



Received on 19 October 2022; received in revised form, 11 April 2023; accepted 19 April 2022; published 01 July 2023

ETHANOPHARMACOLOGY, PHYTOCHEMICALS AND THERAPEUTIC POTENTIAL OF *AILANTHUS EXCELSA* ROXB: AN OUTLOOK

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Keywords:

Ailanthus excels Roxb.,
Phytochemical, Pharmacological
diseases, Phytochemical

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ABSTRACT: The genus *Ailanthus*, which includes both evergreen and deciduous species, is native to both Asia and northern Australia. Traditional medicine relies heavily on this plant, and various components of the plant are utilized to treat a wide range of illnesses. Herbal and ayurvedic drugs have gained worldwide attention over the past decade for their potential health and financial benefits. There are now major worries about the quality, safety, and efficacy of herbs due to their regular and extensive use around the world. As a result, credible scientific data or evaluation is required before health claims made about herbs may be considered valid. The foundation for this tree's status as a plant of heaven includes the traditional assertions, phytochemical studies, pharmacological examination and some ayurvedic formulations. Therapeutic effects are found throughout the plant. The bark is employed in treating dysentery, earaches, skin diseases, rectum problems, fever related to tridosha and alleviating thirst. Furthermore, it is prescribed for patients suffering from bronchitis, asthma, bronchitis, dyspepsia, gout and rheumatism. In Ayurveda, it is recommended for those with a sour palate. Extracts from the bark of the stem were shown to have strong antibacterial and antifungal properties. Flavonoids, quassinoids, alkaloids, terpenoids, sterols and saponins have all been found in this plant. Ethnobotanical research shows that *Ailanthus excelsa* Roxb (*AER*) is full of different chemical compounds that may have a wide range of effects on living things. The traditional claims, as well as the pharmacognostical, phytochemical, pharmacological, and future potential of this plant are discussed in this review. Researchers are still looking for ways to use naturally occurring molecules to treat human diseases, according to new information. This information also points the way toward discovering more naturally occurring and new semisynthetic or synthetic compounds with similar effects.

INTRODUCTION: Traditional medical practices have become increasingly mainstream during the past decade. Traditional practitioners in many poor nations rely extensively on medicinal plants to provide primary health care to a substantial percentage of the population.

For a variety of cultural and historical reasons, herbal remedies continue to be widely used, despite the availability of modern pharmaceuticals. Concerns about these herbal medications' safety, purity, and efficacy in both developed and underdeveloped countries have arisen as their use has increased¹.

Interest has encouraged scientists to investigate medicinal plants' many purported benefits and usage. Before using any recommended medicinal plant as a medicine, regular people and medical experts look for the most recent, reliable information on the plant's safety and effectiveness.

<p>QUICK RESPONSE CODE</p> 	<p>DOI: 10.13040/IJPSR.0975-8232.14(7).3306-13</p> <hr/> <p>This article can be accessed online on www.ijpsr.com</p> <hr/> <p>DOI link: http://doi.org/10.13040/IJPSR.0975-8232.14(7).3306-13</p>
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Our current effort is an overview and compilation of recent data on *Ailanthus excelsa*, a plant with multiple applications in the Indian medical system. Trees belonging to the genus *Ailanthus* are typically rather tall and can be found in Indo-Malaya, China, Japan, and Australia². Antidiarrheal and antispasmodic qualities have made this family famous. The Malay Peninsula and China are home to *Ailanthus glandulosa*, which has coarsely toothed leaflets and filaments that are several times longer than the anther. In India, the genus is represented by *Ailanthus excelsa*, which has coarsely toothed leaflets but shorter filaments, and in Indo-China, *Ailanthus malbarica*, which has entire leaflets and larger filaments. For its similarities to the neem tree, the *Ailanthus excelsa* Roxb (Simaroubaceae) family is often known as the "Mahanimba" (*Azadirachta indica*).

In the Moluccas, one species is known as the Tree of Heaven, or ailanto and the name *Ailanthus* comes from this word. The Latin word *excelsa* means "tall" in English. Tree of Heaven, Ardushi, Aralavo, Maruk, Ghoda Karanj, Aakashneem, Arlu, Peruvagai, Tamil and Peddamanu are just a few of the names for this plant. It's a fast-growing tree that's widely grown in the outskirts of many Indian communities. The tree's native range includes the states of Madhya Pradesh and Gujarat, as well as parts of Andhra Pradesh's coast and the Orissan districts of Ganjam and Puri³. There is a lot riding on this plant commercially and economically.

Several portions of this plant are utilized in traditional medicine to treat many illnesses. The bark is employed in treating dysentery, earaches, skin diseases, rectum problems, fever related to tridosha and alleviating thirst. In addition to its usage in treating asthma and bronchitis, it is also prescribed for gout, rheumatism, dyspepsia and bronchitis. It's used to eliminate a sour taste in the mouth in Ayurveda⁴. According to folk medicine, *Ailanthus* can be used to treat cuts and rashes. Evidence from studies done on mice and in cell cultures shows that the root bark possesses cytotoxic and anticancer properties. Extracts from the bark of the stem were shown to have strong antimicrobial and antifungal properties⁵. High anti-implantation and early abortifacient activity have been observed in alcohol extracts of leaves and stem bark. Recent research shows that the

hepatoprotective impact of ethanol extracts of (*AER*) leaves on experimental liver injury in rats and their antidiabetic action are both promising. Flavonoids, quassinoids, alkaloids, terpenoids, sterols, and saponins have all been identified in the plant. According to ethnobotanical research, (*AER*) has a wide range of chemical compounds with promising biological uses⁶.

Common Names: Araluka, Aralu, Katvanga, Deerghavrinta, Putiveriksha, Mahaneem.

Botanical Distribution: A huge deciduous tree, reaching heights of 18–25 meters, with a straight trunk measuring 60–80 centimeters in diameter and a light gray-brown, rough and aromatically bitter bark on large trees. Large (30-60 cm or more), alternate, pinnately compound leaves; leaflets 8-14 or more in a pair, on long stalks; oblong or widely lance-shaped from a highly uneven base; 6-10/90 cm long, 3-5 cm wide; typically curving, long-pointed; hairy gland; margins coarsely serrated and often lobed. Flowers are widespread, generally male and female on different trees, shorter stalked, greenish-yellow; calyx 5 lobed; 5 narrow petals spreading 6 mm across; 10 stamens; on other flowers, 2-5 separate pistils, each with an oval ovary, 1 ovule and slender type.

The fruit is a single-seeded samara, lance-shaped, flat and pointed at both ends; it is 5 centimetres in length and 1 centimeter in width and is colored a bright copper with prominent veining and a twisted stem^{7, 8, 9}. According to reports, the leaves can be found in *Adhatoda zeylanica*. The bark can stand in for kutaj. It provides substantial shade and is useful for preventing erosion, so it is often grown as an avenue tree. Loamy, well-drained soil is ideal. Seeds and tree stumps can both be used to grow this tree. When selecting soft woods, this species is preferred because of its rapid growth and complete resistance to grazing. The leaves are delicious and nutritious, and a single tree can produce as much as 700 kilograms (1,500 pounds) of green leaves twice a year. The wood is pristine, white, and yellowish, making it ideal for cabinetry¹⁰.

Taxonomical Classification:

Kingdom: Plantae

Phylum: Magnoliophyta

Class: Magnoliopsida

Order: Sapindales

Family: Simaroubaceae

Genus: *Ailanthus*

Species: *Ailanthus excels*

Ethnopharmacology: The bark of (*AER*) is used to treat diarrhea and dysentery in the Chinese medical system, particularly when blood is in the stool¹¹. The bark has been used to treat worms, excessive vaginal discharge, malaria and asthma in traditional Asian and Australian medicine¹². Its antispasmodic and cardiodepressive effects are highly noticeable. The root bark is believed to alleviate symptoms of epilepsy and heart disease. Cramping, epilepsy, tapeworm infestation, and high blood pressure are just some ailments this herb alleviates in Africa¹³.

Leaf and stem bark extract in ethanol has been shown to inhibit implantation and cause abortions in the first stages of pregnancy. Historically, children with fevers would sleep on a mattress made of leaves. The bark and leaves are widely used as a tonic in Bombay, particularly for women feeling weak after giving birth. Dyspepsia, bronchitis and asthma are some of the conditions where they are effective. To alleviate menstrual cramps, the Konkan people drink khir made from leaf juice, which contains the juice of the fresh bark mixed with coconut juice and treacle or with aromatics or honey.

It can also be applied topically to treat wounds and rashes. Irula women in the Mavanahalla area of the Nilgiri district in Tamil Nadu utilize the plant as a natural antifertility agent. For lifelong sterility, a pregnant woman must drink the fresh juice of stem bark combined with honey or sugar for three consecutive evenings.

The nasal rope wound can be cured with a mixture of stem bark, goat milk, and neem oil in the *Kanakpura taluka* of Karnataka. The bark can be used to relieve dysentery, earaches, skin illnesses, rectum problems, fever related to tridosha and thirst. It can also be used as an astringent, an appetizer, an anthelmintic and a febrifuge. As a result, it is also used for gout and rheumatism.

The Ayurvedic practice of using this to eliminate a sour taste in one's mouth *Holarrhena antidysenterica* (Kurchi) bark is a suitable alternative. Both (*AER*) and *Arjuna myrobalans* help the body's own rejuvenation mechanisms. Diarrhea, polyuria, piles, and fever can all be treated with fruit. Cattle, sheep, and goats can digest leaves and twigs just fine. The bassora, or hog gum, that this tree produces is low grade.

The silkworms need this plant as a food source. France cultivates the tree for its leaves, which are given to the larva of the silk-spinning *Ailanthus* moth (*Bombyx cynthia*) to produce stronger and more cost-effective silk than mulberry silk. Short-fiber wood is used in conjunction with long-fiber pulp, like bamboo pulp, in producing paper. In addition, it is essential in the manufacturing of pencils¹⁴.

Phytochemicals of *Ailanthus Excelsa* Roxb:

Many different ailments have been treated with this plant's various parts in traditional medicine. Flavonoids, quassinoids, alkaloids, terpenoids, sterols, saponins, *etc.* are said to be present in the plant **Fig. 1**. Ethnobotanical research suggests that (*AER*) contains a wide range of active chemical components.

Quassinoids: Compounds having a highly oxygenated triterpenoid structure and a bitter flavor, called quassinoids are found in plants belonging to the Simaroubaceae family. "Quassi" popularized the use of the bark of plants in this family for the treatment of fever, and the name "quassin" stuck to the chemical compounds of this type.

Quassinoids have been extensively studied for their potential as therapeutic agents, and these studies have revealed their antitumor, antiviral, anti-inflammatory, anti-amoebic, anti-malarial, insecticidal, anti-tubercular, anti-cancer, amoebicidal, anti-ulcer, herbicidal, antifedant, *etc.* effects¹⁵. Quassinoids such as excelsin, 1,4-dihydroexcelsin, 2,4-dihydroexcelsin, 13,18-dehydroexcelsin, glaucarubin, glaucarubol, ailanthinone, 1,12-deoxy-13-formyl ailanthiol, ailanex A, ailanex B, polyandrol. There is evidence that the fungicidal properties of ailanthone, which is present in this species, assist in protecting plants

from fungal infections¹⁶. Excelsin was found to be highly effective at eradicating *Chenopodium album* and *Amaranthus retroflexus*, two common weeds found in soybean fields. The mice were given *Plasmodium berghei* intraperitoneally, and the Quassinoids from *Simarouba amara* were evaluated *in-vitro* against a multidrug-resistant drug-resistant strain of *Plasmodium falciparum*. Toxicities were exceedingly significant, despite *in-vitro* tests showing action 23–52 times higher than chloroquine. In mice infected with *Plasmodium falciparum* and *Plasmodium vinckeipetteri*, only a small number of the quassinoids isolated from *Simana cedron* showed any significant action.

Depolarization of mitochondrial membranes may account for quinoids' beneficial effects in treating Epstein-Barr virus infection, HIV infection, and neoplasms. By allowing the powdered bark of an ancient (*AER*) tree to air-dry, a viscous oil rich in 2, 6-dimethoxy benzoquinone and malanthin was extracted. This oil yields a colorless crystalline substance called malanthin after being chilled in a mixture of light petroleum and a small amount of benzene. The mother liquor remaining after malanthin crystallization can be saponified to yield 10% saponifiable matter and 90% unsaponifiable material. On alumina column chromatography, the unsaponifiable substance yields 2,6-dimethoxy benzoquinone and sitosterol¹⁴.

Alkaloids: Four different alkaloids, including canthin-6-one, 1-methoxy canthin-6-one, 5-methoxy canthin-6-one, and 8-hydroxy canthin-6-one, were isolated from a methanol extract of root bark that had been chloroform-extracted. Research on these alkaloids for eagle nasopharynx cancer found that none of the substances were effective enough to warrant further investigation. However, these alkaloids have demonstrated substantial cytotoxicity against Epstein-Barr virus early antigen produced by 12-O-tetradecanoylphorbol-13-acetate (EBV-EA). Both canthin-6-one and 4-methoxy canthin-6-one exhibited considerable antinociceptive effects in mice and their robust antiulcerogenic activity in gastric lesion-induced animals¹⁴.

Proteins: Proteins can be extracted from leaves in a number of ways; the cytoplasmic protein fraction can be used for human consumption, while the

unfractionated and chloroplastic fractions can be used as a nourishing feed for ruminants and nonruminants. Among the fresh leaf fractions analyzed, the cytoplasmic protein fraction had 62.71% crude protein. The total leaf, meanwhile, contained just 20.86% protein. Crude fat content was highest in the unfractionated and chloroplastic protein fractions, whereas the whole leaf and pressed cake were the lowest. Protein fractions have a low crude fiber concentration compared to whole leaf and pressed cake. The protein sample's amino acid profile exhibited a healthy distribution of all nine necessary amino acids. In terms of nutritional value, leaf protein fractions were better than the whole leaf, pressed cake, and soya bean protein¹⁷.

Flavonoids: The range of biochemical and pharmacological activity displayed by flavonoids is truly impressive. There are a variety of flavonoids, including kaempferol, luteolin and apigenin, all of which have been detected in the leaves, while quercetin has been found in the fruits. Numerous pharmacological effects, including those of antibacterial, anti-inflammatory, anti-allergic, anti-mutagenic, anti-viral, antineoplastic, anti-thrombotic and vasodilatory, have been attributed to these flavonoids.

Vitexin, one of the flavon-C-glycosides, has been shown to have antioxidant, analgesic and antithyroid effects. Quercetin, on the other hand, has been shown to suppress the proliferation of leukemic cells, ehrlich ascites tumor cells and other ascites tumor cells. It increases the effectiveness of cisplatin and other DNA-damaging anticancer medicines¹⁸.



FIG. 1: *AILANTHUS EXCELSA* ROXB TREE



FIG. 2: FLOWER, LEAVES AND BARK *AILANTHUS EXCELSA* ROXB

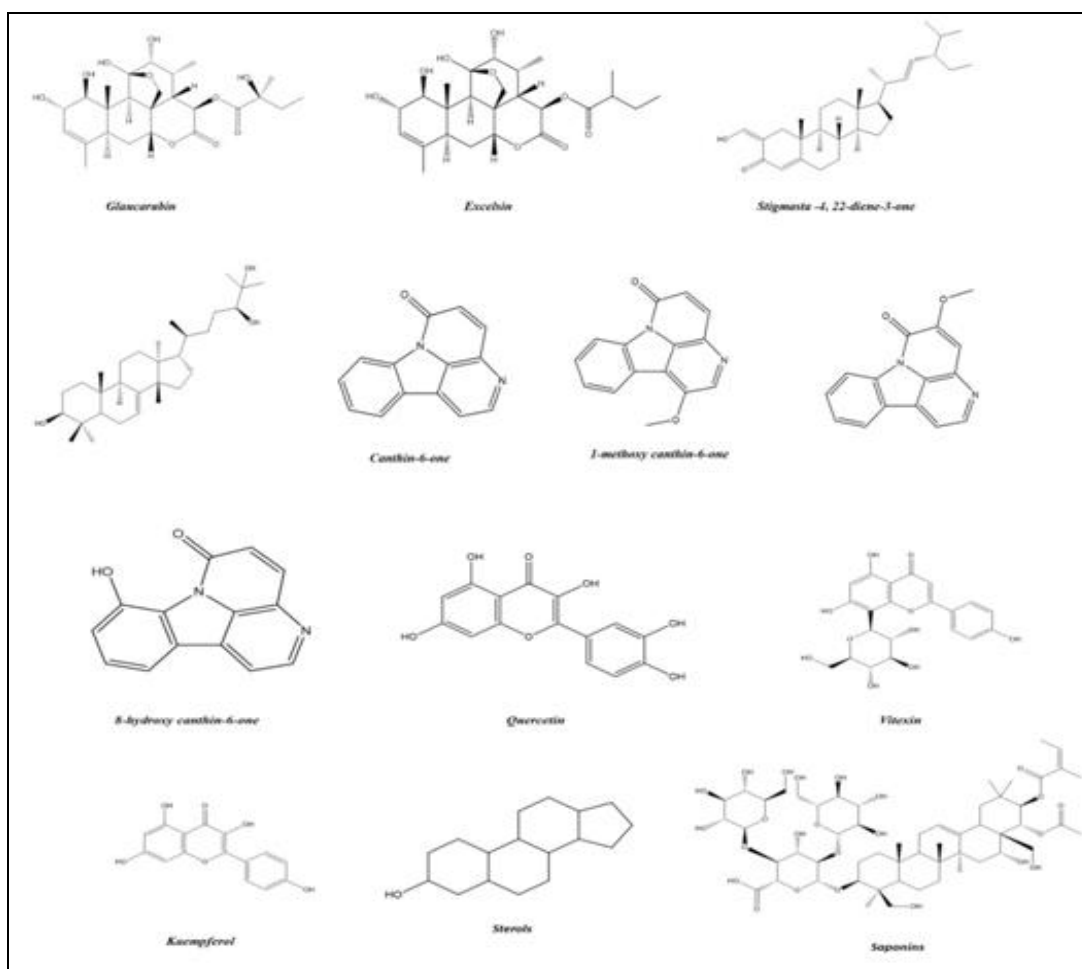


FIG. 3: VARIOUS CHEMICAL CONSTITUENTS OF PLANT *AILANTHUS EXCELSA* ROXB

Therapeutic Potential of *Ailanthus Excelsa* Roxb:

Antioxidant and Antiproliferative Activities:

Said *et al.*; investigated the chemical constituents, antioxidant and antiproliferative activities of (AER). Extracts of (AER) demonstrated significant antioxidant activity in DPPH and FRAP experiments, two separate *in-vitro* systems. The SRB assay was used *in-vitro* to test the possible

antiproliferative activity of the (AER) extract and extracted flavonoids against five different human cancer cell lines (ACHN, COR-L23, A375, C32, and A549) and one normal cell line (142BR). The extract exhibited the greatest inhibitory action ($IC_{50} = 36.5 \mu\text{g ml}^{-1}$) against C32 cells. Quercetin 3-O- β -galactoside Induced activity against COR-L23 ($IC_{50} = 3.2 \text{ g ml}^{-1}$) was observed. Both amelanotic melanoma and malignant melanoma cells were

sensitive to the compounds apigenin and luteolin, which suppressed cell proliferation¹⁹.

Antifertility Activity: Ravichandran *et al.*; evaluated the activity of the stem bark of *Ailanthus excelsa* Roxb via utilization of hydroalcoholic extract. At the doses examined (200 and 400 mg/kg, p.o.), there was significant antiimplantation (72%) and abortifacient (56%). Furthermore, the extract causes a statistically and clinically significant ($P < 0.05$) rise in uterine weight in young ovariectomized rats. When ethinyl estradiol is given alongside the extract, antiestrogenic activity is amplified. These results point to an antifertility action of *Ailanthus excelsa* hydroalcoholic extract²⁰.

Bronchodilator Activity: Kumar *et al.*; utilized the stem bark of (*AER*) to identify the bronchodilator activity. They have tested its bronchodilator efficacy in a variety of animal and human models, including those with milk-induced leukocytosis and eosinophilia, clonidine-induced mast cell degranulation, bronchoalveolar lavage fluid (BALF) and lung histology. Significant action was observed at 100, 200 and 400 mg/kg of the aqueous extract of stem bark²¹.

Antihistaminic Activity: Kumar *et al.*; demonstrated the stem bark activity of *Ailanthus excelsa* Roxb via utilizing of aqueous extract. The antihistamine effects of clonidine *in-vivo* have been studied using models of clonidine-induced catalepsy in mice at 100 µg/mL dosages in an isolated goat tracheal chain preparation and 100, 200, and 400 mg/kg in passive paw anaphylaxis in rats. In the preparation of the goat tracheal chain, an aqueous extract of the stem bark of (*AER*) considerably ($***P < 0.001$) reduces the percentage of contraction. The paw volume at the fourth hour was inhibited by 13.98%, 28.49%, 42.47% and 46.77% when treated with (*AER*) extract (100, 200, and 400 mg/kg oral) and dexamethasone (0.5 mg/kg, i.p.). These results were likewise statistically significant ($**P < 0.01$). At 150 minutes post-clonidine administration, the aqueous extract of (*AER*) stem bark significantly reduced ($*P < 0.05$, $**P < 0.01$) clonidine-induced catalepsy in mice. This effect was seen at 100, 200, and 400 mg/kg p.o. of *A. Excels Roxb*. The antihistaminic (H1-antagonist) properties of an aqueous extract of *A.*

excels Roxb. stem bark is related to its bronchodilatory, anti-inflammatory, adaptogenic properties²².

Anti-asthmatic Activity: Dinesh *et al.*; investigated the activity of *Ailanthus excelsa* Roxb via methanolic extract for the treatment of asthma. *In-vitro*, using a goat tracheal chain preparation paradigm and *in-vivo*, using milk-induced leucocytosis, milk-induced eosinophilia and clonidine-induced catalepsy in mice, a methanolic extract of the stem bark of *Ailanthus excelsa* was tested for its efficacy. Methanolic extract dose-response experiments were performed at 30 µg mL⁻¹ *in-vitro* and at 100, 200 and 400 mg kg⁻¹p.o. *in-vivo* models.

Reduced indications and symptoms were observed after treatment with methanolic extract of *Ailanthus excelsa* stem bark at 30 µg mL⁻¹ *in-vitro* and 100, 200, and 400 mg kg⁻¹ p.o. *in vivo* ($*p < 0.05$, $**p < 0.01$, $***p < 0.001$). Multiple investigations have shown that *Ailanthus excelsa* methanolic extract of stem bark has an antihistamine effect, possibly by lowering histamine-induced contraction in a goat tracheal chain preparation model and by stabilizing mast cells. The antiasthmatic activity is increased because the release of inflammatory mediators is suppressed, lowering the number of total leucocytes and eosinophils²³.

Anti-Allergic and Anticataleptic Activity: Kumar *et al.*; used mice models of milk-induced leucocytosis and eosinophilia and rat models of passive paw anaphylaxis to assess the anti-allergic and anti-cataleptic effects of *Ailanthus excelsa* Roxb. leaves extract. Leucocytosis, eosinophilia, and passive paw anaphylaxis were all significantly ($*p < 0.01$) reduced in the aforementioned experimental animals after the administration of the extract. Mice that were given clonidine experienced significantly ($**p < 0.01$) less catalepsy as a result of the extract. Adaptogenic qualities and the potential therapeutic efficacy of aqueous extract of *Ailanthus excelsa* Roxb. in the treatment of allergic disorders are suggested by these findings²⁴.

Antiasthmatic and Antiallergic Potential: Kumar *et al.*; evaluated the anti-asthmatic and anti-allergic activity of leaves extract of *Ailanthus excels Roxb*. The efficacy of a methanolic extract of (*AER*)

leaves was tested in an *in-vitro* goat tracheal chain production model and *in-vivo*. Rats were subjected to passive paw anaphylaxis and clonidine to produce mast cell degranulation, while mice were given milk to promote leucocytosis and eosinophilia and clonidine to induce catalepsy. The extract tested positive for the presence of alkaloids and steroids in addition to flavonoids, terpenoids, saponins and quassinoids. Flavonoid quercetin was present in the extract and was discovered using standard quercetin on a preparative TLC plate. The methanolic extract of (*AER*) leaves were studied in dose-response trials at 100 $\mu\text{g mL}^{-1}$ *in-vitro* and at 100, 200 and 400 mg kg^{-1} p.o. *in-vivo* models. Significant (* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$) antiasthmatic activity was seen after treatment with a methanolic extract of (*AER*) at varying doses. The ability of (*AER*) leaves to stop or slow the production of inflammatory mediators makes their methanolic extract's antiasthmatic and antiallergic effects even stronger²⁵.

Antiviral Activity: Rashed *et al.*; demonstrated antiviral potential of the extract *Ailanthus excelsa* bark. When tested against herpes simplex virus type 1, the results showed that the chloroform extract of *Ailanthus excelsa* was 82.6% more effective than the methanol 70% extract at a concentration of 50 $\mu\text{g in-vitro}$.

Chloroform and methanol extracts of *Ailanthus excelsa* have been analyzed for their phytochemical properties, revealing the presence of compounds like quassinoids (highly oxygenated triterpenes) and alkaloids. Further analysis of the bioactive chloroform extract led to the isolation of the major alkaloid compound, canthin-6-one. According to the research, Herpes simplex virus type 1 may be treated with *Ailanthus excelsa* extracts²⁶.

Gastroprotective and Antisecretory Activity: Melanchauski *et al.*; used an ethanol-induced gastric lesion model, they compared the gastroprotective efficacy of four (*AER*) bark extracts (petroleum ether, diethyl ether, chloroform, and methanol). Mice pre-treated with (*AER*) extracts (100 mg/kg , oral (p.o.)) showed a 56, 47, and 70% reduction in stomach lesions generated by ulcerogenic agents compared to mice pre-treated with vehicle. Diethyl ether pre-treatment reduced gastric lesion damage by 83%, which is on par with

the conventional antiulcer medicine cimetidine when administered orally at the same dose (100 mg/kg). When administered intraduodenally, cimetidine and a lower dose of diethyl ether extract both dramatically raised pH levels and decreased acid flow from the stomach. The diethyl ether extract of (*AER*) stem bark showed the most gastroprotective activity of the extracts tested because it contains sterols, triterpenes, and quassinoids. In this investigation, they found that (*AER*) is effective in treating stomach ulcers, in line with its traditional uses²⁷.

Hypoglycemic Activity: Cabrera *et al.*; studied the methanolic extract of *Ailanthus excelsa* Roxb on rats. Normal rats' fasting blood glucose levels were not affected by oral administration of the extract at doses of 14, 70, or 350 mg/kg body weight. A significant drop in glycemia was observed 90 minutes after a glucose pulse in an oral glucose tolerance test, suggesting that the extract may have beneficial effects. Diabetic animals showed a strong hypoglycemic response after receiving (*AER*) extract orally once daily for 60 days. Further, the therapy normalized the impaired renal function seen in diabetic control rats. This research provides preliminary evidence that *Ailanthus* leaf extract may be an effective therapy for postprandial hyperglycemia²⁸.

Hypolipidemic Activity: Hukkeri V *et al.*, Studied hypolipidemic activity of ethanolic extract and its fractions of stem bark of *Ailanthus excelsa*, Roxb on triton WR 1339 induced hyperlipidemic model. The results obtained showed a significant effect of ethanolic extract of *Ailanthus excelsa* Roxb (200 + 200 mg/kg) in lowering total cholesterol, triglycerides, High-density lipoprotein, low-density lipoprotein, and Very low-density lipoprotein.

CONCLUSION: In this review, we've tried to compile all the data we could find on *Ailanthus excelsa*, a herb used in traditional Indian medicine, including its botanical and phytochemical properties, nutritional value, ethnopharmacological significance, pharmacological effects, and toxicological profiles. Researchers and medical professionals working with this plant will find this review useful in understanding its nature and applying it appropriately. The cytoplasmic protein fraction from (*AER*) can be used for human

consumption, while the other two can be used as a nutritious feed for ruminants and nonruminants. (AER) extract and purified fractions showed that they stopped plant growth in a big way, which suggests that they could be used as strong, effective, and safe pesticides for agriculture.

ACKNOWLEDGEMENTS: Nil

Funding Source: Nil

CONFLICTS OF INTEREST: None

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How to cite this article:

Agrawal A and Dubey SK: Ethanopharmacology, phytochemicals and therapeutic potential of *Ailanthus excelsa* roxb: an outlook. Int J Pharm Sci & Res 2023; 14(7):3306-13. doi: 10.13040/IJPSR.0975-8232.14(7).3306-13.

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