Pharmacognosy Reviews [Phcog Rev.]
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PHCOG REV.
An official Publication of Phcog.Net

PHCOG REV.: Plant Review

Chemistry and biological activities of *Ailanthus altissima* Swingle: A review

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ABSTRACT

Ailanthus altissima (Mill.) Swingle, [syn. = *A. glandulosa* Desf.] (Simaroubaceae), is a large tree indigenous to China. It is known as the "Tree of Heaven" and has been the subject of several chemical and biological studies. It is used in traditional medicine in many parts of Asia, including China, to treat cold and gastric diseases as diarrhea, dysentery, and endoparasites. It is also used as a bitter-aromatic drug and as an antitumoral. The chemical studies have underlined the presence of various classes of compounds, the main being quassinoids and alkaloids. The extracts of this plant, as well as pure isolated compounds, showed multiple pharmacological activities such as antitumor, antiviral, insecticidal, herbicide and others. In particular, 1-methoxycanthin-6-one has been proposed as an anticancer chemotherapeutic agent. In this review, we have explored chemistry and biological activities of *A. altissima*, in order to comprehend and synthesize its potential image of multipurpose medicinal agent. The plant is widely cultivated to large regions of the world and its importance, as a medicinal plant, is growing up substantially with increasing and stronger reports in support of its multifarious therapeutic uses.

KEY WORDS: *Ailanthus altissima*, Simaroubaceae, Quassinoids, Alkaloids, Chemical constituents, Biological activities.

INTRODUCTION

Ailanthus altissima (Mill.) Swingle (synonym = *A. glandulosa* Desf.), also called tree-of-heaven, Chinese summac, paradise tree, copal tree, stink tree and ghetto palm, is a deciduous tree belonging to the quassia family, Simaroubaceae (1-3).

Botanical description: Tree of heaven is a rapidly growing plant: it can reach a height of 2.5 m in its first year. Adult trees can reach 25-30 m in height. The trees are tipically short-lived (30-50 years), thought some have survived for over 150 years. *A. altissima* has deciduous leaves, odd-pinnately, with 11-41 leaflets. Shape is lanceolate, acuminate and entire, except for 1-5 basal teeth, each leaflet with a prominent dark green gland on the underside near the apex. Both surfaces have minute hairs and glands. Leaflets are 7-13 cm long and 2-5 cm wide. Crushed foliage has an acrid odor. Leaf scars are triangualr with numerous bundle scars. Light brown twigs are very stout and covered with fine hairs when young. Pith is continuous and yellowish in color. Buds are relatively small and solitary; terminal buds are absent. The smooth, striped, gray-brown or light brown bark cracks with age and exhibits light-colored grooves.

Male and female flowers are 0.5 cm long and form large, light green terminal panicles. They are radially simmetrical with 5 or 6 petals. The trees may be polygamous, but most individuals are unisexual. Male flowers have a foul scent. Each tree may produce up to several hundred inflorescences a year. In Europe blooms late may through early June.

Fruit is a 3-8 cm long schizocarp with 2-5 samaroid mericarps. Each fruit contains a single seed; seeds mature in late summer or early fall and form dense, showy pink clusters, that persiste through the winter. Each cluster may contain hundreds of seeds.

Habitat- *Ailanthus altissima* is native of Northeast and Central China as well as Taiwan. The species is remarkable in its ability to rapidly invade and colonize disturbed, often seemingly harsh, habitats. In U.S.A. (southern Pennsylvania, New York, and Connecticut), this tree sometimes invades recently abandoned fields, suppressing growth of other tree species and forming nearly pure stands (4-5). It was first grown in Europe, in about 1751, from seed sent to England from Nankin by a French Jesuit priest, Pierre Nicholas d'Incarville. Among the recipients was Peter Collinson, who grew from them "a stately tree". The Royal Society in London also received seeds, which it distributed to Philip Miller of the Chelsea Physic Garden and to a gardener in Surrey, Mr. Webb, both of whom raised plants from the seeds. Miller and Webb exchanged the plant for "Japanese sumac": a lacquer had been obtained from this plant. Only some years later, in 1786, Desfontaines, of Paris Museum, recognized the error and baptized the plant, "Paint of Japan". *A. altissima* had been introduced in Europe and Italy to start breeding of *Philosamia cyntia*, named "Sfinx of Ailanthus", in place of silkworm. It readily invades and thrives along roadsides, cracks of sidewalks and pavement, in vacant lots, and almost anywhere else sufficient dust or soil has accumulated. *A. altissima* was first introduced into the Unites States from England to Philadelphia, PA, in 1784: therefore, it has become widely naturalized across the continent.

Several characteristics contribute to the fitness of *A. altissima*. It grows very rapidly and readily overtops most competitors. The tree of heaven reproduces sexually, with abundant samaras, and vegetatively, with sprouts from wide-ranging lateral roots (6). Root sprouts may remain suppressed for a considerable time until conditions become favorable. Lateral root growth is tolerant of, or even enhanced by, soil compaction (7). These attributes alone, however, appear inadeguate to explain the invasivness and tenacity of *Ailanthus* at certain sites. The 1943 book *A Tree Grows in Brooklyn* by Betty Smith (8) uses the tree of heaven as its central metaphor, using it as an analogy for the ability to thrive in a difficult environment. At the time as well as now, tree of heaven was common in neglected urban areas. She writes: "There's a tree that grows in Brooklyn. Some people call it the Tree of Heaven. No matter where its seed falls, it makes a tree which struggles to reach the sky. It grows in boarded up lots and out of neglected rubbish heaps. It grows up out of cellar gratings. It is the only tree that grows out of cement. It grows lushly...survives without sun, water, and seemingly earth. It would be considered beautiful except that there are too many of it".

Plant Parts used: The bark of root and leaves.

Synonyms: Ailante, ailanthus, ailanto, ailantus, albero del paradiso, arbol el cielo, Chinese tree-of-heaven, Chinese sumac, copal tree, falso zumaque, gotterbaum, gudstrad, heavenwood, hemelboom, paradise tree, piede di cavallo, stinking chun.

Traditional uses

Tree of heaven was already used in traditional medicine in many parts of Asia including China: the bark and the leaves of this plant had been used for their bitter-tonic, astringent, vermifuge and antitumoral properties. The plant has been employed in case of leucorrhoea, as a vulnerary and an antidiarrhoeal; to treat cold, dysentery, endoparasites and gastric diseases. Melville, in 1944, reported the plant as a species important for a peculiar honey. The wood, rich in cellulose, has been used in paper manufacturing (9).

Phytochemistry

A number of phytochemical studies demonstrated the presence in the plant of several classes of chemical compounds; the main class of these being quassinoids; the second one are alkaloids; following, lipids and fatty acids, volatile compounds and, in minor measure, phenolic compounds, flavonoids and coumarines.

Quassinoids

In the class of quassinoids, the more frequently found compound in *A. altissima* is ailanthone (**I**), extracted from seeds (10), stem bark (11-13) or aqueous root extract (14): the structure of ailanthone is 11β,20-epoxy-1β,11α,12α-trihydroxypicrasa-3,13(21)-diene-2,16-dione (Figure 1). From the fruits of the plant, recently, ailanthone A [11β,20-epoxy-1β,2α,12α-pentahydroxypicrasa-3,13(21)-dien-16-one] was isolated (15).

Other quassinoids, ailanthinone (**II**) (14), ailantinol A (**III**) (16), ailantinol B (**IV**) (14,16), ailantinols C (**V**) and D (**VI**) (17), ailantinols E (**VII**), F (**VIII**) and G (**IX**) (18), ailantinol H (**X**) (19-20), chaparrine (**XI**) (14) and chaparrinone (**XII**) (12) (Figure 2) have been isolated from different parts of *Ailanthus altissima*, and their structures were elucidated from spectral evidence.

From the root bark of the plant other two quassinoid compounds were isolated, shinjudilactone (**XIII**) (21-22) and shinjulactone C (**XIV**) (22-23): their structures were determinated as 13[12→11α]-abeo-picrasane and 1α,12α,5α,13α-dicyclo-9β H-picrasane, respectively. Other bitter compounds, called shinjulactone A (**XV**) [11β,20-epoxy-1β,2α,11α,12α-tetrahydroxypicrasa-3,13(21)-dien-16-one (24)], shinjulactone B (**XVI**) (25-26), shinjulactones D (**XVII**) and E (**XVIII**) (26-27), shinjulactones F (**XIX**) (28, 29), I (**XX**), J (**XXI**) and K (**XXII**) have been isolated from the plant (29).

Shinjulactones G (**XXIII**) and H (**XXIV**) (30), shinjulactone L (**XXV**) (31), shinjulactones M (**XXVI**) and N (**XXVII**) (32) are, subsequently, isolated from root bark of tree of heaven. The structures of compounds **XIII**-**XXVII** are reported in Figure 3.

Althought many quassinoids have been obtained from *A. altissima*, the isolation of glycosides wasn't reported until 1984: Yoshimura et al. (33) isolated four bitter quassinoid glycosides, shinjuglycosides A (**XXVIII**), B (**XXIX**), C (**XXX**), and D (**XXXI**) (Figure 4) from the seeds of the plant and their structures were established, from spectral data and enzymic or acid-catalyzed hydrolysis, to be 2-β-D-glucopyranosides of chaparrine, shijulactone A, amarolide 11-acetate, and amarolide, respectively.

Other two shinjuglycosides, E (**XXXII**) and F (**XXXIII**) (Figure 4), were isolated from the root bark of *A. altissima*. Their structure were established as 2-O-(β-D-glucopyranosyl)-2α,11α,12α-trihydroxypicrasane-1,16-dione and 2-O-(β-D-glucopyranosyl)-2α,12β dihydroxypicrasane-1,11,16-trione, respectively (34).

Alkaloids

The second more representative class of compounds isolated in *A. altissima* is alkaloid one. In the 1970's, a series of alkaloids were isolated and identified from the wood (35) of the plant (Figure 5): canthin-6-one (**XXXIV**), canthin-6-one 3-oxid (**XXXV**) and 1-methoxycanthin-6-one (**XXXVI**). Canthin-6-one was isolated, also, from other parts of the plant: root bark (36-37) and leaves (38). Canthin-6-one 3-oxid was isolated from the root bark of plant too (37). Another alkaloid, strictly correlated to canthin-6-one, was isolated next: 1-hydroxycanthin-6-one (**XXXVII**) (Figure 5) (39). The alkaloid 1-methoxycanthin-6-one is, absolutely, the most studied in the plant (14, 36-37, 40-41); several its derivates have been isolated from the root bark: 5-hydroxymethylcanthin-6-one (**XXXVIII**) (42) and 1-methoxycanthin-6-one-3N-oxide (**XXXIX**) (Figure 5) (37).

Zhang et al. (43) isolated two new alkaloidal glycosides from the root bark of *A. altissima*, canthin-6-one-5-O-β-D-xylopyranosyl-(1→6)-β-D-glucopyranoside (**XL**) and canthin-6-one-1-O-β-D-xylopyranosyl-(1→6)-β-D-glucopyranoside (**XLI**), named ailantcanthinosides A and B, respectively (Figure 6).

Carboline alkaloids (Figure 7) were also found in the plant: 1-acetyl-4-methoxy-β-carboline (**XLII**) (37, 44), 1-(2'-hydroxyethyl)-4-methoxy-β-carboline (**XLIII**) and 1-(1',2'-dihydroxyethyl)-4-methoxy-β-carboline (**XLIV**) (37, 39) were isolated from the root bark of tree of heaven (Figure 7). Ohmoto and co-workers isolated also 1-(2-hydroxy-1-methoxy)-ethyl-4-methoxy-β-carboline (**XLV**) (42). Another indole alkaloid, 4-methoxy-1-vinyl-β-carboline (**XLVI**) was isolated from the plant (38).

Lipids and fatty acids

Fruits of *A. altissima* contain sterol derivatives. These compounds include stigmast-4-ene-3,6-dione, β-sitosterol, 6βhydroxystigmast-4-en-3-one, 5α,8α-epidioxyergosta-6,22-dien-3β-ol, stigmast-4-ene-3β,6β-diol, 9,19-cyclolanost-23(Z)-ene-3β,25-diol, 3-epi-ursoloic acid, 12β,20(S)-dihydroxydammar-24-en-3-one, and daucosterol (45).

Zhao et al. (46) describe the isolation of seven stigmasterols from the fruits of *A. altissima*. These have been identified as 5α-stigmastane-3,6-dione, 3β-hydroxystigmast-5-en-7-one, stigmast-5-ene-3β,7α-diol, 6α-hydroxystigmast-4-en-3-one, 5α-stigmastane-3β,6β-diol, stigmast-4-ene-3β,6α-diol, stigmast-5-ene-3β,7α,20ξ-triol.

Also the seeds contain sterol compounds, ailanthusterol A and ailanthusterol B (47). Their structures have been established as stigmasta-5,20(21)-diene-3β-ol (**XLVII**) and stigmast-5-ene-3β,20-diol (**XLVIII**) on the basis of spectral data (Figure 8).

Moreover, in *A. altissima* seeds the total lipids represented about 39% of dry weight, being located in both cotyledons and endosperm. Of total lipids, 93% and 89% consisted of triacylglycerols in endosperm and cotyledons, respectively. Of the polar lipids, phospholipids constituted the major components and galactolipids were found only in cotyledons. The main fatty acids were linoleic, oleic and palmitic (48). Fatty acids have been previously extracted also from the fruits (49). The bark of the plant contain fatty acids and about 27% of these compounds are C_{22} acids (50). The secretion from the glandular trichomes of *A. altissima* contained bound lipids (mainly monogalactosyldiacylglycerol) as well as oleic, palmitic, and linoleic acids in the free state (51).

The freshly cut wood contains fatty acids; among these compounds, 9-cis,12-cis-octadecadienoic acid was the major constituent (51.1%), followed by pentadecanoic acid (29.5%) (52).

Other compounds

2,6 Dimethoxyquinone was found in the plant. (53). The volatile oils from leaves (54) and seeds have been characterized (55). The main constituents of the oil were aliphatic C_6-compounds (aldehydes, acids, esters), sesquiterpene compounds and oxygenated compounds.

Flavonoid derivates have been found in *A. altissima* leaves: isoquercetin (56) and a flavone glycoside gallate, luteolin 7-O-β-(6"-galloylglucopyranoside) (57). El-Baky and co-workers (58) isolated from the leaves of *A. altissima* kaempferol, quercetin, kaempferol-3-O-glucoside, quercetin-3-O-glucoside and rutin together with β-sitosterol, ceryl alcohol and β-sitosterol glucoside.

Also coumarin derivatives, altissimacoumarin A (**XLIX**) and altissimacoumarin B (**L**), have been isolated from the plant (59) (Figure 9).

In 2006, a new cerebroside and 3 known cycloartan triterpenes were isolated from fruits of *A. altissima*. Their structures were identified as 1-O-β-D-glucopyranosyl-(2S,3R,4E,9E)-2-(2'R-hydroxyhexadecenoy)-4,9-octadecadiene-1,3-diol, 9,19-cyclolanost-23(Z)-ene-3β,25-diol (**LI**), cycloart-25-ene-3β,24R-diol (**LII**), and cycloart-25-ene-3β,24S-diol (**LIII**) (Figure 10) (60).

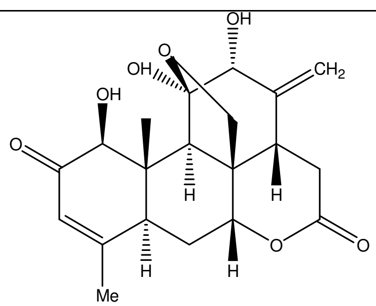
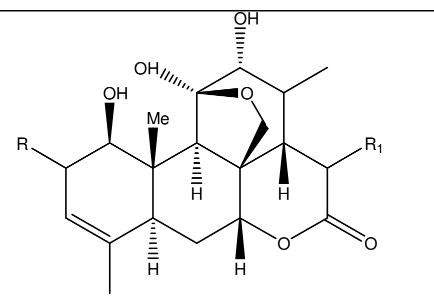
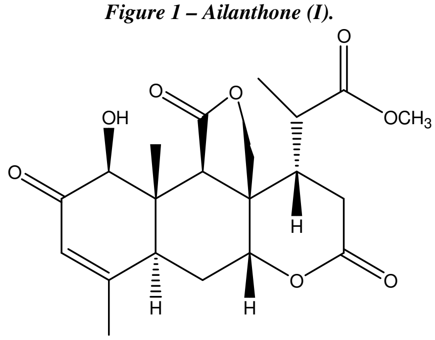


Figure 1 – Ailanthone (I).

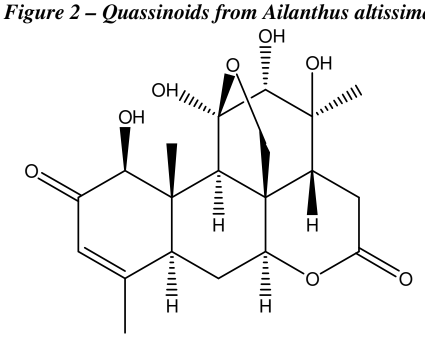


Ailanthinone (**II**) R= =O; R_1= $OCOCH(CH_3)C_2H_5$
Chaparrine (**XI**) R= OH; R_1= H
Chaparrinone (**XII**) R= =O; R_1= H

Figure 2 – Quassinoids from Ailanthus altissima



Ailantinol A (**III**)



Ailantinol B (**IV**)

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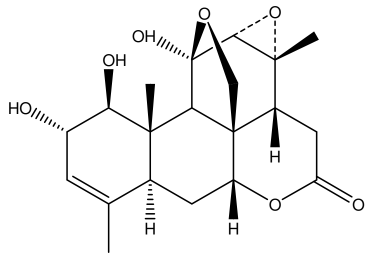
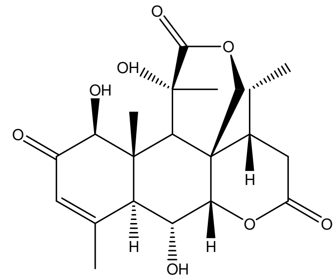
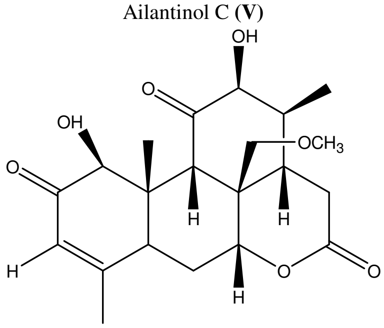


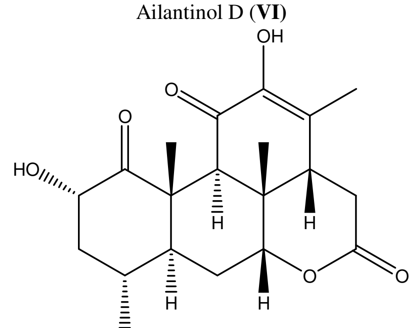
Ailantinol C (**V**)



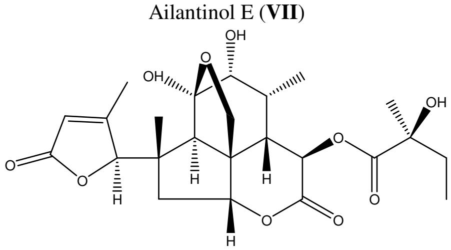
Ailantinol D (**VI**)



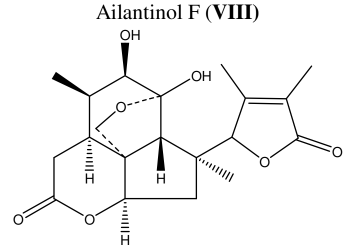
Ailantinol E (**VII**)



Ailantinol F (**VIII**)

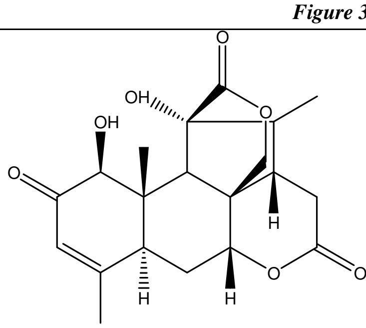


Ailantinol G (**IX**)

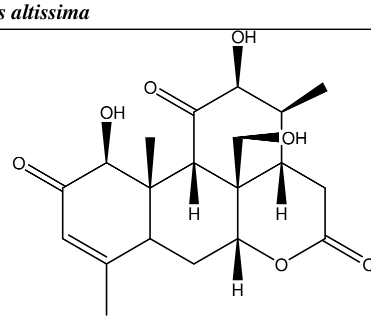


Ailantinol H (**X**)

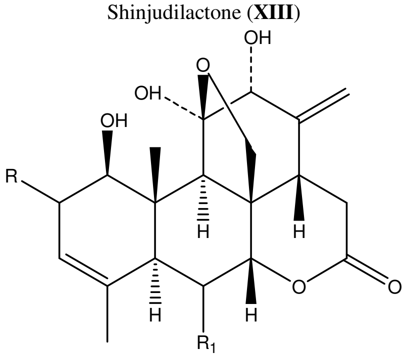
Figure 3 – Quassinoids from Ailanthus altissima



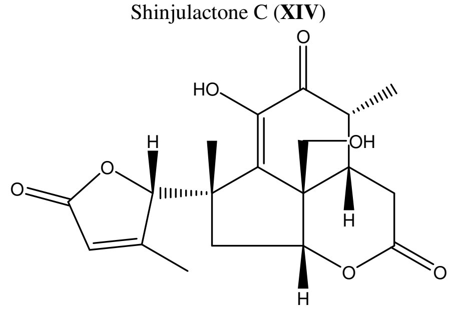
Shinjudilactone (**XIII**)



Shinjulactone C (**XIV**)



Shinjulactone A (**XV**) R= OH; R_1= H;
Shinjulactone E (**XVIII**) R= =O; R_1= OH



Shinjulactone B (**XVI**)

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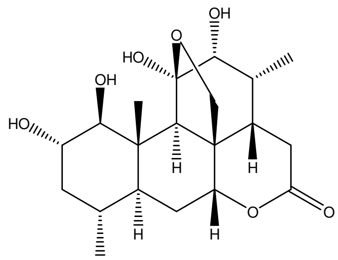
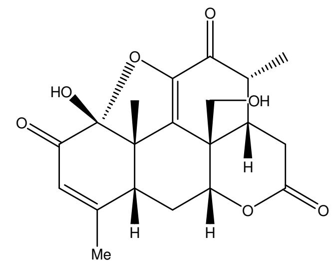
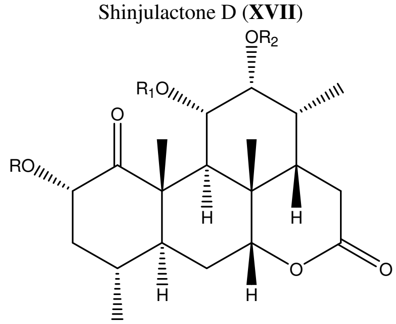


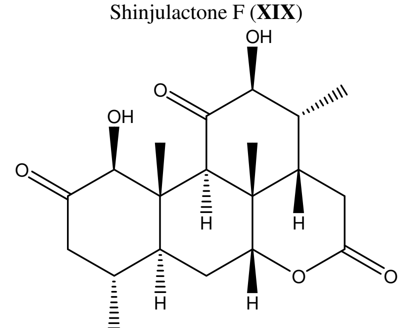
Shinjulactone D (**XVII**)



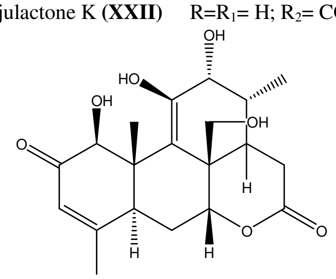
Shinjulactone F (**XIX**)



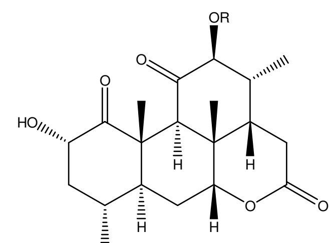
Shinjulactone I (**XX**) R=R_2= H; R_1= $COCH_3$
Shinjulactone K **(XXII)** R=R_1= H; R_2= $COCH_3$



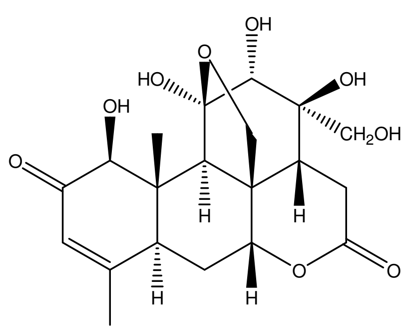
Shinjulactone J (**XXI**)



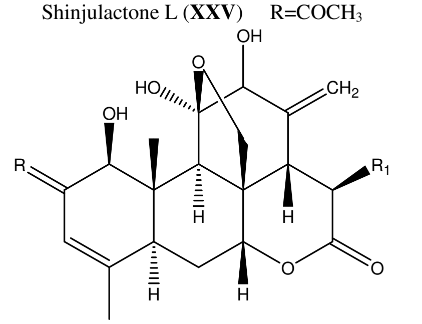
Shinjulactone G (**XXIII**)



Shinjulactone H (**XXIV**) R=H
Shinjulactone L (**XXV**) R=$COCH_3$

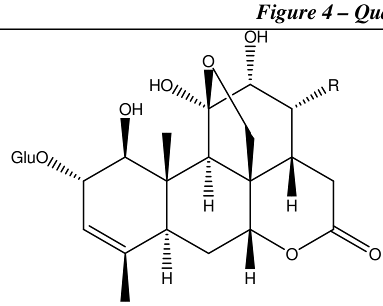


Shinjulactone M (**XXVI**)

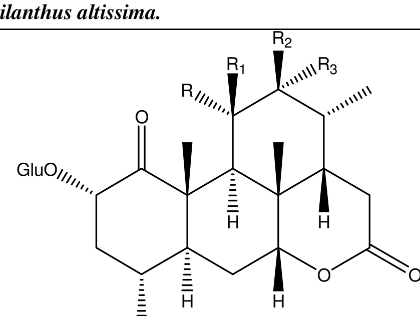


Shinjulactone N (**XXVII**) R= α –OH, β –H; R_1= OH

Figure 4 – Quassinoid glycosides from Ailanthus altissima.



Shinjuglycoside A (**XXVIII**) -R=CH_3



Shinjuglycoside C (**XXX**) R=R_1= $OCOCH_3$; R_2=R_3= =O

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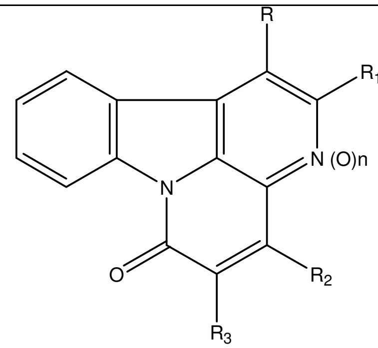
Shinjuglycoside B (**XXIX**) -R= $=CH_2$

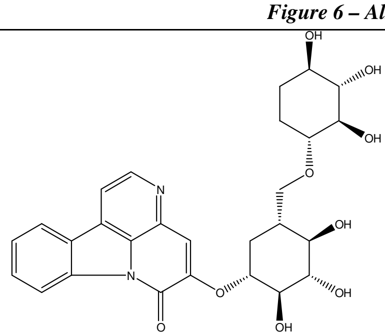
Shinjuglycoside D (**XXXI**) $R=R_1= H; R_2=R_3= =O$
Shinjuglycoside E (**XXXII**) $R=R_3= OH; R_1=R_2= H$
Shinjuglycoside F (**XXXIII**) $R=R_1= =O; R_2= OH; R_3= H$

Figure 5 – Alkaloids from Ailanthus altissima.

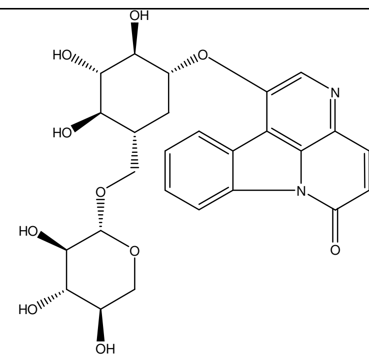


Canthin-6-one (**XXXIV**) $R=R_1=R_2=R_3= H$ n=0
Canthin-6-one 3-oxid (**XXXV**) $R=R_1=R_2=R_3= H$ n=1
1-Methoxycanthin-6-one (**XXXVI**) $R=OCH_3; R_1=R_2=R_3= H$ n=0
1-Hydroxycanthin-6-one (**XXXVII**) $R=OH; R_1=R_2=R_3= H$ n=0
5-Hydroxymethylcanthin-6-one (**XXXVIII**) $R=CH_3; R_1= OH; R_2=R_3= H$ n=0
1-Methoxycanthin-6-one-3N-oxide (**XXXIX**) $R=OCH_3; R_1=R_2=R_3= H$ n=1
4,5 Dihydrocanthin-6-one (**LIV**) $R=R_1= H; R_2=R_3= OH$ n=0
5-Hydroxycanthin-6-one (**LV**) $R=R_1=R_2= H; R_3= OH$ n=0
2-Hydroxycanthin-6-one (**LVIII**) $R=R_2=R_3= H; R_1= OH$ n=0
4-Hydroxycanthin-6-one (**LIX**) $R=R_1=R_3= H; R_2= OH$ n=0

Figure 6 – Alkaloid glycosides from Ailanthus altissima.

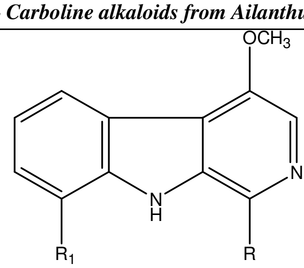


Ailantcanthinoside A (**XL**)



Ailantcanthinoside B (**XLI**)

Figure 7 – Carboline alkaloids from Ailanthus altissima.



1-Acetyl-4-methoxy-β-carboline (**XLII**) $R= COCH_3; R_1= H$
1-(2'-Hydroxyethyl)-4-methoxy-β-carboline (**XLIII**) $R= CH_2CH_2OH; R_1= H$
1-(1',2'-Dihydroxyethyl)-4-methoxy-β-carboline (**XLIV**) $R= CH(OH)CH_2OH; R_1= H$
1-(2-Hydroxy-1-methoxy)-ethyl-4-methoxy-β-carboline (**XLV**) $R= CH(OCH_3)CH_2OH; R_1= H$
4-Methoxy-1-vinyl-β-carboline (**XLVI**) $R= OCH_3; R_1= H$
β-Carboline-1-propionic acid (**LVI**) $R= CH_2CH_2COOH; R_1= H$
4-Methoxy-β-carboline-1-carboxylic acid methyl ester (**LVII**) $R= COOCH_3; R_1= H$
4,8-dimethoxy-β-carboline-1-carboxylic acid methyl ester (**LX**) $R= COOCH_3; R_1= OCH_3$

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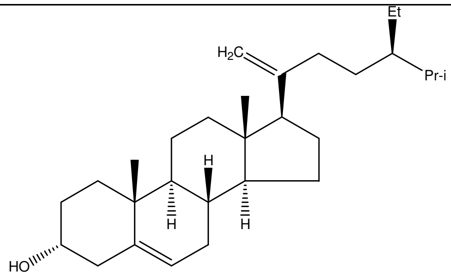
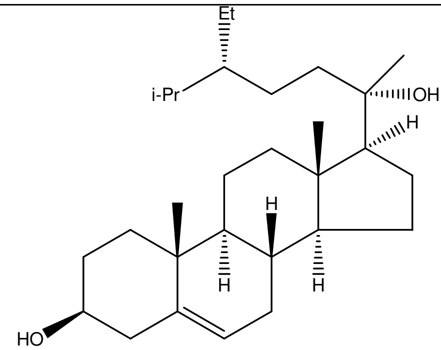
Figure 8 - Stigmasta-5,20(21)-diene-3β-ol (XLVII) and stigmast-5-ene-3β,20-diol (XLVIII)

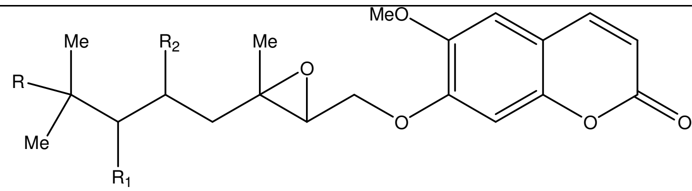


XLVII



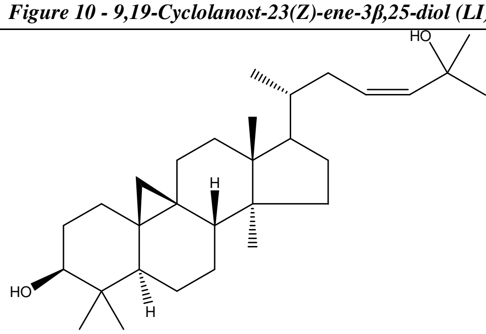
XLVIII

Figure 9 - Altissimacoumarin A (XLIX) and Altissimacoumarin B (L).

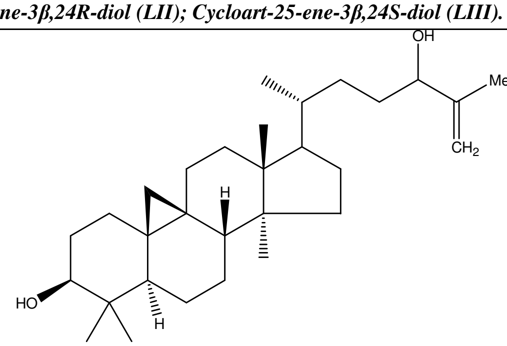


XLIX R= OH; R_1R_2= bond
L RR_1= bond; R_2= H

Figure 10 - 9,19-Cyclolanost-23(Z)-ene-3β,25-diol (LI); Cycloart-25-ene-3β,24R-diol (LII); Cycloart-25-ene-3β,24S-diol (LIII).



LI



LII
LIII

Pharmacology

Pharmacological tests have confirmed that *Ailanthus altissima* has a surprisingly broad range of biological effects, some of them very interesting for possible future development.

Antitumoral and cytotoxic activities

Ohmoto and Koike (42) reported the antitumoral activity of 1-(2-hydroxy-1-methoxyethyl)-4-methoxy-B-carboline and its salts. Short-term *in vitro* assays for tumor and antitumor promoters were carried out for 14 quassinoids isolated from *A. altissima*.

The cytotoxicity of canthin-6-one, 1-methoxycanthin-6-one, 5-methoxycanthin-6-one, and canthin-6-one-3-N-oxide to guinea pig ear keratinocytes were compared, and the IC_{50} values ranged from 1.11 to 5.76 μg/mL. There is no significant difference in activity among these four cytotoxic alkaloids (61).

Some quassinoids, including ailantinol B, ailantinol C, ailanthone and shinjulactone A showed moderate activity at a molar ratio of 1:100 (TPA/quassinoids), and the results led to the elucidation of the structure-activity relationships (62). Also ailantinols E, F, and G have been evaluated for their antitumor promoting effects against Epstein-Barr virus early antigen activation introduced by 12-O-tetradecanoylphorbol-13-acetate in Raji cells: they have demonstrated a potent activity without showing any cytotoxicity (18). It has been reported that the water extract of *A. altissima* induced apoptotic cell death in Jurkat T-acute lymphoblastic leukemia cell (63). Our research group also evaluated tree-of-heaven for its cytotoxic and antiproliferative activities by a bioassay-oriented study. The cancer cells, HeLa (human cervical carcinoma cell line), SAOS (human osteosarcoma cell line), U87MG (human glioma cell line) and U937 (human monocytic leukemia cell line), incubated for different times with the active extract, fraction or pure alkaloid isolated from *A. altissima* showed a remarkable increase in the apoptosis (40). Therefore, the same group evaluated the apoptosis-inducing activity by 1-methoxy-canthin-6-one on several cell lines [Jurkat (human leukemia), ARO and NPA (thyroid carcinoma) and HuH7 (hepatocellular carcinoma)] and demonstrated its involvement in inducing of caspase 3. Its synergism with TRAIL get 1-methoxy-canthin-6-one to be a candidate for *in vivo* studies of monotherapies or combined antineoplastic therapies (41).

Antiviral activity

A. altissima was tested for its antiviral activity: in 1972, Chirkina and Degtyareva (64) identified a phenolic protein as the antiviral compound of the plant against tobacco mosaic virus (TMV). The plant was tested also for its antiherpes activity: the β-carboline alkaloids resulted active against herpes simplex virus (HSV) (65). A methanol extract of stem bark of tree-of-heaven showed a potent HIV1-cell fusion inhibitory activity (74% of inhibitory activity) between the HIV-1 envelope glycoprotein gp120/41 and the cellular membrane protein CD4 of T lymphocytes (66-67).

Antimalaric activity

A crude extract of *A. altissima* was tested *in vitro* in an antimalarial test against *Plasmodium falciparum* (68-69) and against *P. berghei* (69) infections in mice. The activity of the chloroform extract *in vitro* and *in vivo* is due principally to the presence of ailanthone. Isolated compounds from seedlings of *Ailanthus altissima*, were assessed for antiplasmodial activity *in vitro*: ailanthone and 6α-tigloyloxychaparrinone showed *in vitro* activity against both chloroquine-resistant and chloroquine-sensitive strains of *Plasmodium falciparum* (70).

Antimicrobic activity

An ethanol extract and stigmasterols isolated from fruits of *A. altissima* were tested for their antimicrobial activity (46): the extract was strongly active against the bacteria assayed while single compounds exhibited a moderate activity.

Antimycotic activity

Canthin-6-one from *Ailanthus altissima* was inhibited the growth of *Aspergillus* sp. at low concentrations (5-80 μg/ml) (71).

Inhibition of phosphodiesterase

Alkaloids from the plant were tested as inhibitors of cAMP phosphodiesterase: major alkaloids in *A. altissima* showed the most potent inhibitory activity, equal to or greater than that of papaverine used as a reference (72). For this activity some alkaloids (β-carboline-1-propionic acid) of the plant were evaluated for their effect on the rate of blood flow (73) of intestine and stomach, whereas other alkaloids from *Picrasma quassinoides* increased only the rate of intestinal blood flow.

Nematicidal, bactericidal and fungicidal activity

Kraus et al. (74) tested nematicidal, bactericidal and fungicidal activities of extracts and pure compounds of *A. altissima*, without significant results.

Acaricide activity

Extracts of *Ailanthus altissima* are acaricides against *Rhipicephalus bursa* and *Hyalomma anatolicum* (75).

Anti-inflammatory activity

An ethanol extract of *A. altissima* inhibited generation of the cyclooxygenase-2 (COX-2) dependent phases of prostaglandin D_2. In addition, the same extract inhibited leukotriene C_4 production and degranulation reaction. The ethanol extract reduced the eosinophil infiltration into the airway and the eotaxin, IL-4, and IL-13 mRNA expression levels. These results suggest that the anti-inflammation activity of *A. altissima* may occur in part *via* the down regulation of TH_2 cytokines and eotaxin transcripts as well as the inhibition of inflammatory mediators (76).

Antiulcer activity

Ailanthone, the main quassinoid of *Ailanthus altissima*, and its α-epoxide were revealed to have antiulcer activity (77).

Antitubercolosis activity

Rahman and co-workers (78) tested some quassinoids isolated from *A. altissima* for their anti-tubercolosis activity: shinjulactone K, ailanthone and shinjudilactone were the most potent. The resulting data provided a picture of structure–activity relationships.

Central nervous-depressant activity

Various solvent extracts of the root bark of *A. altissima* had central nervous-depressant activity in mice. The differences in their activity were related to differences in alkaloid content. Various cell cultures of *A. altissima* had central nervous-depressant activity in mice. The high activity of a fraction from the cell cultures was due to the presence of 4,5-dihydrocanthin-6-one, a precursor of canthin-6-one. The limited activity of another cell culture fraction was due to the presence of β-carboline-1-propionic acid (79).

Allelopathic activity

Heisey (80) found that *A. altissima* contains one or more phytotoxic compounds in roots and leaves. Activity is higher in roots, where it occurs primarily in the bark. Extracts from the fresh leaves of the plant showed a strong plant germination/growth inhibitory effect in laboratory bioassays against alfalfa (*Medicago sativa*). The effect was greater in the light than in the dark (81). Extracts of *Ailanthus altissima* stem bark was evaluated in two outdoor trials (82). Ailanthone and chaparrinone were identified as the active constituents in *A. altissima* (12). Particularly, ailanthone exhibits promising potential for development as a natural-product herbicide (13). Moreover, ailanthone was sprayed post-emergence onto seedlings of 17 species of weeds and crops, showing a non selective activity (83). Our research group tested the antigerminative activity against radish, garden cress and purslane, of compounds isolated from the plant: ailanthone, ailanthinone, chaparrine and ailantinol B. Our data confirmed that the compound with greatest inhibitory activity is ailanthone (14).

Insecticidal activity

Reed and co-workers (84) tested various extracts of *A. altissima* against the stopped (*Diabrotica undecimpunctata*) and striped (*Acalymma vittata*) cucumber beetles. Non polar extracts of aerial parts of the plant provoked 70-100% of mortality when applied topically at a dose of 3 μg/*Tribolium castaneum* Herbst (85). An extract of fresh leaves was slightly insecticidal against yellow fever mosquito larvae (*Aedes aegypti*) (81). Petrol and methanol extracts from the seeds of *A. altissima* and the main components (chaparrinone and ailanthone) of the methanol one were tested for their antifeedant, insecticidal, insect growth regulating (IGR). The experiments showed that ailanthone turned out to be a potent antifeedant, too, but seems to be also an insect growth-inhibitor at lower concentration (74).

Allergy to *Ailanthus altissima* pollen

Ballero and co-workers (86) suggested that the pollen of *A. altissima* needs to be considered as a possible allergenic source and its extract should be introduced in the diagnostic screening panels in areas where this tree is widespread.

Cell cultures of *Ailanthus altissima*

Cell cultures of *A. altissima* have been of particular interest for their remarkable ability to produce high amounts of its different classes of compounds: quassinoids (87-88) and alkaloids (Figures 5 and 7) such as canthinone and 1-methoxycanthinone (89), canthin-6-one (**XXXIV**) (61, 90-92), 1-methoxycanthin-6-one (**XXXVI**) (61, 91-92), 4,5 dihydrocanthin-6-one (**LIV**) (79), canthin-6-one-3-oxide (**XXXV**) (90, 92), 1-methoxycanthin-6-one-3-oxide (**XXXIX**) (90), 1-hydroxycanthin-6-one (**XXXVII**) (90, 92), 5-hydroxycanthin-6-one (**LV**) (90), β-carboline-1-propionic acid (**LVI**) (79, 90), and 4-methoxy-β-carboline-1-carboxylic acid methyl ester (**LVII**) (90, 92), normally found as very minor constituents. Moreover Crespi-Perellino and co-workers (90) isolated from cell cultures of the plant three new alkaloids, 2-hydroxycanthin-6-one (**LVIII**), 4-hydroxycanthin-6-one (**LIX**), and 4,5-dihydrocanthin-6-one (**LIV**).

Bucar and co-workers (92) isolated, from callus cultures of the plant, 6-β-OH-stigmasta-4-en-3-one, 6-β-OH-stigmasta-4,22-dien-3-one and 4,8-dimethoxy-β-carboline-1-carboxylic acid methyl ester (**LX**) (Figure 7).

Conclusions

A number of characteristics undoubtedly contribute to the fitness of *Ailanthus altissima*. These characteristic, alone, appear inadequate to explain the invasiveness and tenacity of the plant: it is probably that an arsenal of biochemical defenses may also contribute to the fitness of *A. altissima.* Many plants produce secondary compounds capable of inhibiting other plants, pathogens, or herbivores. Much evidences suggests allelopathy is important in the establishment and persistence of this plant. The literature showed that extracts or purified compounds of *A. altissima* were strong plant growth inhibitors, therefore good candidates as potential environmentally safe and effective agricultural pest management agents.

On the other hand, the vast pharmacological literature suggests that *A. altissima*, coluld be employed in various applications as cancer, viral disease like HIV and others. It is very important to underline the antitumoral activity of the plant: it is probably that, in major cases, its antitumoral effect occur via apoptosis. Some of other activities traditionally attributed to the plant have been confirmed by experimental data and other biological activities have been demonstrated.

Taking great concern of the useful benefits of the plant, it can be advocated as a safe, highly important, medicinal plant for general mankind.

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