Pharmacogn. Res., 2024; 16(3):472-482.
https://www.phcogres.com

Review Article

A Comprehensive Review of Ethnomedicinal, Phytochemical and Pharmacological Activity Profile of *Achyranthes aspera*

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ABSTRACT

For centuries, humans have harnessed the healing properties of plants to address diverse health conditions. Ancient systems like Ayurveda and Unani medicine hold a rich repository of knowledge extolling the virtues of herbal remedies. *Achyranthes aspera,* one prolific native herbaceous plant in the South America, Asia and Africa often prospers as one common weed. Its many applications in traditional medicine for treating various diseases are at the heart of this global research. *Achyranthes aspera* is diverse many chemical ingredients, including terpenoids, alkaloids, steroids, saponins and flavonoids. This paper provides a thorough examination and elucidation of the phytochemical composition across different parts of *Achyranthes aspera*, delving into its traditional uses and expounding upon its pharmacological properties.

Keywords: *Achyranthes aspera*, Antidiabetic activity, Anti-oxidant, Anti-inflammatory activity, Anti- microbial activity.

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Received: 02-10-2023;
Revised: 21-11-2023;
Accepted: 13-05-2024.

INTRODUCTION

Throughout history, nature has served as a wellspring of medicinal compounds, yielding a notable array of innovative drugs.[1] Recent times have witnessed a remarkable surge in the production and utilization of plant derived health products, both in developed and developing nations. This surge has led to an exponential growth in the global herbal product market. The World Health Organization (WHO) has identified a staggering 22,000 species of medicinal plants in its endeavor to catalogue global usage.[2]

According to a survey conducted by the WHO, a striking 80% of the population in developing countries predominantly relies on traditional herbal medicine for their healthcare needs.[3] The exploration of plant chemical constituents and subsequent pharmacological assessments forms the bedrock for discovering potential leads in the development of new therapeutic agents. Many of today's life-saving drugs in modern medicine are derived from plants.[4]

Because of the cumulative and persistent side effects associated with modern medications, there has been a notable trend toward herbal medicines in recent years. However, this natural reservoir and the traditional knowledge associated with it face escalating threats from urbanization, population surges and the ongoing exploitation of these herbal reserves.[5] Presently, the evaluation of plants based on their traditional uses plays a pivotal role in the quest for novel drug agents. One such plant under scrutiny is *Achyranthes aspera,* commonly known as prickly chaff flower in English and Chirchira in Hindi. This article aims to provide information about the chemical constituents found in the different parts of *Achyranthes aspera*, as well as elucidate its various pharmacological effects, which underlie its many applications. Its use in the treatment of many diseases is well-documented.

Geographical distribution

Achyranthes aspera thrives as a common weed in India and other regions, growing along roadsides, field edges, and in abandoned areas at altitudes of up to 2,100 m. Its presence is not limited to India but can also be found in Australia, Bangladesh, South

DOI: 10.5530/pres.16.3.57

Figure 1: Morphology of Achyranthes aspera.

Andaman Islands, America, Ceylon, Africa and various parts of tropical Asia.[6]

Plant characteristics

Achyranthes aspera is characterized as a perennial or sometimes annual herbaceous plant, with a prostrate or erect habit (Figure 1).[7]

Seeds: The seeds possess a brown hue, featuring a truncated apex and a rounded base. They are endospermic and sub-cylindric in shape.[8]

Height: Typically, it attains a height ranging from 0.2 to 2.0 m, often supported by a woody base.[9]

Leaf: The leaves are arranged oppositely, bearing a velvety, tomentose texture. They take on an obovate form, with undulating margins and a white hairy surface. The leaf petiole has a crescent-shaped outline and consists of a single-layer cuticle with a thick cuticle. The midrib has a single-layer epidermis, surrounded by 4 to 5 layers of parenchyma on the upper surface and 2 to 3 layers of parenchyma on the lower surface.[10] Leaf dimensions vary, with an average length of 5.22 cm and width of 2.5 cm.[11] They can be found in assorted sizes, featuring anomocytic stomata on the lower epidermis.[12]

Branch: The branches are either terete or quadrangular, marked by striations and a pubescent surface. They support thick leaves.

Roots: The root system comprises secondary and tertiary roots. These roots are cylindrical in shape, exhibiting a diameter ranging from 0.1 to 1.0 cm. They possess a somewhat ribbed texture, gradually tapering towards the ends and are tinted yellowish-brown.[13] Flowers: Arranged in spikes, the flowers vary in length from 8 to 30 cm, with a width of 3 to 7 mm. They are bisexual, presenting a greenish-white hue and occur in numerous quantities. The flowers are sessile, bracteate and have two bracts, one of which has a spiny lip. They exhibit optical symmetry and subcellular arrangement. The perianth comprises five membranous segments, while there are five stamens with short filaments and a two-celled anther. Flowering typically occurs in the summer season.

Trunk: The stem is simple or branched, has ribs, angular borders and is often purple in color. Fruit: The fruits are dry indehiscent capsules, enclosed in persistent bracts and perianths. They contain a seeded drupe or utricle.[14]

Traditional uses

Achyranthes aspera finds mention in both Ayurvedic and Chinese medicinal traditions.[15] In Ayurvedic texts known as "Nighantus," The plant is described for its medicinal properties as a digestive aid, purgative, medicine for internal inflammation, itching, haemorrhoids, cervical gland hypertrophy and abdominal enlargement.[16] Hindus use ash taken from the whole plant to make caustic alkaline preparations.[17]

European and Indian doctors know the plant's diuretic properties.[18] In cases of general edema and renal edema, a decoction of the plant is used as a diuretic.[19] In the Philippines, this herb is used to treat toothache, gastrointestinal problems and dysentery.[20] The plant is used for many therapeutic purposes, including the treatment of asthma, indigestion, bronchitis, flatulence and menstrual disorders. It also acts as an expectorant, analgesic, purifying, anthelmintic, diaphoretic and gastric suppressant.[21] The roots are used to treat coughs, stomach tumours and stomach-related diseases.[22]

In the tribal communities of Chitoor district of Andhra Pradesh, this herb is used to treat epilepsy, Scorpion bite. Additionally, a remedy made from its seeds and milk, known as Payasam Kheer, is considered effective for brain-related ailments.[23]

Achyranthes aspera serves various therapeutic roles, acting as a diuretic, astringent, purgative and remedy for conditions such as abdominal pain, ascites, haemorrhoids[24] and skin rashes.[25] It also acts as a laxative[26] and as an antidote for snakebites, In addition, it is also used in the treatment of bone fractures,[27] whooping cough, respiratory problems[28] asthma[29] and leukaemia.[30] The inflorescence is employed in cases of hydrophobia[31] and cough,[32] while the fruit is used to address hydrophobia.[33] The seeds find application in treating gonorrhea, insect bites, fear of water, cough (especially whooping cough) and anti- asthma.[34] They are also known for their cathartic, purgative and emetic properties.[35] The leaves are used to treat conditions such as dog bites, intermittent fever, asthma, ulcers, wounds and typhoid, For whooping cough, tonsillitis, haemorrhage,[36] cough and hydrophobia,[37] the roots are used as an anti-asthma,[38] diuretic, diaphoretic and anti- syphilis drug.[39]

Phytochemistry

The whole *Achyranthes aspera* plant was analyzed, showing its solubility in water and chloroform. Initially, the component known as achyranthine was identified as a betaine derivative of

Table 1: Taxanomic Classification.

Kingdom:	Plantae
Subkingdom:	Tracheobionta
Phylum:	Angiosperms
Class:	Eudicots
Subclass:	Core Eudicots
Order:	Caryophyllales

N-methylpyrrolidine-3-carboxylic acid.[40] Subsequent studies clarified that betaine, not achyranthine, is soluble in water.[41] Further studies demonstrated that the chloroform-soluble fraction consisted of a mixture of two unidentified alkaloid compounds.[42] The ethanolic extract of the plant contained alkaloids and saponins, while tannins and flavonoids were not detected.[43] Employing gas chromatography-mass spectrometry (GC-MS) technology, a separate study elucidated the phytochemical constituents within the hydro- alcoholic extract of *A. aspera's* whole plant.[44] This analysis revealed the presence of 15 distinct phytocompounds, which are detailed in Table 1.[45]

Shoot

From the shoots of *Achyranthes aspera*, a unique aliphatic dihydroxyketone named.[46] Dihydroxyhenpentacontan-4 was synthesized along with tritriacontane. Another study showed the production of dihydroxy ketones from shoots.[47] identified as 36,37- dihydroxyhenpentacontan-4-one and triacontanol.[48] Additionally, a new long-chain alcohol, 17-pentatriacontanol.[48] and an essential oil yield four distinct compounds: 4- methylheptatriacon-1-en-10-ol, 16-hydroxy-2 6-methylheptacosan-2-one and tetracontanol-2. Shoots also produce the fatty alcohol, 17-pentatriacontanol.[49]

Stem

From the chloroform extract of the stem, unique compounds including pentatriacontanone, 6- pentatriacontanone, hexatriacontane and triacontane were successfully isolated, Ecdysterone, a distinctive component, was identified in the stem, employing ethyl acetate as the extracting agent, the stem yielded 3-acetoxy-6-benzoyloxyapangamide,[50] a compound characterized by its distinct chemical structure.

Inflorescence

Alkaloids and flavonoids have been found in inflorescences.[51]

Seeds

The seeds were found to be a rich source of protein, with a content of 24.8% and a calorific value of 3.92/g, comparable to Bengal seeds.[52] Protein hydrolysis in the seeds revealed the presence of essential amino acids, with leucine, isoleucine, phenylalanine and valine contents equivalent to those of Bengal gram. Notably, tryptophan and sulfur amino acid (methionine and Cystine) contents exceed those of most legumes, while arginine, lysine and threonine are relatively lower than those in whole eggs.[53] The composition of saponin sugar moieties includes glucose, galactose, xylose and rhamnose, the seeds contain a portion of crude sapogenin, which secretes oleanolic acid.[54] Further research led to the isolation of two oleanolic saponins,[55] identified as saponin A and saponin B. They are characterized as α-l-rhamnopyranosyl (1→4)-β'-D -glucopyranosyl (1→4)-β'-D glucuronopyranosyl (1→3)-oleanolic acid and β-D-galactopyranosyl (1→28) ester of saponin A, respectively.[56] Acid hydrolysis of total saponins confirmed the presence of oleanolic acid.[57] A rapid procedure for isolating triterpenoid saponins from plants has been described based on partition chromatography.[58]

In the seeds, hexatriacontane, 10-octacosanone, 10-triacosanone and 4-triacosanone have been identified as constituents.[59] The fatty fraction of seed oils includes lauric, myristic, palmitic, stearic, arachidic, behenic, oleic and linoleic acids, Additionally, the seeds were found to contain Ecdysterone.

Roots

Various preliminary studies have been conducted to discern the chemical composition of the root. It was noted that the saponin fraction contains oleanolic acid as its aglycone component, Additionally, analyses revealed the presence of saponins and alkaloids in both the root and shoot, with no detectable flavonoids.[60] In a separate investigation, alkaloids were identified in the root, while saponins and tannins were not reported, Another preliminary chemical study unveiled the presence of steroids, flavonoids, alkaloids, saponins and terpenoids in the root, with no glycosides detected.[61] Notably, β-sitosterol was also identified in the root, furthermore, Ecdysterone was reported to be present in the root in a separate study.

Pharmacology

Antimicrobial properties

Diverse preliminary investigations have unveiled the multifaceted antibacterial attributes of *Achyranthes aspera*. The entire plant, along with the constituent achyranthine, demonstrated significant antibacterial efficacy against *Streptococcus haemolyticus, Staphylococcus aureus* and *Bacillus typhosus*.[62] Aqueous and alcoholic extracts of the leaves showed notable antibacterial activity against *Staphylococcus Aureus* and *E. coli*.[63] Seeds grown on cow manure showed antibacterial activity against *Salmonella typhimurium, Pseudomonas cichorii* and *B. subtilis* strains, In addition, 80% concentrated ethanolic extract of leaves and stems inhibited the growth of *B. subtilis* and *S. yellow*.[64]

Additionally, diethyl ether extract from the leaves of *A. aspera* has demonstrated inhibitory effectiveness against a variety of microorganisms including *T. rubrum, E. floccosum, Enterobacter* sp., *S. aureus, Salmonella* sp., *Shigella* sp., *Trichophyton*

mentagrophytes, Aspergillus sp., *T. tonurans, P. vulgaris, Klebsiella* sp. to *E. coli*.[65] The finished fabric derived from *Achyranthes aspera* displayed a notable reduction in bacterial count against *Staphylococcus aureus* and *Escherichia coli*.[66] Furthermore, saponin extracted from the ethyl acetate extract of *A. aspera* exhibited larvicidal properties against mosquitoes.[67,68] In *in vivo* experiments, aqueous extracts of the leaves showed specific antibacterial activity against Proteus vulgaris.[69] with no apparent effect against *Pseudomonas aeruginosa, Escherichia coli*, or *Klebsiella aerogenes*.[70] Another water residue from leaves was found to have no effect on a variety of bacteria, including *Escherichia coli, Klebsiella aerogenes, Cytophaga* sp., *Pseudomonas aeruginosa, Vibrio parahaemolytica, Aeromonas hydrophilla, Damsela, Bacillus cereus* and *Streptococcus pyogenes*.[71] Additionally, leaf extracts also demonstrated antibacterial effects against *E. coli, S. citri* and aerobic spores found in soft drinks.[72] Additionally, essential oil extracted from the buds demonstrated antifungal activity against *Aspergillus cameus*, inhibiting its mycelial growth, In a comparative study of herbal fumigants, *Achyranthes aspera* significantly reduced microbial colonies in air samples compared to formalin.[73]

The leaf extracts of *Achyranthes aspera*, along with other plant species, displayed varying levels of larvicidal activity against *Aedes aegypti* L. and *Culex quinquefasciatus* early fourth- instar larvae.[74] In addition, the plant has exhibited significant antibacterial and antifungal properties in dried leaf extracts, particularly in chloroform, petroleum ether and methanol.[75] Phytochemical analyses revealed that *Achyranthes aspera* extracts demonstrated the most prominent inhibition of *E. coli* growth.[76] Additionally, the root extract was found to possess potent hormonal actions associated with insect molting, displaying high larvicidal activity against *Boophilis microplus* tick larvae.[77]

Anti-inflammatory activity

"The alcohol extract of *Achyranthes aspera* exhibited significant anti-inflammatory effects in albino male rats,[78] as demonstrated in studies utilizing cotton pellet granuloma and carrageenin-induced hind paw oedema models.[79] Additionally, the ethanolic extract of *A. aspera* demonstrated anti-inflammatory and anti-arthritic activities within the dosage range of 100-200 mg/kg.[80] Achyranthine, a water-soluble alkaloid found in *A. aspera*, was evaluated for its anti-inflammatory and antiarthritic properties in rats across various models,[81] showing notable efficacy although not surpassing the performance of phenylbutazone and betamethasone.[82] Moreover, achyranthine led to alterations in organ weights, including reductions in the thymus, spleen and adrenal glands,[83] accompanied by elevated concentrations of ascorbic acid and cholesterol in the adrenal gland,[84] similar to the effects of betamethasone.[85] All three medications under examination induced a decrease in food intake without significant effects on urination, mortality rate, or fecal output.[86] Notably, betamethasone exhibited a higher incidence of gastric ulcers compared to achyranthine.[87] Furthermore, additional studies have corroborated the anti-inflammatory properties of *A. aspera*.[88] In a chronic study, the alcohol extract of *A. aspera* demonstrated notable inhibition of edema in carrageenin-induced rat paw oedema.[89] with 65.38% and 72.37% reductions observed at doses of 375 and 500 mg/kg, respectively.[90]

In terms of immunomodulatory activity, the extract of *Achyranthes aspera* exhibited an enhanced induction of humoral antibody responses specific to Ovalbumin (OVA) in mice. This response displayed a dose-dependent trend, resulting in significantly elevated levels of IgM, IgG 1 and IgG 3 antibodies, albeit with a decrease in anti-OVA PCA titers. Notably, extracts from the seed and root of the plant demonstrated particularly robust activity.[91] In studies involving fish, *Achyranthes aspera* seed supplementation led to notable enhancements in various immune parameters, including RNA/DNA ratios, hemagglutination antibody titters and anti-trypsin activity. Additionally, serum globulin levels were significantly elevated in the *Achyranthes*-treated group, indicating an augmentation of immune function in catla.[92] Similar positive effects on immune parameters were observed in Labeo rohita, rohu fingerlings, where *Achyranthes* supplementation resulted in increased superoxide anion generation, lysozyme levels and serum bactericidal activity, among other markers. Furthermore, the extract showed potential in enhancing resistance to infection.[93] Finally, it has been shown that hydroalcoholic extract of *A. aspera* enhances the cell-mediated immune system by enhancing phagocytic function.[94]

Ant-ifertility activity

The ethanol extract of *Achyranthes aspera* root demonstrated potent antifertility activity when administered orally to fertile albino female rats during days 1-7 of pregnancy. At a dosage of 200 mg/kg body weight, it exhibited an impressive 83.3% anti-implantation activity, resulting in complete prevention of successful pregnancies.[95] In addition, when tested in immature female albino mice that had undergone ovariectomy, the ethanolic extract showed estrogenic properties.[96]

In a separate investigation, the acetone and methanolic extracts from the roots of *A. aspera* exhibited notable anti-implantation effects, with 50% and 60% inhibition observed, respectively, in mice.[97] Additionally, a synthetic extract derived from the leaves and roots of *A. aspera* and *Stephania hernandifolia*, in a ratio of 1:3, showed that sperm had the ability to quickly immobilize within 2 min after administration at a concentration of 0.32 g/mL. This effect was irreversible, indicating spermicidal rather than spermiostatic properties.[98] Moreover, the extract significantly reduced sperm viability, rendering them nonviable after 30 min. At the highest concentration, it also led to a notable decrease in hypo-osmotic swelling, suggesting potential damage to the sperm plasma membrane.[99]

The methanolic extract of *A. aspera* leaves was assessed for its impact on various indicators of antifertility activity in female rats. The extract induced significant increases in pituitary and uterine weights in ovarectomized rats, demonstrating abortifacient effects. However, it had no noticeable influence on serum levels of ovarian hormones or different lipid profiles, except for a reduction in HDL at the doses tested.[100]

In a distinct trial, the benzene extract of *A. aspera* stem, when orally administered, resulted in 100% prevention of conception on post-coitum or day 1 in rats.[101] The stem's crude benzene extracts also exhibited a strong abortifacient effect in mice.[102] Additionally, the ethanolic extract (excluding the root) of the plant demonstrated a 60% antifertility effect in rats when administered orally at doses ranging from 100 to 200 mg/kg body weight. Subsequent tests further supported its potential.[103]

The aerial fraction of n-butanol has demonstrated an anti-pregnancy effect in female rats when administered orally at doses of 75 mg/kg or more on days 1 to 5 postcoitus, although it was found to be ineffective in hamsters, even at higher doses.[104] up to 300 mg/kg. The aqueous portion did not show an anti-fertility effect in hamsters or rats. In ovariectomized rats, the extract showed strong estrogenic activity, leading to noticeable stimulation of uterine weight even at a dosage as low as 3.75 mg/kg.[105]

In another study, male rats fed a 50% ethanolic *Achyranthes aspera* extract showed no significant effects on sperm motility or HMG CoA reducing activity. However, this leads to decreased sperm count, epididymal weight, serum testosterone levels and 3beta-hydroxysteroid dehydrogenase activity in the testicles. Elevated urinary 17-ketosteroid concentrations, fecal bile acids, testicular liver cholesterol concentrations and increased incorporation of labeled acetate into cholesterol suggest reproductive toxicity, possibly through inhibition of synthesis protein Androgen.[106]

Whole plant extracts exhibited abortifacient effects in mice, with the benzene extract demonstrating the highest activity, specifically by interfering with corpus luteum function in the ovaries. However, no such effects were observed in rats. Furthermore, co-administration of progesterone or pituitary extract did not prevent abortions in mice, indicating species-specific action.[107] In rabbits, a benzene fraction of the extract demonstrated abortifacient effects at a single dose of 50 mg/kg.[108] Additionally, oral administration of both ethanol and chloroform extracts of *A. aspera* exhibited estrogenic properties as well as a 100% anti-implantation effect.[109]

The alkaloid fraction obtained from the alcoholic extract of the root bark inhibited the oxytocin response in isolated rat uterus. However, it did not affect uterine responses to histamine or serotonin in guinea pigs, nor to acetylcholine in rats.[110] Benzene extract of the whole plant (excluding roots) also showed anti-implantation activity in female albino rats.[111]

Anti-hyperlipidemic activity

The alcoholic extract derived from *Achyranthes aspera* demonstrated significant lipid-lowering effects in both hyperlipidemic and healthy rats. In rats with triton-induced hyperlipidemia, the extract led to notable decreased Phospholipid (PL), Triglyceride (TG), Total blood Cholesterol (TC) and Total Lipid (TL). Specifically, PL, TC, TL and TG% serum concentrations decreased by 62%, 56%, 67% and 68%, respectively. After chronic administration for 30 days. Furthermore, hepatic lipids also showed a significant decrease. This effect is attributed to the extract's ability to prompt rapid bile acid excretion, resulting in reduced cholesterol absorption, indicating a potential mechanism of action for its cholesterol-lowering properties.[112]

Additionally, the hypolipidemic potential of *Achyranthes aspera* was assessed in rats fed with sesame oil, known to induce lipid peroxidation. The alcoholic extract, administered at a dose of 100 mg/kg, effectively reduced blood levels of triglycerides, phospholipids, total lipids and total cholesterol, highlighting its efficacy in mitigating lipid abnormalities.[113]

Anti-feedent activity

The crude ethanolic extract of *A. aspera* was evaluated for its effectiveness against cauliflower borer and brinjal borer larvae. Detailed observations were made on the initial and final weights of the larvae, mortality rates and death rates. Notably, the extract led to a significant reduction in both food consumption and excreted feces. Interestingly, there was a sudden increase in the total body weight of the larvae by 600 µg and 800 µg. However, at the higher concentration of 800µg, the larvae exhibited signs of distress and unhealthy growth. By the third day, the larvae exposed to the 1000 µg concentration had succumbed to the extract's effects. Furthermore, the amount of excreted feces was notably decreased at the highest concentration of 1000 µg. In conclusion, the plant extract demonstrated substantial antifeedant properties and exhibited a lower level of larvicidal activity against *Spodopter litura*.[114]

Anti-diabetic activity

The 50% ethanolic extract of the entire plant demonstrated hypoglycemic effects in rats during preliminary biological investigations.[115] However, it showed no discernible impacts on respiration, Cardiovascular System (CVS), Central Nervous System (CNS), or isolated guinea pig ileum. Additionally, the extract did not exhibit anti-helminthic, anti-tumor, anti-protozoal, or anti-viral properties. The Maximum Tolerated Dose (MTD) of the extract in rats was determined to be 1000 mg/kg body. Weight when administered orally, in another study, a substantial dose-dependent hypoglycemic effect was observed with oral administration of 2-4 g/kg of whole plant powder in both normal and alloxan-induced diabetic rabbits. Additionally, water and methyl alcohol extracts of the plant reduced blood sugar

levels in both healthy rabbits and rabbits with alloxan-induced diabetes.[116]

The hypoglycemic effect of the plant in diabetic rabbits may be due to the fact that it provides essential nutrients such as zinc, manganese, magnesium, calcium and copper to beta cells. Furthermore, administration of plant seeds to high-dose fructose-fed rats showed alterations in the redox and oxidation states of plasma and other tissues.[117]

In experiments involving normoglycemic albino rats, diabetes was induced by intraperitoneal injection of a dose of 150 mg/kg body weight of alloxan monohydrate after a 12 hr fasting periods. This dose of alloxan resulted in sustained hyperglycemia after four days of monitoring blood and urine samples to determine glucose levels.[118] The *A. aspera* water extract group (administered at a dose of 500 mg/kg) showed significantly lower blood glucose and HbA_{1c} levels than the control group.

To induce diabetes in adult Wistar rats, *Streptozotocin* was administered intravenously at a dose of 60 mg/kg body weight. This agent caused diabetes to develop within three days by damaging the beta cells.[119] It was reported that an ethanol extract of *A. aspera* (administered at 600 mg/kg) significantly reduced blood glucose levels.

Diuretic activity

Mice were treated with 10 to 20 mg/kg intramuscularly (i.m) of the saponin derived from *A. aspera* seeds exhibited significantly increased urine production at 2, 6 and 24 hr compared to untreated rats. Notably, Mersalyl at a concentration of 3 mg/kg also induced a diuretic effect of comparable magnitude. The optimal dosage for the saponin was determined to be 10 mg/kg. Furthermore, rats administered oral doses of the saponin (at 5-10 mg/kg) demonstrated a substantial elevation in urine output, akin to the effect observed with acetazolamide at 10 mg/kg. Importantly, the diuretic effects of the saponin were comparable to those of acetazolamide and were accompanied by an increase in the excretion of potassium and sodium in the urine.[120]

Activity on Cardiovascular system

Incorporation of isolated saponins extracted from *A. aspera* seeds demonstrated a significant increase in contractile force in hearts isolated from guinea pigs, frogs and rabbits. Pronethalol effectively blocks the stimulant effects of lower doses of saponins (from 1 to 50 µg), while mepyramine partially attenuated these effects. This resulted in enhanced contraction force of failing papillary muscle and heightened tone in hypodynamic hearts due to the presence of saponins. Notably, compared to the effects of digoxin, the onset of action of saponins was quicker and of shorter duration.[120] Further investigations into the phosphorylase activity of perfused rat hearts revealed that saponin, much like adrenaline, stimulated this activity, indicating a comparable effect on cardiac function.[121]

In an earlier study, the roots of *A. aspera* were found to induce a sudden reduction in blood pressure in anesthetized dogs, without notable effects on respiration. However, at higher doses, a slight depression in respiratory rate was observed. The hypotensive effects of the extracts could be counteracted with atropine sulfate. Additionally, the extracts exerted temporary negative chronotropic and ionotropic effects on the frog's heart. In addition, the extract increased both the intensity and amplitude of contractions in the uterus of pregnant and non- pregnant albino rats, guinea pigs and rabbits, as well as induced contractions in the ileum of an isolated rabbit. When administered orally to rabbits, the plant extract significantly increased urine output.[122]

In anesthetized dogs, the water-soluble alkaloid achyranthine, found in *A. aspera*, is reported to increase respiratory rate and amplitude while lowering blood pressure, impairing cardiac function and dilating the heart. Blood vessels, another study showed that saponins derived from *A. aspera* seeds exhibited cardio stimulatory activity and increased contractile force in both isolated and intact hypokinetic hearts.[123] However, it should be noted that cardiovascular toxicity has been reported from leaf decoctions. In tropical West Africa, this plant was observed to activate the cardiovascular system.[124]

Analgesic and Anti-pyretic activities

Achyranthes aspera leaves exhibit both analgesic and antipyretic effects, equivalent to those of aspirin, at doses of 25 mg/kg for analgesic effects and 125 mg/kg for antipyretic effects. These effects were determined using the hot plate method and the yeast induction method.[125] Another study corroborates the analgesic activity of *Achyranthes aspera* leaves and seeds.[126] Specifically, when evaluated by the hot plate method and the acetic acid-induced torsion response, the leaves and seeds demonstrated analgesic effects in rats. Furthermore, hydroalcoholic extract obtained from the roots and leaves of *Achyranthes aspera* showed centrally acting analgesic effects in adult male albino rats, as evidenced by the results of tail flicking, hot plates and acetic acid-induced contraction of peripheral analgesic activity, aspirin. Is the standard drug.[127]

Anti-carcinogenic activity

Scientists have explored the leaves of the *Achyranthes aspera* plant for their potential chemo preventive properties. In laboratory studies, methanol extract, alkaloid, non-alkaloid fractions and saponins were shown to effectively reduce early Epstein-Barr virus antigen activation by the tumor promoter 12-O-tetradecanoylphorbol-13-acetate in Raji cells (in concentration 100 µg). Notably, the alkaloid-free fraction, consisting mainly of nonpolar molecules, had the most significant inhibitory activity (96.9%; with a viability of 60 µL). Furthermore, in a two-step *in vivo* skin carcinogenesis assay in mice, the whole methanol extract demonstrated potent anticancer activity (76%).[128]

Additionally, non-alkaloid constituents of the plant have been identified as potential anti- cancer agents, exhibiting inhibitory activity on human pancreatic cancer cells when extracted in methanol, highlighting these properties. Its anti-proliferative and anti-cancer effects.[129] In experiments evaluating the anti-cancer activity of *A. aspera*, Swiss albino mice were intraperitoneally injected with mineral oil.[130] While the whole methanol extract showed significant anti-cancer effects in *in vivo* studies using rat skin carcinogens, the alkaloid-free fraction, consisting only of non-polar molecules, demonstrated the strongest inhibitory effect in *in vitro* tests.

Renal Disorders

Achyranthes aspera shows an inhibitory effect on the mineralization of urinary stones, including calcium oxalate, calcium carbonate and calcium phosphate. Specifically, methanol extract demonstrated protective properties against lead-induced nephrotoxicity in albino rats.[131] The plant root was evaluated for its effectiveness in inhibiting the nucleation and growth of calcium oxalate crystals *in vitro*, as well as protecting against oxalate-induced injury in NRK-52E (kidney epithelial model). (Mouse tube). Additionally, a hydroalcoholic extract of the plant has been studied for its effect in inhibiting the crystallization of calcium oxalate in synthetic urine, suggesting its potential as an anti-kidney stone drug.[132]

Anti-Dandruff Activity

The efficacy of polyherb hair conditioner containing methanol leaf extract of *A. aspera* (PHO) was evaluated for anti-dandruff effectiveness. Clinical studies have demonstrated that coumarin; a component found in the crude extract of *Achyranthes aspera*, effectively reduces dandruff and inhibits the growth of Pityrosporum ovule.[133]

Anti-Depressant Activity

Rats were subjected to doses of 200, 400 and 600 mg/kg of the methanolic extract derived from *A. aspera* and their total immobility time was recorded. Notably, the oral administration of the methanolic extract of *Achyranthes aspera* at a dosage of 600 mg/kg led to a significant reduction in immobility time, indicating its potential for producing antidepressant-like effects.

Miscellaneous

The effects of *Achyranthes aspera* leaf extract were studied on various parameters including body weight, Lipid Peroxidation (LPO), liver protein content, Catalase (CAT) activity, Superoxide Dismutase (SOD), as well as blood Thyroxine (T4), Triiodothyronine (T3) and glucose concentration. The extract demonstrated significant thyroid activity, elevating thyroid hormone levels, serum glucose levels, body weight and liver protein content. Interestingly, it did not cause any notable effects on the antioxidant enzymes SOD and CAT, suggesting its direct free radical scavenging ability.[134] The water-soluble alkaloid of the plant, achyranthine, isolated from it, has a spasmolytic effect on the rectal muscles of frogs and a cathartic and diuretic effect on albino rats. However, no significant effects were observed in isolated guinea pig, rat and rabbit ileum, as above the Central Nervous System (CNS), with only a slight antipyretic effect noted,[135] Furthermore, experiments revealed that the leaf extract lacked anti-protozoal and antiviral properties and had no effects on Cardiovascular System (CVS), respiratory, central nervous system and membranes initiate preganglionic stimulation. The LD_{50} of the extract in rats was found to be greater than 1000 mg per kg i.p.[136] Additionally, fresh leaf extracts of *Achyranthes aspera* were assessed for their impact on Alternaria alternate, the pathogen causing *Vicia faba* leaf spot disease, resulting in observed growth inhibition.[137]

The alkaloid fraction derived from the alcoholic extract of the root bark of *Achyranthes aspera* showed an inhibitory effect on the oxytocin response in isolated rat uterus. However, this fraction showed no inhibitory effect on the response to histamine in the guinea pig uterus, nor to serotonin and acetylcholine in the rat uterus.[138] Additionally, the total chloroform-soluble fraction (alkaloid residue) of *Achyranthes aspera* has demonstrated mild antidiuretic activity in rats and has an antispasmodic effect against various spasmolytic agents on the myocardium. guinea pigs' intestines and intestines. No specific effects on the central nervous system were observed in rats and rats exposed to this fraction did not exhibit analgesic effects.

CONCLUSION

For centuries, medicinal plants have played an important role in humanity's survival. Knowledge about using plants to treat various diseases has been passed down from generation to generation. In modern times, a combination of indigenous wisdom and modern techniques are used to explore the medicinal properties, effectiveness and safety of plants.

Achyranthes aspera is one of the herbs widely used in Unani, Ayurvedic and Siddha systems of medicine to treat a variety of diseases. This herb acts as an astringent, diuretic and cleanser and is used in the treatment of conditions such as hemorrhoids, ascites and skin rashes. In addition, it is also used to treat snakebites, broken bones, respiratory problems and whooping cough. It also acts as a laxative in the treatment of leukemia and asthma. With a rich variety of chemical constituents including flavonoids, alkaloids, steroids, saponins and terpenoids, there is significant potential to develop innovative therapies and drugs to treat various diseases.

However, further exploration of the chemical composition of *Achyranthes aspera* is necessary as very little research has been done on this subject. The available botanical and analytical studies on this plant are rare. This provides many opportunities to conduct further research such as phytopharmacology of different

extracts, standardization of extracts, identification and isolation of specific compounds. These studies may be followed by the development of lead molecules, as well as their incorporation into specific botanical formulations for intended use.

AUTHOR CONTRIBUTION

NKJ and SA planned the review outline, content, and structure. NKJ, SA, PK, and SK wrote the manuscript and created the figures. AS, MB, DD, and SY contributed to the literature search and data collection. SY, HK, and SM created the figures and tables. All authors approved the manuscript for publication.

ACKNOWLEDGEMENT

The authors extend their appreciation to the authorities of ITM University for providing the necessary support and resources.

CONFLICT OF INTEREST

All authors declare that there is no conflict of interest.

ABBREVIATIONS

GC-MS: Gas Chromatography-Mass Spectrometry; **TCA:** Tricarboxylic Acid Cycle; **HDL:** High-Density Lipoprotein; **IgG:** Immunoglobulin G; **HMG-CoA:** 3-Hydroxy-3-Methyl-Glutaryl-Coenzyme A; **OAR:** Oxidation and Reduction; **CNS:** Central Nervous System; **CVS:** Cardiovascular System; **PL:** Phospholipids; **TG:** Triglycerides; **TL:** Total Lipids; **MTD:** Maximum Tolerated Dose; **HbA_{1c}:** Hemoglobin A1c; **NRK52E:** A specific cell line used in research; **Pho:** Phosphorylation; **LD_{50}:** Median Lethal Dose; **ED_{50}:** Effective Dose 50%; **LPO:** Lipid Peroxidation; **CAT:** Catalase; **SOD:** Superoxide Dismutase; **T3 and T4:** Triiodothyronine and Thyroxine (Hormones produced by the thyroid gland).

SUMMARY

Achyranthes aspera, belonging to the family Amaranthaceae. Native to Asia, including India, it is also found in various parts of Africa, Australia and the Americas. This robust, erect and often prickly herbaceous plant is characterized by its distinctive lance-shaped leaves, which are typically arranged oppositely along the stem.

The plant has a long history of traditional medicinal use in various cultures. It contains a rich array of bioactive compounds, including alkaloids, flavonoids, saponins and triterpenoids, which contribute to its therapeutic properties. In traditional medicine, *Achyranthes aspera* has been employed to treat a wide range of ailments, including inflammatory conditions, digestive disorders, respiratory issues and skin problems.

One of its notable uses is in traditional Ayurvedic medicine, where it is known as "Apamarga." It is valued for its diuretic, analgesic and anti-inflammatory properties. Additionally, the plant has been investigated for its potential as an antimicrobial and anti- diabetic agent.

In modern times, *Achyranthes aspera* has attracted attention from the scientific community due to its pharmacological potential. Research has focused on various aspects, including its cancer-fighting, anti-oxidative, anti-microbial and anti-inflammatory qualities. Additionally, studies have explored its potential applications in the treatment of conditions like diabetes, hypertension and gastrointestinal disorders.

Furthermore, *Achyranthes aspera* is used in traditional agricultural practices. It is known to possess allelopathic properties, meaning it can release chemicals that inhibit the growth of competing plants. This characteristic has led to its use in organic farming as a natural herbicide.

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Cite this article: Jain NK, Anand S, Keshri P, Chopra N, Bajhaiya MK, Harsha GSS, *et al*. A Comprehensive Review of Ethnomedicinal, Phytochemical and Pharmacological Activity Profile of *Achyranthes aspera*. Pharmacog Res. 2024;16(3):472-82.