strain (MIC 2.5 μg/ml) when compared with the positive control amphotericin B (an antifungal drug, MIC 1-2 μg/ml). In contrast, the lowest minimum fungicidal concentration (MFC) value recorded in this study was 20 μg/ml, which was nearly 10 times higher than the lowest MIC value (2.5 μg/ml) given by the ethanol extract (against *C. krusei*). These MFC values were documented in the ethyl acetate, ethanol, methanol, and water extracts of *A. triphysa* against *C. krusei*. On the other hand, the *A. triphysa* extracts appeared to have a broad spectrum of antifungal activity, as they showed inhibitory activity against all the fungi used in this study [25].

4.5. Cytotoxic activity

A study evaluated the anti-angiogenic and cytotoxicity of extracts from several medicinal plants, *A. malabarica* being one of them. The results showed that all the plant extracts were evaluated for their toxicity against a panel of human cancer cell lines by MTT assay, and none of them exhibited acute toxicity. The methanol extract of *A. malabarica* exhibited IC_{50} values > 200 µg/ml against all the cancer cell lines. Similarly, the plant had relatively low anti-angiogenic activity. Therefore, no further studies were conducted on this extract [87]. In a preliminary study on the cytotoxic activity of *A. triphysa* against cancer cell lines (human hepatocarcinoma (HepG2), human lung cancer (A549), human cholangiocarcinoma (Thai; HuCCA-1), and non-adhesive T-lymphoblast (MOLT-3) cell lines), the dichloromethane-methanol extracts (1:1) and dichloromethane from the stem and stem bark of this plant showed good inhibitory activity (63-90% at 30 μg/mL) against all four cancer cell lines. However, when testing the cytotoxic activity of the compounds isolated from this species, including compounds **16**, **19**, **24-28**, **30**, **37**, **43**, **45**, **48**, **51-57**, **65**, **72** and **81** against cancer cell lines *in vitro*, none of the tested compounds showed good cytotoxic activity. The newly isolated cycloapotirucallanes **43** and **45** with a tricyclo[4.3.1.0]decane skeleton were inactive in all cell lines (IC_{50} > 50 μg/mL, assumes no cytotoxic effects) [14]. Malabaricol (**16**) showed good cytotoxic activity (IC_{50} 10.91 μg/ml) against the A549 cell line when compared with the control doxorubicin (IC_{50} 9.10 μg/ml) [24].

In another report, the cytotoxic activity of different extracts of *A. triphysa* against the Vero cell line (kidney epithelial cells extracted from an African green monkey) was evaluated. The results showed that all extracts of *A. triphysa* were significantly cytotoxic to the Vero cells. The chloroform extract of *A. triphysa* exhibited the best cytotoxic activity among all the tested extracts (the cell viability of 67.7 % ± 2.30 % was recorded at the lowest concentration used of 5 μg/ml). The extent of toxicity of this extract was also reflected by its median cytotoxic concentration value (9.7 ± 0.4 μg/ml), which was the lowest among all the extracts in the study [25].

5. CONCLUSION

This article summarizes recent scientific publications on the chemical composition and pharmacological activities of *A. triphysa*. A total of 92 chemical compounds have been identified, and classified into major groups such as alkaloids, triterpenoids, quassinoids, steroids, flavonoids, and benzopyranoids. Many of these compounds exhibit valuable biological activities, including antibacterial, antioxidant, antifungal, anti-inflammatory, anticancer, and cytotoxic activities. This review highlights the chemical diversity and broad spectrum of biological activities of *A. triphysa*.

CRediT authorship contribution statement. The authors have contributed equally.

Declaration of competing interest. The authors declare no conflict of interest.

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