

## PHYTOCHEMISTRY AND PHARMACOLOGICAL POTENTIAL OF *ACHYRANTHES ASPERA*- A REVIEW

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### Abstract

Many herbal remedies individually or in combination have been recommended in various medical treatises for the cure of different diseases. *Achyranthes aspera* Linn. (Amaranthaceae) is an indigenous medicinal plant of Asia, South America and Africa and is commonly used by traditional healers for the treatment of fever, malarial fever, dysentery, asthma, hypertension and diabetes. The root extract is well reputed for its pronounced insect molting hormonal activity. A decoction of the whole plant is described to have diuretic properties and the aqueous extract is given for pneumonia. The dried herb is used to treat children for colic and also as an astringent in gonorrhea treatment. The root of *Achyranthes aspera* Linn., is reported to have application in infantile diarrhea and cold while dry leaves are employed against asthma. Leaf extracts are reported to possess hypoglycemic, thyroid-stimulating and anti-peroxidative properties. It is claimed to be significant abortifacient activity in ancient Indian literature. This paper explains the evidence-based information regarding the phytochemistry and pharmacological activity of this plant.

**Keywords:** *Achyranthes aspera*, Phytochemistry, Pharmacological activity, Traditional uses.

### Introduction

Ayurveda is the most ancient health care system and is practiced widely in India, Sri Lanka and other countries. According to the WHO survey 80% of the populations living in the developing countries rely almost exclusively on traditional medicine for their primary health care needs. Exploration of the chemical constituents of the plants and pharmacological screening may provide us the basis for developing the leads for development of novel agents. In addition, herbs have provided us some of the very important life saving drugs used in the armamentarium of modern medicine. However, among the estimated 250,000-400,000 plant species, only 6% have been studied for biological activity, and about 15% have been investigated phytochemically(1). This shows a need for

planned activity guided phyto-pharmacological evaluation of herbal drugs. *Achyranthes aspera* Linn. (*A.aspera*) is an annual, stiff erect herb, about 0.3 to 0.9 m high and found commonly as a weed throughout India.

*Achyranthes aspera* Linn. (Amaranthaceae) is commonly found as a weed on way side and at waste places throughout India. It is widely used for asthmatic cough, snakebite, hydrophobia, urinary calculi, rabies, influenza, piles, bronchitis, diarrhoea, renal dropsy, gonorrhoea and abdominal pain(2-6). A powder of dried leaf mixed with honey is useful in the early stages of asthma(7). One of the drugs from Siddha system of medicine, Naayuruvi kuzhi thailum has *A. aspera* as the primary constituent is reported to be quite effective in the management of asthma(8).

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### Traditional Uses

The plant is used in dropsy, piles, skin eruptions, colic, as diuretic, astringent and purgative(9-11), as an antidote to snake bite<sup>12</sup>, in fractured bones(13-15), whooping cough, respiratory troubles(16), in asthma(17), laxative(3) and in leucoderma(18). The inflorescence is used in cough(19) and in hydrophobia(15). Fruit is used in hydrophobia(3). The seeds are employed as an emetic, purgative, and cathartic, in gonorrhoea, for insect bite and in hydrophobia(18,20), cough including whooping cough(20), as an anti-asthmatic(20). The leaves are used in wounds, injuries(21), in intermittent fever, as an anti-asthmatic, for urination, dog bite(13,15) and in typhoid(19). The root is used in whooping cough, tonsillitis(13,15), Hemorrhage(18), cough and hydrophobia, as an antiasthmatic(13), diuretic, diaphoretic, and antisiphilitic(9).

### Phytochemistry of *Achyranthes aspera*

#### Whole plant

The plant is reported to yield a water-soluble base and a chloroform soluble base. The former was earlier designated as achyranthine(22). It was characterized as a betaine derivative of N-methylpyrrolidine-3-carboxylic acid(22). Later studies showed that the water-soluble base was betaine and not achyranthine(23). The chloroform soluble basic fraction was shown to be a mixer of two uncharacterized alkaloid entities(24). The ethanol extract of the plant contained alkaloids and saponin while flavonoid and tannin were found absent(25).

#### Shoot

The shoot yielded a new aliphatic dihydroxyketone, characterized as 36, 47-dihydroxyhenpentacontan-4 one together with tritriacontanol(26). An essential oil; a new long chain alcohol characterized as 17-pentatriacontanol(27-28) four new compounds characterized as 27-cyclohexylheptacosan-7-ol, 16-hydroxy-26-methylheptacosan-2-one, 4-

methylheptatriacont-1-en-10-ol and tetracontanol-2(27-28).

#### Stem

The chloroform extract of the stem led to the isolation of n pentatriacontan, 6-pentatriacontanone, hexatriacontane and triacontane(29)

#### Inflorescence

The inflorescence is reported to contain flavonoids and alkaloids(30).

#### Seed

The food value of the seeds in terms of its protein quality is also reported. The composition of the seeds has close similarity to Bengal gram with a protein content of 24.8 and calorific value of 3.92/g. The hydrolyse contains the usual amino acids. The values obtained for ten essential amino acids and cystine shows that the seed protein can be compared favourably with Bengal gram in its leucine, isoleucine, phenylalanine and valine content, while its tryptophan and sulphur amino acid (methionine and cystine) content are higher than most of the pulses. It is however, deficient in arginine, lysine and threonine as compared to the whole egg protein(31). The defatted seeds are reported to yield a saponin in a yield of 2%, which was identified as oleanolic acid-oligosaccharide. The sugar moiety of the saponin was composed of glucose, galactose, xylose and rhamnose(32-33). Isolated a crude sapogenin fraction from the seeds, which yielded oleanolic acid(34). Later, investigation led to the isolation of two oleanolic acid based saponins, saponin A and saponin B which were characterized as  $\alpha$ -L-rhamnopyranosyl (1→4)- $\beta$ '-D-glucopyranosyl (1→4)- $\beta$ '-D-glucuronopyranosyl(1→3)-oleanolic acid and  $\beta$ -D-galactopyranosyl (1→28) ester of saponin A, respectively(35). In another study, the total saponins were hydrolysed with acid and the genin was identified as oleanolic acid(35). A rapid procedure for the separation of triterpenoid saponin based on partition chromatography from the plant has been described(36). The seeds are reported to contain

hexatriacontane, 10- octacosanone, 10-triacosanone and 4-triacontanone(29).

### Root

The chemical constituents of the root varied in different preliminary studies carried out. The root was found to contain oleanolic acid as the aglycone from the saponin fraction(34). Both root and shoot of the plant were found to contain saponin and alkaloids but no flavonoids. The root of the plant was found to contain alkaloids but indicated absence of saponin and tannins(37-38). In yet another preliminary chemical study, the root was reported to contain alkaloids, flavonoids, saponins, steroids and terpenoids. Glycosides were found to be absent(39). Isolation of  $\beta$ -sitosterol was also reported from the root(38). Various parts of the plant, viz., seeds, stem, leaves and root are reported to contain ecdysterone(40-41). A new six compound isolated from the ethanol extract of the roots are strigmasta-5, 22 dien-3- $\beta$ -ol, trans-13-docasenoic acid, n-hexacosanyl n-decaniate, n-hexacos-17-enoic acid, n-hexacos-11-enoic acid and n-hexacos-14-enoic acid(38).

### Pharmacological Activity of *Achyranthes aspera*

#### Anti-microbial activity

The aqueous solution of the base achyranthine as well as the entire plant of *A. aspera* showed antibacterial activity against *Staphylococcus aureus*, *Streptococcus hemolyticus* and *Bacillus typhus*(22). While the alcoholic and the aqueous extract of the leaves showed antibacterial activity against *S.aureus* and *E. coli*. The seeds growing on cattle dung revealed antibacterial activity against bacterial strains of *B. subtilis*, *Pseudomonas cichorii* and *Salmonella typhimurium*(42). In another study, the 80 percent ethanolic extract of the leaves and stem of the plant inhibited *B. subtilis* and *S. aureus* bacterial strains at a concentration of 25 mg/ml(43). Diethyl ether extract of *Achyranthes aspera* Linn. showed antibacterial and antifungal activities

against the organisms, *E. coli*, *Enterobacter sp.* *P. aeruginosa*, *P. vulgaris*, *S. aureus*, *Klebsiella sp.* *Salmonella sp.* *Shigella sp.* *Trichophyton mentagrophytes*, *T. rubrum*, *T. tonsurans*, *Aspergillus sp.* *E. Floccosum*, *C. neoformans* and *Candida albicans*(44). The antimicrobial activity of the finished fabric from *Achyranthes aspera* was assessed against bacteria that normally exist in the textile environment like Gram positive, *Staphylococcus aureus* (ATCC 6538) and Gram negative, *Escherichia coli* (ATCC 11230) by both quantitative method (AATCC 100) and qualitative methods like Parallel Streak (AATCC 147) and Agar Diffusion method (SN 195 920). The finished cotton fabrics showed the bacterial reduction percentage of 92 and 50 against *S. aureus* and *E. coli*, respectively(45). Saponin from the ethyl acetate extract of *A. aspera* showed mosquito larvicidal activity(46).

#### Anti inflammatory activity

An alcohol extract of *Achyranthes aspera* Linn., showed the anti-inflammatory activity on carrageenin-induced hind paw oedema and cotton pellet granuloma models in albino male rats(47). It is also reported that the ethanolic extract of *A. aspera*, in the doses of 100-200mg/kg possess anti-inflammatory and anti-arthritic activity(48). The water-soluble alkaloid achyranthine isolated from *A. aspera* was screened for its anti inflammatory and anti-arthritic activity against carrageenin-induced foot oedema, granuloma pouch, formalin induced arthritis and adjuvant arthritis in rats. It showed significant anti-inflammatory activity in all the four models employed but was less active than phenylbutazone and betamethasone. Further, achyranthine significantly reduced the weight of adrenal gland, thymus and spleen and raised the adrenal ascorbic acid and cholesterol contents. The effects were qualitatively similar to betamethasone. All the three drugs tested reduced food intake but had no significant effect on urinary and

faecal output and mortality rate. Incidence of gastric ulcers was maximum with betamethasone and minimum with achyranthine(49).

### **Immunomodulatory activity**

The extract of *Achyranthes aspera* Linn., was found to enhance the induction of ovalbumin (OVA)- specific humoral antibody response in mice, on intraperitoneal injection of extract along with OVA. Furthermore, the plant extract was found to increase the induction of OVA-specific antibody response in a dose-dependent manner. A significant elevation of IgM, IgG 1 and IgG 3 antibodies was observed; however, interestingly, the anti-OVA PCA titres were suppressed. The adjuvant property of the extract was further examined in different strains of mice and a significant elevation of the OVA-specific IgG antibody response in all strains tested was found. When the extracts of different parts of the herb were tested, the seed and root extracts appeared to exhibit relatively higher activity(50). Catla, were fed a diet containing seed of *Achyranthes aspera* (0.5%) and control diet without *A. aspera* for four weeks prior to and after i.p injection with chicken erythrocytes. Hem agglutination antibody titers, anti-trypsin activity due to total serum protease inhibitors, alpha1-antiprotease, RNA/DNA ratio of spleen and kidney were significantly higher in the test group of fishes compared with the control group. Serum globulin levels were significantly higher in the test group than control group on days 14 and 21. All these results confirm that *A.aspera* enhances the immunity of catla(51). Immunomodulatory activity of *Achyranthes aspera* seed was studied by incorporating it in the diets of Labeo rohita, rohu fingerlings. Super oxide anion production, serum bactericidal activity, lysozyme, ALP, serum protein, albumin: globulin ratio (A/G) were enhanced in *Achyranthes* treated groups compared to the control group. SGOT and SGPT levels were elevated in control group, but in *Achyranthes* treated groups

the levels were similar to the uninfected-control group. Higher cumulative mortalities were observed in the control group (77%) up to day-9 after infection. This gradually decreased with increasing dose of *Achyranthes* indicating that *Achyranthes aspera* stimulates immunity and increases resistance to infection in *L. Rohita*(52-53). In another study, *Achyranthes aspera* was incorporated in artificial fish diet, and fed to Catla. *Achyranthes* has significantly ( $P<0.05$ ) enhanced the BSA-specific antibody titers than the untreated control group throughout the study period. The efficiency of antigen clearance was also enhanced in *C. catla* treated with *Achyranthes*(54).

### **Anti fertility activity**

The ethanol extract of the root was screened for antifertility activity in proven fertile female albino rats at 200 mg/kg body weight and given orally on days 1-7 of pregnancy. The ethanol extract exhibited 83.3% anti-implantation activity when given orally at 200 mg/kg body weight. The rats, which continued their pregnancy, did not deliver any litters after their full term. Hence the combined antifertility (antiimplantation and abortifacient) activity of ethanol extract was 100%. The ethanol extract also exhibited estrogenic activity tested in immature ovariectomised female albino rats(52). The methanolic extract of the root revealed 60 percent anti implantation activity in rats while the acetone extract of the root prevented implantation in 50 percent of rats(55-56). The effect of a composite plant extract of the leaf of *Stephania hernandifolia* and the root of *Achyranthes aspera* on sperm motility and function in a ratio of 1:3 by weight at different concentrations was studied. At a concentration of 0.32 g/ml, this composite extract showed the promising results by complete sperm immobilization within 2 min after the application of the extract. The effects were spermicidal but not spermiostatic as sperm immobilization

effect was found to be irreversible. Sperm viability was decreased significantly and was found to be nonviable after 30 min when treated with the composite extract at a concentration of 0.32 g/ml. The hypo-osmotic swelling of these sperm was reduced significantly at this highest concentration, indicating that the crude extract may probably cause injury to the sperm plasma membrane(57). The methanolic leaves extract of *Achyranthes aspera* on some indicators for anti-fertility activities such as abortifacient, estrogenicity, pituitary weight, and ovarian hormone level and lipids profile in female rats was investigated. The extract showed significant abortifacient activity and increased pituitary and uterine wet weights in ovariectomized rats. The extract, however, did not significantly influence serum concentration of the ovarian hormones and various lipids except lowering HDL at doses tested(58). The benzene extract of stem bark at 50 mg/kg prevented pregnancy (100%) in mice when given orally either on day 1 or 6 post-coitum(59). The crude benzene extract of the stem was found to have potent abortifacient effect in mice(52). Various chromatographic fractions were tested for anti fertility activity in female mice. The maximal activity was found to be located in the fraction eluted with 50 percent benzene in petroleum ether(52-53,60). The ethanolic extract of the plant (excluding root) at a dose of 100-200 mg/kg body weight administered orally revealed 60 percent anti fertility activity on early pregnancy in rats. Further, the plant also showed potent activity at secondary testing level(60). The n-butanol fraction of the aerial parts prevented pregnancy in adult female rats when administered orally at a daily dose of 75mg/kg or more on 1-5 d post coitum, but was ineffective in hamsters up to 300 mg/kg dose. No anti fertility activity was observed in the aqueous fraction in either rats or hamsters. In ovariectomized immature female rats, the extract exhibited potent estrogenic

activity at a dose of 75mg/kg. It induced marked stimulation in uterine weight. Marked uterotrophic effect was discerned even at a dose of 3.75 mg/kg(61). It was found that feeding 50% ethanolic extract of *A. aspera* to male rats resulted in reduced sperm counts, weight of epididymis, serum level of testosterone and testicular activity of 3beta-hydroxysteroid dehydrogenase, while motility of the sperm and activity of the HMG CoA reductase were not affected. Cholesterol level in the testis, incorporation of labelled acetate into cholesterol, 17- ketosteroids in urine and hepatic and fecal bile acids were increased suggesting reproductive toxicity in male rats and the action may be by suppressing the synthesis of androgen(62). Extracts of the whole plant had shown an abortifacient effect in mice. Maximal activity was in the benzene extract which was tested. Ovaries contained prominent corpus luteum, indicating that the drug had prevented pregnancy. In rats, no effect was observed. Progesterone or pituitary extract given along with the drug did not prevent abortions in mice suggesting that drug is species-specific in that no abortifacient effect was found in rats. A benzene fraction of the benzene extract of the whole plant showed abortifacient activity in rabbit at a single dose of 50 mg/kg(63-64). The chloroform and ethanol extracts of *A. aspera* exhibited 100% anti-implantation activity at 200 mg/kg body weight orally and also exhibited estrogenic activity(65).

#### **Anti-hyperlipidemic activity**

The alcoholic extract of the plant *A. aspera* at 100mg/kg dose lowered total serum cholesterol (TC) and phospholipids (PL), triglyceride (TG) and total lipids (TL) levels by 60, 51, 33 and 53 percent, respectively in triton-induced hyperlipidemic rats. The chronic administration of the extract at the same doses to normal rats for 30 days, lowered serum TC, PL, TG, and TL by 56,62,68



and 67 %, respectively followed by significant reduction in the levels of hepatic lipids. The possible mechanism of action of cholesterol lowering activity of the plant might be due to rapid excretion of bile acids causing low absorption of cholesterol(66).

#### **Anti-feedant activity**

The crude ethanolic extract of the *A. aspera* was tested on cauliflower borer, brinjal borer. The mortality rate, the initial and final weight of the larvae was recorded. There was a marked decrease in the food consumption and faecal matter in excreta rate. The overall body weight of the worm increased abruptly in 600µg and 800µg. The larvae attained abnormal size in 800µg. The larvae of 1000µg concentration were not alive after the 3rd day. The faecal matter excreted also showed considerable reduction in 1000µg. Therefore the plant extract showed high antifeedant and less larvicidal activity on spodopter litura(67).

#### **Anti-diabetic activity**

The 50% ethanolic extract of entire plant was screened for preliminary biological activities. It showed hypoglycemic activity in rat. It was devoid of anti bacterial, anti fungal, anti protozoal, anthelmintic, antiviral and anticancer activities and effects on isolated g. pig ileum, respiration, CVS and CNS in experimental animals. The MTD on the extract was found to be 1000 mg/kg orally in mice(68). It was found that oral administration of 2-4 g/kg of whole plant powder produced a significant dose-related hypoglycemic effect in normal as well as alloxan treated diabetic rabbits. The aqueous and methyl alcohol extracts of the plant also decreased blood glucose levels in normal and alloxan diabetic rabbits(69).

#### **Diuretic activity**

The saponin isolated from the seed of *A. aspera* in 10-20 mg/kg i. m. doses in rats caused significant increase in urine output after 2, 6 and 24h as compared to untreated rats. The diuretic effect was comparable to that observed with 3mg/kg dose of mersalyl. The optimum dose of the

saponin was 10 mg/kg. After oral administration of the saponin (5-10 mg/kg) in rats, a significant increase in urine output was observed which was comparable to that of 10 mg/kg oral dose of acetazolamide. The diuretic effect of saponin, like acetazolamide, was associated with an increase in the excretion of sodium and potassium in the urine(70).

#### **Activity on Cardiovascular system**

The mixture of saponins isolated from the seeds of *A. aspera* caused a significant increase in force of contraction of the isolated heart of frog, g. pig and rabbit. The stimulant effect of the lower dose (1 to 50) of the saponins was blocked by pronethol and partly by mepyramine. The effect of higher dose was not blocked by pronethol. The saponin increases the tone of the hypo dynamic heart and also the force of contraction of failing papillary muscle. The effect was quicker in onset and shorter in duration in comparison to that exerted by digoxin(70). The effect of saponin on the phosphorylase activity of the perfuse rat heart has been investigated and compared with that of adrenaline. The saponin has been found to stimulate the phosphorylase activity of the heart and its effect was comparable to that of adrenaline(71). In a preliminary study, the aqueous and alcoholic extracts of the roots of *A. aspera* caused a sharp and transient fall in blood pressure without any significant action on the respiration of anaesthetized dogs. In higher doses, there was slight respiratory depression. Atropine sulphate blocked the hypotensive effect of the extracts. On frog heart the extracts had a temporary negative inotropic and chronotropic effects. The extracts produced spasm of isolated rabbit ileum, increased the tone and amplitude of contractions in gravid and non-gravid uteri of albino rats, guinea pigs and rabbits. Oral administration of the drug significantly increases the urine output in rabbits(72). The total chloroform soluble basic fraction (alkaloid residue) obtained from the plant *A. aspera* raised the blood pressure of

anaesthetized dog, caused initial transitory stimulation of respiration and increased the amplitude of cardiac contractions of isolated guinea pig heart(73). The water-soluble alkaloid, achyranthine isolated from the plant was found to lower blood pressure, depress the heart, dilate the blood vessels and increase the rate.

#### **Analgesic and Antipyretic activities**

*Achyranthes aspera* leaves shows analgesic activity by using hot plate method and antipyretic by using brewers yeast induced method and compare with Aspirin as a standard in a dose of [25mg/kg] for analgesic and [125mg/kg] for antipyretic effect respectively(74).

#### **Anti-carcinogenic activity**

*Achyranthes aspera* leaves have been assessed for chemo preventive activity. The methanolic extract, alkaloid, non-alkaloid and saponin fractions exhibited significant inhibitory effects (concentration 100) on the Epstein-Barr virus early antigen activation induced by the tumor promoter 12-O-tetradecanoylphorbol-13-acetate in Raji cells. In this in vitro assay the non-alkaloid fraction containing mainly nonpolar compounds showed the most significant inhibitory activity (96.9%; 60% viability). In the in vivo two-stage mouse skin carcinogenesis test the total methanolic extract possessed a pronounced anticarcinogenic effect (76%) (75).

#### **Miscellaneous**

The effects of *Achyranthes aspera* leaf extract on body weight, hepatic protein content, and lipid peroxidation (LPO), superoxide dismutase (SOD) and catalase (CAT) activities and on serum triiodothyronine (T3), thyroxine (T4) and glucose levels were evaluated. The extract exhibited significant prothyroidic activity as it enhanced the levels of both the thyroid hormones along with an increase in serum glucose concentration, body weight and hepatic protein content. On the other hand, it decreased hepatic LPO without altering the activities of the two antioxidant enzymes, SOD and CAT

significantly, suggesting a direct free radical scavenging activity of the extract(76). The water-soluble alkaloid, achyranthine isolated from the plant showed spasmogenic effect on frog rectus muscle and diuretic as well as purgative action in albino rats. No effect was observed on isolated rabbit, g. pig and rat ileum and on CNS. The drug exerted a slight antipyretic effect(77). The ethanolic extracts of leaves were screened for preliminary biological activities. The leaf extract was found to be devoid of anti protozoal and antiviral activities and effects on respiration, preganglionically stimulated nictitating membrane, CVS and CNS in experimental studies. The LD50 of the latter extract was >1000 mg/kg i. p. in mice(78).

#### **CONCLUSION**

Medicinal plant has always played a big role for the survival of mankind. Humans have been using many species of plants medicinally for centuries. Through personal experience and knowledge passed down for generations, indigenous people have learned which species of plants may help alleviate certain ailments such as toothaches, induce labor, or cure malaria. In recent years, there has been an explosion of interest regarding plants and their medicinal value, efficacy and safety. Modern science has added many techniques to evaluate the efficacy of new compounds of medicinal plant through phytochemical investigation, biological evaluation on experimental animal models, toxicity studies, investigation of molecular mechanism of action of isolated phyto-principles and their clinical trials. *Achyranthes aspera* has used in Ayurveda, Unnani, Siddha system of medicine to cure many ailments. Efforts have been made by the researchers to explore the therapeutic potential of this plant.

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