PHYTO-PHARMACOLOGICAL PROFILE OF *AILANTHUS EXCELSA*

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Summary

Over the past decade, herbal medicine has become an item of global importance, with both medicinal and economic implications. Widespread use of herbs throughout the globe has raised serious concerns over their quality, safety and efficacy. Thus, accurate scientific assessment has become a prerequisite for acceptance of herbal health claims. *Ailanthus excelsa* Roxb is a tree, indigenous to central and southern India, belongs to family Simaroubaceae is widely used in Ayurveda and evidence based phytotherapy. The tribal population uses the plant for antifertility, anthelmintic and rejuvenating purpose. Alkaloids, flavonoids, triterpenoids and bitter principles like quassinoids are reported in this plant. Several quassinoids from Simaroubaceae are designated as potent antimalarial especially against the chloroquine-resistant Plasmodium falciparum. The roots of this plant also serve as substitute for *Oroxylum indicum*, one of the constituents of an ayurvedic formulation Dasmularista. In the present review an attempt has been made to explore different aspects of Ailanthus excelsa.

Key Words: *Ailanthus excelsa*, Quassinoids, Anticancer, Simaroubaceae, Canthin alkaloids, Antimalarial.

Introduction

Ailanthus is a genus of tall, lofty trees, distributed in Indo-Malaya, China, Japan and Australia[1]. The genus is noted for its antidiarrhoel and antidysenteric properties[2]. Different species of the genus are *Ailanthus glandulosa* in Malay Peninsula and China, (leaflets very coarsely toothed at the base and filaments several times exceeding the anther), *Ailanthus excelsa* in India (leaflets coarsely toothed and filaments shorter than anthers) and *Ailanthus malbarica* in Indo-china (leaflets entire and filaments larger than anthers)[1]. *Ailanthus excelsa* Roxb (Simaroubaceae) is commonly known as "Mahanimba" due to its resemblance with neem tree (*Azadirachta indica*). The term Ailanthus is from ailanto which means "Tree of Heaven" and is the name for one of the species in the Moluccas, while in Latin excelsa means tall. The plant is known by different names like, tree of heaven in English, ardusi, aralavo in Gujarati, maruk, ghoda karanj, aakashneem, arlu in Hindi, peruvagai in Tamil and peddamanu in Telgu[1]. It is a fast growing tree extensively cultivated in many parts of India towards the vicinity of villages. The tree is indigenous to central and southern India and is distributed in Madhya Pradesh, Gujarat, some costal districts of Andhra Pradesh, Ganjam and Puri districts of Orissa[3]. The plant is known for its high commercial and economic importance[4].

PHYTOCHEMICAL STUDIES

Quassinoids

Plants from Simaroubaceae are known to contain compounds with highly oxygenated triterpenens and bitter taste called as quassinoids[5]. Initially the compounds of such chemical nature were known by the term "quassin" after the physician "Quassi" who used the bark of plants from this family for the treatment of fever. Studies on quassinoids have shown their promising role as therapeutic agents as an antitumor, antiviral[6,7] anti-inflammatory, antiamoebic[8,9] antimalarial[10,11] insecticidal, antitubercular[12] ,anticancer[13], amoebicidal[6], antiulcer[14], herbicidal and anti feedent, etc[15]. Stem bark of *A. excelsa* contains quassinoids like excelsin, 1,4-dihydroexcelsin[16,17], 2,4-dihydroexcelsin, 3,4-dihydroexcelsin[18], 13,18-dehydroexcelsin, glaucarubin[19], glaucarubol[20], ailanthinone,

1,12-deoxy-13-formyl ailanthiol, ailanex A, ailanex B, polyandrol and glaucarubolone[21,22] while the root bark is reported to contain ailanthinone, glaucarubinone and mixture of glaucarubin-15-isovalerate, 13,18-dehydroglaucarubol-15-isovalerate[23]. Ailanthone is toxic to some fungi and may therefore acts to protect plants against fungal pathogens and is associated with the observed toxicity of this species[24,25]. A total control on *Chenopodium album* and *Amaranthus retroflexus*, the two weeds associated with soybean was observed with excelsin[20]. Quassinoids from *Simarouba amara* were tested in vitro against a multi drug resistant strain of *Plasmodium falciparum* and in vivo against *Plasmodium berghei* in mice. Although the in vitro studies indicated activity in the region of 23-52 times greater than that for chloroquine, the toxicity was found to be very high[26]. Few quassinoids isolated from *Simana cedron* showed good activity against chloroquine-resistant and chloroquine sensitive strains of *Plasmodium falciparum* and *Plasmodium vinckei* petteri in mice.[27] Quassinoids also play an important role in treating Epstein-Barr virus infection[28], HIV infection[29,31], and neoplasms[32] possibly by depolarization of mitochondrial membranes[33].

2, 6-dimethoxy benzoquinone and malanthin

Yellowish green viscous oil was obtained by percolation of air dried powder of trunk bark from an old tree of *A. excelsa*. This oil after refrigeration in minimum amount of benzene and light petroleum gives colorless crystalline malanthin. Saponification of the mother liquor left after malanthin crystallization gives 10 % saponifiable matter and 90 % unsaponifiable material. The unsaponifiable material upon column chromatography on alumina gives 2,6-dimethoxy benzoquinone and β–sitosterol[34,37].

Steroidal compounds

The petrol extract of stem bark on column chromatography over silica gel gives β–sitosterol and Stigmasta-4,22-diene-3-one with hexane-ethyl acetate (9:1)[36]. **Triterpine**

Root bark showed the presence of a new triterpene alcohol, 3S, 24S, 25-trihydroxytirucall-7-ene[17, 37,38].

Triacontane and Hexatriacontane

Stem bark showed the presence of triacontane and hexatriacontane[39].

Figure: Ailanthus excelsa

Alkaloids

Methanol extract from root bark after solvent extraction with chloroform gave four alkaloids viz., canthin-6-one, 1-methoxy canthin-6-one, 5-methoxy canthin-6-one and 8-hydroxy canthin-6-one[40,42]. These alkaloids were studied for nasopharynx carcinoma in Eagles but none of the compounds were sufficiently active to meet the required criteria. On the other hand these alkaloids have shown significant cytotoxicity against 12-O-tetradecanoylphorbol-13-acetate induced Epstein-Barr virus early antigen (EBV-EA). Canthin-6-one and 5-methoxy canthin-6-one showed potent antiulcerogenic activity in gastric lesions induced animals, as well as significant antinociceptive activity in mice[43,44].

Proteins

Leaves contain considerable amount of proteins where, cytoplasmic protein fraction can be used for human consumption; while the unfractionated and chloroplastic fractions could be utilized as a nutritious feed for ruminants and nonruminants. Proximate analysis of various fractions of fresh leaves showed 62.71 % crude protein in cytoplasmic protein fraction, while whole leaf showed 20.86 % protein. The unfractionated and fractions from chloroplastic protein contained more crude fat than the whole leaf and pressed cake. Compared to whole leaf and pressed cake, protein fractions were low in crude fiber content. The amino acid compositions of protein sample, showed an excellent balance of essential amino acids. The leaf protein fractions were nutritionally superior to the whole leaf, pressed cake as well as soyabean protein[45,46] **(Table-1).**

Table 1. Amino acid composition of the fractionated leaf protein concentrate (grams per 16 gram of nitrogen).

S.No.	Amino acid	Unfractionated LPC*	Chloroplastic LPC	Cytoplasmic LPC	Soyabean Protein
1	Lysine	6.17	5.99	7.75	6.40
2	Threonine	4.72	4.69	4.85	4.10
3	Serine	4.87	4.71	4.38	5.60
4	Glutamic acid	12.27	12.26	12.53	19.10
5	Glysine	6.57	7.19	6.89	4.20
6	Alanine	6.67	6.65	6.79	4.30
7	Valine	7.20	7.08	7.20	5.00
8	Isoleucine	6.18	6.09	6.16	4.00
9	Leucine	10.75	11.27	10.10	7.80
10	Tyrosine	5.98	5.90	6.01	3.80
11	Phenylalanine	7.87	8.25	7.65	5.20
12	Methionine	1.79	1.65	2.11	1.40
13	Cystine	1.00	0.96	1.58	1.80
14	Aspartic acid	10.80	10.80	11.13	11.60
15	Arginine	6.37	6.21	8.01	7.70
16	Histidine	2.43	2.41	2.98	2.80

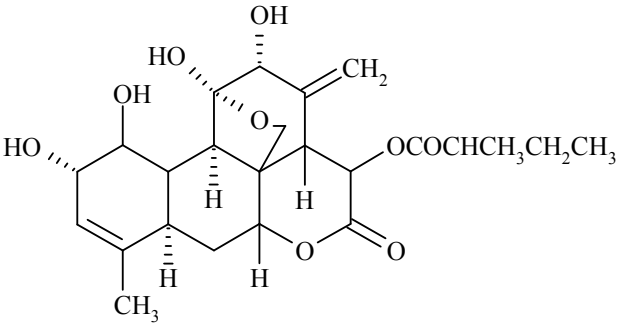
LPC* = Leaf Proteins Concentrate

Flavonoids

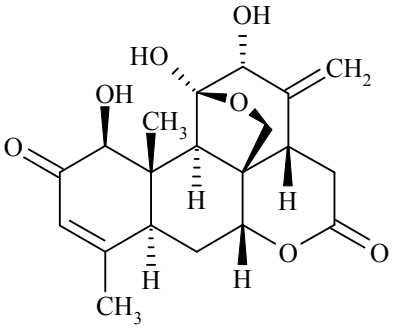
From a pharmaceutical perspective flavonoids possess a remarkable spectrum of biochemical and pharmacological activities. The leaves were reported to contain different flavonoids like kaempferol (5',4',5,7-Tetrahydroxy flavone), luteolin (3',4',5,7-tetrahydroxy flavone), apigenin (4',5,7-trihydroxy flavone) while fruits contains quercetin[47,48]. These flavonoids were reported to possess many biological activities such as antibacterial, anti-inflammatory, anti-allergic, anti-mutagenic, antiviral, anti-neoplastic, anti-thrombotic and vasodilatory properties. The flavon-C-glycosides like vitexin show antioxidant, analgesic and antithyroid activities[49,51], where as quercetin inhibits the growth of leukemic cells, ehrlich ascites tumor cells, and other ascites tumor cells[52,55]. It potentates the cytotoxicity of DNA-damaging anticancer drugs, such as cisplatin[56,59].

Ailantic acid

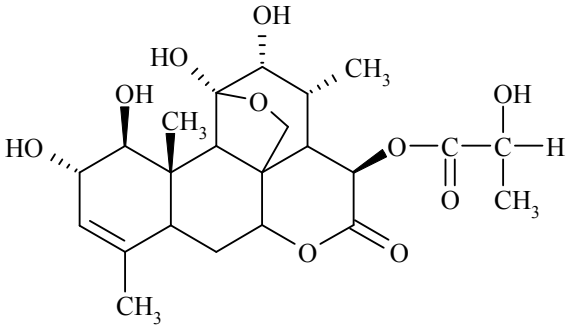
Bark contains wax like, reddish brown, water soluble bitter principle, known as ailantic acid. It is given as a tonic and alterative in dyspepsia and constipation[3].



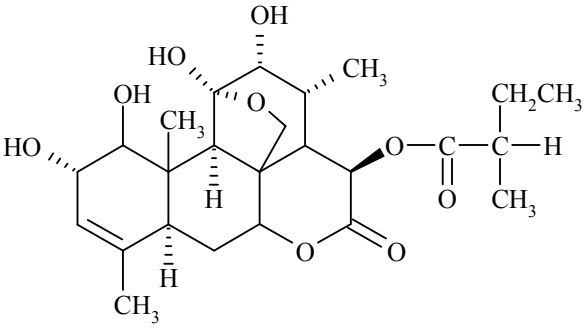
13,18 - dehydroexcelsin



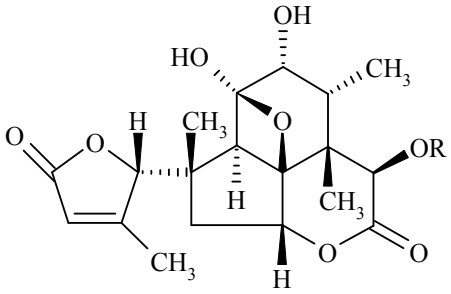
Ailatnthone



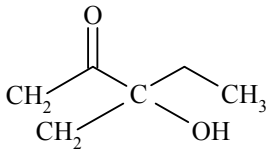
Glaucarubin



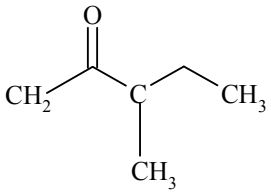
Excelsin



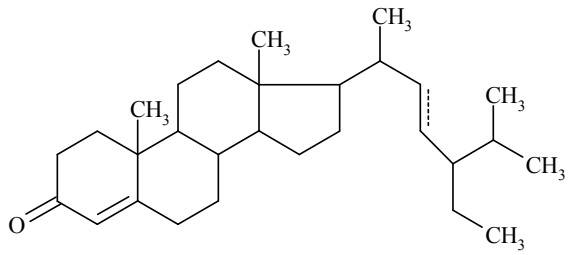
Ailanex A, R =



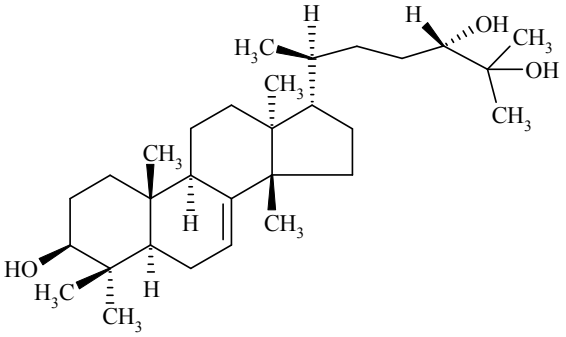
Ailanex B, R =



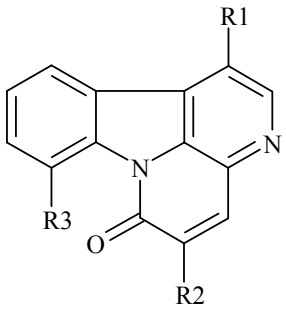
Polyandrol, R = H



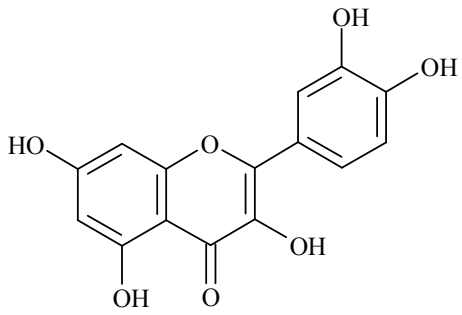
Stigmasta-4,22-diene-3-one



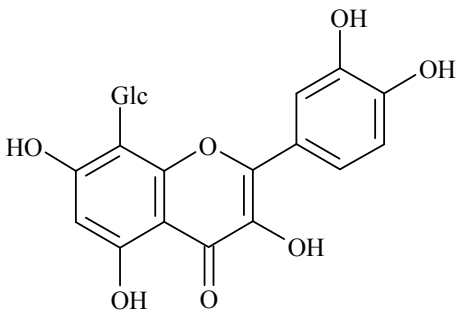
3S, 24S, 25-trihydroxytirucall-7-ene



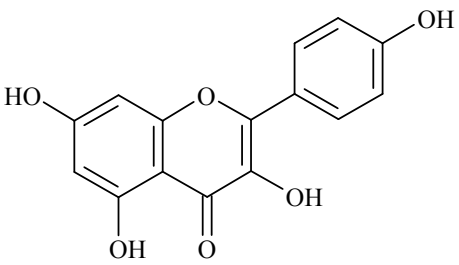
	R1	R2	R3
Canthin-6-one	H	H	H
1-methoxy canthin-6-one	OCH_3	H	H
5-methoxy canthin-6-one	H	OCH_3	H
8-hydroxy canthin-6-one	H	H	OH



Quercetin



Vitexin



Kaempferol

PHARMACOLOGICAL STUDIES

Anti fertility activity

The alcoholic extract of the leaf and stem bark at a dose of 250 mg/kg body weight exhibited a remarkable anti-implantation and early abortificient activity in female albino rats[60].

Antifungal activity

Chloroform fraction of the methanol extract of stem bark showed significant fungistatic and fungicidal activity against *Aspergillus fumigatus, Penicillium frequentence, Aspergillus niger, Penicillium notatum* and *Botrytis cinerea*[61].

Antimalarial activity

It has been considered as a great discovery that several quassinoids possess potent antimalarial activity especially against the chloroquine-resistant *Plasmodium falciparum*[62,67]. Excelsin was found to inhibit the growth of malarial parasites even at a concentration of 0.2 μM[21]. Glaucarubinone is much more potent than that of chloroquine and acts by inhibiting the protein synthesis in mammalian cells as well as in malaria parasites. It has been suggested that this effect also accounts for their amoebicidal activity[68,69]. However, their antimalarial action is different from that of cytotoxicity, as some quassinoids have shown greater selectivity against *P. falciparum* than against KB cells[70,71]. The cytotoxicity of glaucarubinone against KB cells is 285 times of its activity against *P. falciparum*[72]. All quassinoids inhibits protein synthesis more rapidly than nucleic acid synthesis in the *P. falciparum* infected human erythrocytes which is mainly due to its effects upon ribosome rather than upon nucleic acid metabolism. Inhibition of nucleic acid synthesis was observed following the failure of protein synthesis. As chloroquine does not affect protein synthesis so the chance of cross-resistance of malaria between quassinoids and chloroquine is less[68].

Antibacterial activity

Ethyl acetate fraction of dried stem bark inhibited the growth of *Staphylococcus aureus, Escherichia coli* and *Bacillus subtilis* (MIC: 6 mg/disc). Three active principles, excelsin, 13,18-dihydroexcelsin and 1,12- deoxy-13-formylailanthinol, isolated from bark are said to be responsible for this activity. The antibacterial activity of all three compounds was more pronounced than the antifungal potency[73,75].

Hypoglycemic activity

A single administration of leaves or stem bark extracts of *A. excelsa* lowered the blood glucose of normal rats in a glucose tolerance test. Administration of each extract for 60 days produced a significant hypoglycemic effect on STZ-induced diabetic rats, with improved renal parameters which suggest of its potential use in the treatment of diabetes[76].

Insect feedent-deterrent

Bioassay directed fraction of the methanol extract of the stem bark led to the isolation and identification of antifeedent constituent excelsin. A leaf disc method of bioassay showed the potency of excelsin to prevent feeding was 75.94 % at a concentration of 1000 ppm against *Spilosoma oblique*. This insect is a destructive lepidopterous pest in the northern parts of India, attacking a wide range of crops. The ED_{50} of excelsin was found to be 0.563 %[46]. Structure activity correlation indicates that cytotoxicity might be involved in the mode of action of these compounds. Ailanthone acts as a feeding deterrent to herbivores because of its extremely bitter taste[77,81].

Antipyretic activity

Ethanol extract of *A. excelsa*, showed moderate to significant degree of antipyretic activity against yeast suspension induced hyperthermia in an experimental rat model[82].

Leishmanicidal

A genus of parasitic flagellate protozoans causes leishmania. In man it invades the cells of the lymphatic system, spleen, and bone (kala-azar). Canthin-6- one alkaloid from Ailanthus was found to be active against these protozoans[83].

Antitumor and cytotoxicity

Aqueous extracts of roots when screened by the brine shrimp lethality assay it showed significant toxicity to the brine shrimp (<60 μg/ml)[84]. The quassinoids like Ailanthione, glaucarubinone and a mixture of glaucarubol-15-isovalerate have shown substantial antitumor and cytotoxic activities against the P 388 lymphocytic leukemia and KB test system respectively[70,85]. The observed antitumor activity is by inhibiting the protein synthesis of ribosomal peptidyl transferase leading to the termination of chain elongation[86].

Hepatoprotective activity

Ethanol extract of leaves showed protective effects against CCl_4 induced liver injury as evidenced by a significant reduction in the CCl_4 induced elevated enzyme levels of serum glutamate oxaloacetate transaminase (SGOT), serum glutamate pyruvate transaminase (SGPT) and serum alkaline phosphatase. The presence of phenolics might be the responsible factor for the above activity[87, 88].

References

1. Kirtikar K.R, Basu B.D, *Indian Medicinal Plants*, (International Books Distributor, Dehradun, Vol-1, 1995; 505-507.
2. Chopra R.N, Handa L.K, Kapoor L.D, *Indigenous Drugs of India,* U N Dhur and Sons, Calcutta, 1958 ; 493.
3. Nadkarni K.M, *Indian Materia Medica,* Bombay Popular Prakashan, 1976; 56.
4. Singh U, Wadhwani A.M, Johri B.M, *Dictionary of Economic Plants in India,* Indian Council of Agricultural Research, New Delhi, 1983; 9.
5. Khosa R.L, Shai M. and Bhatia N.. Studies on *Ailanthus excelsa*. *Indian Drugs*. 1985;22: 395
6. Polonsky J. Quassinoid bitter principle-II. *Fortschr. Chem. Org. Naturst*. 1985;47: 237
7. Apers S, Cimanga K, Berghe D.V, Meenen E.V, Longanga A.O, A., Foriers Vlieti A. and Pieters L.. Antiviral Activity of Simalikalactone D, A Quassinoid from *Quassia Africana*. *Planta Med*. 2002,**68**: 20-24 .
8. Duriez R. Glaucarubin in the treatment of amoebiasis. *Presse Med*. 1962,**70**: 1291.
9. Gillin F.D. and Reiner D.S. In vitro activity of certain quassinoid anti-tumor agents against *Entamoeba histolytica*. *Arch. Invest. Med.* 1982,**13**(3): 43-49 .
10. Chulabhorn M., Poolsak S. and Somsak R.. Bioactive natural products from Thai plants. *Pure & Appl. Chem.* 1994,**66**(10/11): 2353-2356 .
11. Phillipson D.J. Review of Drug Discovery from Plants. New drugs from old plants. *Herbs.* 1997,**22**(2): 17-19 .

12. Rahman S. Anti-tuberculosis activity of quassinoids. *Chem. Pharm. Bull.* 1997,**45**(9): 1527-9 .
13. Valeriote F.A. Anticancer activity of glaucarubinone analogues. *Oncol Res.* 1998,**10**(4): 201-8 .
14. Toma W, De Souza A.J. Gracioso, A.F. Donisete Pezzuto De Andrade, Hiruma-Lima C.A., Wagner Vilegas C. and Monteiro Souza Brito A.R.. Antiulcerogenic activity of four extracts obtained from the bark wood of *Quassia Amara* L. (Simaroubaceae). *Biol. Pharm. Bull.* 2002,**25**(9) 1151-155 .
15. Heisey R.M. Allelopathic and herbicidal effects of extracts from the tree of heaven *Ailanthus altissima*. *American Journal of Botany.* 1990,**77**: 662-670 .
16. Tripathi A.K. and Jain D. C. Excelsin an insect feeding deterrent isolated from *Ailanthus excelsa* (Simaroubaceae). *Phyto. Research.* 1993,**7**(4): 323-325 .
17. Khan S.A, Zuberi S.S. and Shamsuddin K.M. Isolation and structure of Excelsin, a new quassinoid from *Ailanthus excelsa*. *Indian J. Chem.* 1980,**19B**: 183-184 .
18. Bhatia N, Sahai M. and Khosa R.L., Chemical studies on *Ailanthus excelsa*. *J. Indian Chem. Soc.* 1985,**62**: 75 .
19. Khan S.A, Shamsuddin K.M. Quassinoids from *Ailanthus excelsa*. *Indian J. Chem.* 1978,**16B**: 1045 .
20. Khan S.A, Shamsuddin K.M. Isolation and structure of 13, 18-dehydroexcelsin, a quassinoid, and glaucarubol from *Ailanthus excelsa*. *Phytochemistry*. 1980,**19**: 2484-2485 .
21. Joshi Pandey. B, Sharma R.P. and Khare A.. New quassinoids from *Ailanthus excelsa. Med. Chem. Res.* 2004,**13**(8/9): 781-789 .
22. Joshi B.P, Pandey A, Sharma R.P. and Khare A. Quassinoids from *Ailanthus excelsa*. *Phytochemistry.* 2003,**62**: 579-584.
23. Suroor A.K. and Shamsuddin M.K.. Quassinoids from *Ailanthus excelsa*. *Indian J. Of Chem*. 1978,**16B**: 1045-1046 .
24. Ogura M., Cordell G.A., Kinghorn A.D. and Fransworth N.R. Potential anticancer agents VI. Constituents of *Ailanthus excelsa*. *Lloydia*. 1977,**40**: 579-84 .
25. Kubota K.. Two new quassinoids, Ailanthinols A and B, and related compounds from *Ailanthus altissima*. *Journal of Natural Products*. 1996,**59**: 683-686 .
26. Ang H.H., Chan K.L. and Mak J.W.. In vitro antimalarial activity of quassinoids from *Eurycoma longifolia* against

Malaysian Chloroquine-resistant *Plasmodium falciparum* isolates. *Planta Med*. 1995,**61**: 177-8 .
27. Sianne S. and Fanie R. Van .. Antimalarial activity of plant metabolites. *Nat. Prod. Rep.* 2002,**19**: 675-692 .
28. Tamura S., Fukamiya N, Okano M., Koyama J, Koike K. and Tokuda H.. Three new quassinoids, ailanthiol E, F, and G, from *Ailanthus altissima*. *Chem. Pharm. Bull.* (Tokyo). 2003,**51**: 385-9 .
29. Chang Y.S. and Woo E.R.. Korean medicinal plants inhibiting to human immunodeficiency virus type 1 (HIV-1) fusion. *Phytother Res.* 2003,**17**: 426-9. .
30. Morre D. J.. Effect of the quassinoids glaucarubolone and simalikalactone D on growth of cells permanently infected with feline and human immunodeficiency viruses and on viral infections. *Life Sci.* 1998,**62**(3): 213-9 .
31. Geoffrey A.C, Cindy K.A. and John M.P. Recent studies on cytotoxic, anti-HIV and antimalarial agents from plants. *Pure & App/. Chem.* 1994,**66**(10/11): 2283-2286 .
32. George R.P, Cherry I.S, Polonsky J. and John A.R. The Antineoplastic quassinoids of *Simba cuspidate*. Suruce and *Ailanthus grandis*. Prain. *J. of Nat. Prod.* 1980, **43** (4): 503-508 .
33. Rosati A, Quaranta E., Ammirante M, Turco M.C, Leone A. and De Feo V. Quassinoids can induce mitochondrial membrane depolarisation and caspase 3 activation in human cells [Letter]. *Cell Death Differ*. 2004,**2**(16-81): 1.
34. Bhatia N, Mohan Y. and Khosa R.L. Chemical studies on *Ailanthus excelsa* Roxb. Bark. *Indian Drugs.* 1983,**20**: 240.
35. Rastogi R.P. and Dhar M.L, Studies on the chemical composition of *Ailanthus malbarica* DC. *J. Sci. Industrial. Res.* 1957,**16B**: 74-80 .
36. Mandal S, Das P.C, Joshi P.C, Das S.R. and Mallik B. A Steroidal constituent of *Ailanthus excelsa* Roxb (Simaroubaceae). *J. Of Indian Chem. Soc*. 1999,**76** (10): 509-510 .
37. Jain D.C. Mahendra Kumar. Chemical evaluation of *Ailanthus excelsa*. *Indian J. of chem.* 1964, **2**: 40 .
38. Sherman M.M, Borris R.P, Ogura M, Cordell G.A. and Fransworth N.R.. 3S, 24S, 25-trihydroxytirucall-7-ene from *Ailanthus excelsa*. *Phytochemistry*. 1980,**19**: 1499 .

39. Mehta C.R. and Patel C.N. Chemical examination of the bark of *Ailanthus excelsa*, Roxb. Part I. *Indian J. Pharm.* 1959,**21**: 143-145 .
40. Haynes H.F., Nelson E.R. and Price J.R.. Alkaloids of the Australian Rutaceae; *Pentaceras australis* Hook F. I. Isolation of the Alkaloids and Identification of Canthin-6-one. *Aust. J. Sci. Res.* 1952,**5**(2): 387-400 .
41. Ogura M., Cordell G.A. and Fransworth N.R.. Alkaloid constituents of *Ailanthus excelsa. Lloydia.* 1978,**41**: 166 .
42. Ogura M., Cordell G.A. and Fransworth N.R. Lymphocyty-Leukaemia in mice.*J. of Nat. Prod.* 1980,**19**: 1499 .
43. Murakami C, Fukamiya N, Tamura S, Okano M, Bastow K.F, Tokuda H, Mukainaka T, Nishino H. and Lee K.H. Multidrug-resistant cancer cell susceptibility to cytotoxic quassinoids, and cancer chemopreventive effects of quassinoids and canthin alkaloids. *Bioorg Med Chem.* 2004,**12**(18): 4963-8 .
44. Anderson L.A. and Phillipson J.D. Production of cytotoxic canthin-6-one alkaloids by *Ailanthus altissima* plant cell cultures. *J. Nat. Prod.* 1983,**46**: 374-378 .
45. Brule D. and Savoie L. Soya proteins- In-vitro digestibility of proteins and amino acids in protein mixture. *J. Sci. Food. Agric.* 1988,**43**: 361-372 .
46. Nag, Matai S. *Ailanthus excelsa* Roxb (Simaroubaceae) A promising source of leaf proteins. *J. Agric. Food. Chem*. 1994,**42**: 579-584 .
47. Kapoor S.K, Ahmad P.I. and Zaman A. Chemical constituents of *Ailanthus excelsa*, *Phytochemistry.* 1971,**10**: 3333 .
48. Khan M.S, Kallm Y, J, Khan I.U. and Khan M.H. Chemical investigation of fruits and leaves of *Ailanthus excelsa* Roxb (Simaroubaceae) *Indian Drugs* 1994,**31**(3): 125-126 .
49. Gaitan E, Cooksey R.C, Legan J. and Lindsay R.H.. Antithyroid effects in vivo and in vitro of vitexin: a C-glucosylflavone in millet. *J. Clin. Endocrinol. Metabol*. 1995,**80**(4):1144-1147 .
50. Sethuraman M. G, Sulochana N. and Ramaswamy S. Analgesic activity of Vitexin *J. Res. Edu. Ind. Med.* 1990; 61-63 .

51. Wagner H. New approaches in Phytopharmacological research. *Pure Appl. Chem.* 1999,**71**(9): 1649-1654 .
52. Suolinna EM, Buchsbaun RN. and Racker E. The effect of flavonoids on aerobic glycolysisand growth of tumor cells. *Cancer Res.* 1975,**35**:1865-1872 .
53. Castillo MH, Perkins E. and Campbell JH. The effects of the bioflavonoid quercetin on squamous cell carcinoma of head and neck origin. *American J. Surg.* 1989,**188**: 351-355 .
54. Bibby MC, Double JA. Flavone acetic acid-from laboratory to clinic and back. *Anticancer Drugs* 1993,**4**: 3-17 .
55. Leighton T, Ginther CH, Fluss L, Harter W, Cansado J, Notario V. Molecular characterization of quercetin and quercetin glycosides in Allium vegetables (Phenolic Compd. Food Their Eff. Health II). Their effects on malignant cell transformation. *ACS Symp*. 1992,**507**: 220-238 .
56. Scambia G, Ranelletti FO. and Benedetti PP. Synergistic antiproliferative activity of quercetin and cisplatin on ovarian cancer cell growth. *Anticancer Drugs* 1990,**1**: 45-48 .
57. Teofili L., Pierelli L. and Iovino MS. The combination of quercetin and cytosine arabinoside synergistically inhibits leukemic cell growth. *Leuk. Res.* 1992,**16**: 497-503 .
58. Hofmann J, Fielig HH, Winterhalter BR, Berger DR. and Grunicke H. Enhancement of the antiproliferative activity of cis-diammine dichloro platinum (II) by quercetin. *Int. J. Cancer*. 1990,**45**: 536-539 .
59. Yoshida M, Yamato M. and Nakaido T.. Quercetin arrests human leukemic T-cells in late G1 phase of the cell cycle. *Cancer Res.* 1992,**55**: 6676-6681 .
60. Dhanashekaran S, Suresh B, Sethuraman M. and Rajan S.. Antifertility activity of *Ailanthus excelsa* Roxb, in female albino rats. *Indian J. Of Exper. Biology*. 1993,**31**: 384-385 .
61. Joshi BC, Pandey A, Chaurasia L, Pal M, Sharma RP. and Khare A. Antifungal activity of stem bark of *Ailanthus excelsa*. *Fitoterapia*. 2003,**74**: 689-691 .
62. Ang HH, Chan KL. and Mak JW. In vitro antimalarial activity of quassinoids from *Eurycoma longifolia* against Malaysian chloroquine-resistant *Plasmodium falciparum* isolates. *Planta Med.* 1995,**61**: 177-178 .

63. O'Neill MJ. Plants as sources of antimalarial drugs, Part 6. Activities of *Simarouba amara* fruits. *J. Ethnopharmacol.* 1988,**22**(2): 183-90 .
64. O'Neill MJ. The activity of *Simarouba amara* against chloroquine-resistant *Plasmodium falciparum* in vitro. *J. Pharm. Pharmacol*. 1987,**39**: 80 .
65. Trager W. and Polonsky J. Antimalarial activity of quassinoids against chloroquine resistant *Plasmodium falciparum* in vitro. *J. Am. J. Trop. Med. Hyg.* 1981,**30**: 531-537 .
66. Kirby GC. In vitro studies on the mode of action of quassinoids with activity against chloroquine-resistant *Plasmodium falciparum. Biochem. Pharmacol.* 1989,**38**(24): 4367-74 .
67. Cabral JA, McChesney JD. and Milhous WK.. A new antimalarial quassinoid from *Simaba guianensis*. *J. Nat. Prod.* 1993,**56**: 1954-1961 .
68. Kirby GC, O'Neill MJ, Phillipson JD. and Warhurst DC. *Biochem. Pharmacol.* 1989,**38**: 4367 .
69. Monjour. Therapeutic trials of experimental murine malaria with the quassinoid, glaucarubinone. *C. R. Acad. Sci.* 1987,**304**(6): 129-32 .
70. Anderson MM, O'Neill MJ, Phillipson JD. and Warhurst DC. In vitro cytotoxicity of a series of quassinoids from *Brucea javanica* fruits against KB cells. *Planta Med.* 1991,**57**: 62-74 .
71. Kardono LBS, Angerhofer CK, Tsauri S, Padmawinata K, Pezzuto J.M. and Pezzuto AD. Kinghorn, Cytotoxic and antimalarial constituents of the roots of *Eurycoma longifolia*. *J. Nat. Prod.* 1991,**54**: 1360-1367 .
72. Wright CW. Quassinoids exhibit greater selectivity against *Plasmodium falciparum* than against *Entamoeba histoyltica*, *Giardia intestinalis* or *Toxoplasma gondii* in vitro. *J. Eukaryot. Microbiol.* 1993,**40**(3): 244-46 .
73. Patel RD. and Alex RM, Antimicrobial activity of *Ailanthus excelsa* Roxb. *Indian J. Med. Sci.* 1967,**21**: 229-31 .
74. Bhatia N and Khosa LR. Identification and microbiological studies on *Ailanthus excelsa* Roxb. bark. *Indian Drugs*, 1989,**26**(8): 443-445 .

75. Shrimali M, Jain DC., Darokar MP. and Sharma RP. Antibacterial activity of *Ailanthus excelsa* Roxb. *Phytother. Res.* 2001,**15**: 165-166 .
76. Genta S, Cabrera W, Said A, Farag A. and Rashed K. Hypoglycemic activity of leaves and stem bark extracts of *Ailanthus excelsa* in normal and diabetic rats. *Abstracts Biocell.* 2005,**29**(1): 86 .
77. Udert Z. and Wing K.. Insect antifeedent and growth inhibitory activity of agricultural pests of forty-Six quassinoids on two species. *J. of Nat. Prod*. 1987,**50**(3): 442-448 .
78. Heisey RM. Identification of an allelopathic compound from *Ailanthus altissima* (Simaroubaceae) and characterization of its herbicidal activity. *American Journal of Botany* 1996,**83**:192-200 .
79. Klocke JA. Growth inhibitory, insecticidal and antifeedent effects of some antileukemic and cytotoxic quassinoids on two species of agricultural pests. *Experientia.* 1985**,41**(3): 379-82 .
80. Daido M, Fukamiya N, Okano M, Tagahara K, Hatakoshi M. and Yamazaki H.. Antifeedent and insecticidal activity of quassinoids against diamondback moth (*Plutella xylostella*). *Biosci. Biotech. Biochem.* 1995,**57**: 244-246 .
81. Leskinen V, Polonsky J. and Bhatnagar S.. Antifeedent activity of quassinoids. *J. Chem. Ecol.* 1984,**10**: 1497-1507 .
82. Suresh B, Dhanasekaran S., Elango K. Anti-pyretic activity of some plants in female albino rats: A preliminary report. *Ancient Sci. Life.* 1995,**14**: 253-7 .
83. Thouvenel C, Hocquemiller R, Fournet A. Leishmanicidal activity of two canthin-6-one alkaloids, two major constituents of *Zanthoxylum chiloperone* var. angustifolium. *J. Ethnopharmacol*. 2002,**80**(2-3): 199-202 .
84. Krishnaraju AV, Rao1 TVN, Sundararaju1 D, Vanisree M, Tsay H. and Subbaraju GV. Biological screening of medicinal plants collected from Eastern Ghats of India using *Artemia salina* (Brine Shrimp Test). *Intern. J. of Appl. Sci. and Eng.* 2006,**4**(2): 115-125 .
85. Asolkar LV, Kakkar KK. and Chakre OJ, *Glossary of Indian medicinal Plants with active Principles,* Council of Scientific and Industrial Research, New Delhi, Part-I, 1992 ; 34.

86. Hall IH, Liou YF., Lee KH, Chaney SG. and Willingham JW. Antitumor activity of quassinoids. *J. Pharm. Sci.* 1983,**72**: 626 .
87. Lavhale MS, Hukkeri VI. and Jaiprakash B. Comparative study of leaves and bark of *Ailanthus excelsa.* Roxb for hepatoprotective activity. *Indian Drugs*. 2003,**40**(6): 355-357
88. Lavhale MS, Hukkeri VI. and Jaiprakash B. Hepatoprotective activity of leaves of *Ailanthus excelsa.* Roxb on experimental liver damage in rats. *Indian J. Pharm. Edu.* 2003,**37**(2): 105-106 .