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ACHYRANTHES ASPERA: A POTENT IMMUNOSTIMULATING PLANT FOR TRADITIONAL MEDICINE

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Achyranthes aspera, ecdysterone, Betaine, chemical constituents, pharmacological properties, hepatoprotective

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ABSTRACT: Achyranthes aspera L. (family: Amaranthaceae), an erect and much branched diffuse herb is a medicinal plant, frequently found in tropical and warmer regions as weed. The plants are reported to contain following major classes of compounds: fatty acids, a number of oleonic acid, bisdesmosidic, triterpenoid based saponins, ecdysterone, n-hexacos-14- enoic, oleanolic acid, triacontanol, spinasterol, dihydroxy ketones, spathulenol, alkaloids, Dglucuronic, Betaine, Achyranthine and various amino acids. This acrid, bitter plant has been used as indigenous medicine and commonly used by traditional healers for the treatment of various diseases. Though almost all of its parts are used in traditional systems of medicines, seeds, roots and shoots are the most important parts which are used medicinally. The present article gives an account of updated information on its classification, morphology, geographical sources, phytochemical and pharmacological properties. The review reveals that wide numbers of phytochemical constituents have been isolated from the plant which possesses activities like antiperiodic, antiasthmatic, hepatoprotective, antiallergic, expectorant, stomach tonic, laxative, antihelmintic, diuretic, linthontriptic, sudorific, demulcent, anti-inflammatory, anticataract, antifungal, antibacterial, hypoglycemic, antihyperlipidemic and haematinic and various other important medicinal properties. For the last few decades or so, extensive research work has been done to prove its biological activities and pharmacology of its extracts.

INTRODUCTION: Nature has been a source of medicinal agents for thousands of years and an impressive number of modern drugs have been isolated from natural sources ¹. India is a land of rich biodiversity, the total number of lower and higher plants in India is about 45,000 species. The plants are potential source of medicines since ancient times ²

A medicinal plant is factually any plant which in one or more of its parts contains substances that can be used for therapeutic purposes or which are precursors for the synthesis of direct therapeutic agents. Approximately 25% of drugs in modern pharmacopoeia were derived from plants and many others were synthetic analogues built on prototype compounds isolated from plants. Infectious diseases



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A medicinal plant is factually any plant which in one or more of its parts contains substances that can be used for therapeutic purposes or which are precursors for the synthesis of direct therapeutic agents. Approximately 25% of drugs in modern pharmacopoeia were derived from plants and many others were synthetic analogues built on prototype compounds isolated from plants. Infectious diseases are the world's leading cause of premature deaths³. Therefore, there is a continuous and urgent need to discover new antimicrobial compounds with diverse chemical structures and novel mechanisms of action. Medicinal plants represent a rich source of antimicrobial agents. Plants are used medicinally in different countries and are a source of many potent and powerful drugs ^{3,4,5}.

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investigated by a number of researchers worldwide. In recent years the interest to evaluate plants possessing antibacterial activity for various diseases leprosy, diarrhea, scabies, venereal disease, ulcers, is growing and it has also been proved that various bacterio-static plants extracts possess bactericidal effects ⁶ and most of the plants contain **CLASSIFICATION**, many bioactive compounds. Plants are potent biochemical factories and have been components of Linn. (Family: Amaranthaceae) is a stiff erect annual phyto medicine. Plants based natural constituents can be derived from any part of plant like bark, leaves, flowers, roots, fruits, seeds, etc⁷.

Herbal drugs constitute a major part in all traditional systems of medicines. Herbal medicine is a triumph of popular therapeutic diversity. Plants above all other agents have been used for medicine from time immemorial because they have fitted the immediate personal need, are easily accessible and inexpensive According to a WHO report, about 70-80% of the world's populations rely on non-conventional medicine mainly from herbal sources in their primary health care. It is specially the case in developing countries where the cost of consulting a western style doctor and the price of medication are beyond the means of most people ⁹. World Health Organization has made an attempt to identify all medicinal plants used globally and listed more than 20,000 species and more than 80 % of the world's population relies on traditional herbal medicine for their primary health care ^{10, 11}

Plants continue to serve as possible sources for new drugs and chemicals derived from various parts of plants ¹². In recent times, there has been a marked shift towards herbal cures because of the pronounced cumulative and irreversible reactions of modern However, to drugs. due over population, urbanization and continuous exploitation of these herbal reserves, the natural resources along with their related traditional knowledge are depleting day by day. The ethnic and rural people of India have preserved a large bulk of traditional knowledge of medicinal uses of plants growing around them. This knowledge is handed down to generations through word of mouth and is extensively used for the treatment of common diseases and conditions and it has occupied a pivotal position in Indian culture and folk medicine ¹³.

The antimicrobial properties of plants have been Indian folk medicine comprises of numerous prescriptions for therapeutic purposes such as healing of wounds, inflammation, skin infections, snake bite, etc ¹⁴.

> **MORPHOLOGY AND GEOGRAPHICAL SOURCE:** Achyranthes aspera herb (fig. 1). Stems are angular, ribbed, and simple or branched from the base, often with tinged purple colour, branches (1-2 m height) terete or absolutely quadrangular, striate, pubescent and with thick leaves. The plant is known by different names in various parts of the world. Chaff-flower, prickly chaff flower in English, Achyranth a feuilles rudes, collant, gendarme in French, Mosotillo, rabo de gato, rabo de chango, rabo de raton in Spanish, Naeem, Noeim, Mahoot, Wazer in Arabian, Hangod in Philippines, Khare-vazhun in Persian, Atkumah in Arabian, Achyranthes aspera in Latin. Apamargah in Sanskrit, Puthkanda, Latjira, Chirchira, Lamchichra, Sonpur in Hindi, Kutri, in Punjabi, Apang in Bengali, Safad Aghedo in Gujarati, Uttaraene in Telugu, Chirchitaa in Unani, Apaamaarga, Chirchitaa, Shikhari, Shaikharika in Ayurvedic ^{13, 15,}

> Plant Achyranthes aspera has been classified in the following order;

Kingdom – Plantae Division – Mangoliophyta Class – Mangoliophsida Order – Caryophyllales Family – Amaranthaceae Genus – Achyranthes Species – Aspera.





FIG. 1: DIAGRAM OF ACHYRANTHES ASPERA PLANT

The plant grows in tropical and warmer regions. It is found in tropical Asian and African countries, in Baluchistan, Ceylon, Australia and America ^{17, 18}. In India, it predominantly grows as a weed on road sides, in vacant agricultural land, especially in uncultivated lands and along the boundaries of the cultivated fields. It grows up to an altitude of 2100 m *Achyranthes aspera* is found in South Andaman Islands ^{19, 20}.

PHYTOCHEMISTRY: Achyranthes aspera is traditionally valued as a potent medicinal agent. Chemical constituents of various parts of the plant has been isolated and identified.

ROOT: A phytoecdysteroid 20-Hydroxyecdysone (ecdysterone or 20E) has been isolated from the methanolic extract of roots of *Achyranthes aspera* ²¹. An aliphatic acid n-hexacos-14- enoic acid is obtained from the ethanolic extracts of roots ²². Some other compound like strigmasta-5, 22-dien-3-E-ol, trans-13-docasenoic acid, n-hexacosanyl n-decaniate, n-hexacos-17-enoic acid and n-hexacos-11- enoic acid are also isolated from the root (**fig. 2**). Phytosterol strigmasta-5, 22-dien-3- E-ol is isolated from petroleum ether: benzene (75:25) elute as a colourless crystalline mass. It responds positively to Liebermann Burchard test for sterols. Oleanolic acid (0.54%) is found in *Achyranthes aspera* root extracts ^{23, 24}.

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N-HEXACOS-14-ENOIC ACID

STIGMASTA-5, 22-DIEN-3-OL

$$_{\mathrm{HO}\,_{2}\mathrm{C}}$$
 (CH $_{2}$) 11 $_{\mathrm{CH}\,_{2}}$ $_{\mathrm{CH}\,_{2}}$ $_{7}$ Me

TRANS-13-DOCASENOIC ACID

FIG. 2: DIFFERENT CONSTITUENTS PRESENT IN THE ROOT OF ACHYRANTHES ASPERA

STEM: Dihydroxy ketones-36, 37dihydroxyhenpentacontan-4-one, and Triacontanol, aliphatic alcohol, 17-pentatriacontanol, pentatriaontane, 6-pentatriacontanone, Hexatriacontane, Tritriacontane, tetracontanol-2 $(C_{40}H_{82}O),$ methoxyheptatriacont-1-en-10-ol $(C_{33}H_{76}O)$, sitosterol and spinasterol ^{25, 26, 27} are isolated from the shoots of the plant (fig. 3). Triacontanol was also isolated along with 36. 47dihydroxyhenpentacontan-4-one ²¹. Two long chain compounds, isolated from the shoots, have been characterized as 27-cyclohexylheptacosan-7-ol and 16-hydroxy-26-methyleheptacosan- 2000^{29} Kunert et al. reported has three bisdesmosidic saponins (I-III), 20hydroxyecdysone and quercetin-3-O-β-D galactoside in the methanol extract of the aerial

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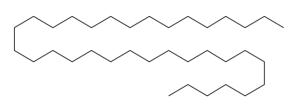
parts of *Achyranthes aspera* their structures are established on the basis of NMR spectroscopic analysis; the complete 1H and 13C assignments of the compounds are achieved by means of 2D NMR studies. Aziz *et al*, 2005 ¹⁷ has been isolated 3-Acetoxy-6 benzoyloxyapangamide from an ethyl acetate extract of the stem of *Achyranthes aspera*. The extract shows mild antibacterial activity against *Bacillus cereus*.

17-PENTATRIACONTANOL

TETRACONTANOL-2

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SPINASTEROL



PENTATRIAONTANE

FIG. 3: DIFFERENT CONSTITUENTS PRESENT IN STEM OF ACHYRANTHES ASPERA

LEAVES: Rameshwar, 2007 30 isolated chemical compounds of the volatile oil from *Achyranthes aspera* leaves. Hydroquinone (57.7%) is the chief constituent; others are p-benzoquinone, spathulenol, nerol, α -ionone, asarone and eugenol (**Fig. 4**). Alkaloids, flavonoids, saponins, tannins and phenolic compounds are found in the leaves 31 .

P-BENZOQUINONE

HYDROQUINONE

ASARONE

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EUGENOL

FIG.4: DIFFERENT CONSTITUENTS PRESENT IN THE LEAF OF ACHYRANTHES ASPERA

SEED: Phytochemical investigations of the seeds (**Fig. 5A**) show the presence of triterpenoid Saponins A and B. Saponins C and D are reported from unripe fruits 32,21 . Its carbohydrate components are the sugars D-glucose, L-rhamnose, D-glucuronic acid (Saponin A). Saponin B is identified as β-D galactopyranosyl ester of D-Glucuronic acid. The seeds also contain water soluble base, betaine and a water soluble alkaloid (Fig.5B) Achyranthine, 10-tricosanone, 10-octacosanone and 4-tritriacontanone 21 .



FIG. 5A: NAKED SEED OF ACHYRANTHES ASPERA

Three oleonolic acid glycosides: α -L-rhamnopyranosyl- $(1\rightarrow 4)$ - $(\beta$ -D-glucopyranosyluronic acid)- $(1\rightarrow 3)$ -oleanolic acid, α -L-rhamnopyranosyl- $(1\rightarrow 4)$ - $(\beta$ -D-glucopyranosyluronic acid)- $(1\rightarrow 3)$ -oleanolic acid-28-O- β -D-glucopyranosyluronic acid)- $(1\rightarrow 3)$ -oleanolic acid-28-O- β -D-glucopyranosyl- $(1\rightarrow 4)$ - $(\beta$ -D-glucopyranosyl- $(1\rightarrow 4)$ - $(1\rightarrow 4$

BETAINE

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ACHYRANTHINE

HO, OH OH HO OH OH SAPONIN

(3-BETA)-3-HYDROXYOLEAN-12-EN-28-OIC ACID

FIG. 5B: DIFFERENT CONSTITUENTS PRESENT IN THE SEED OF ACHYRANTHES ASPERA

SAPOGENIN

Medicinal use of different parts of *Achyranthes aspera*: *Achyranthes aspera* is a popular folk remedy in traditional system of medicine throughout the tropical Asian and African countries ³⁴. The whole plant and its different part like root, seeds, leaves, roots, flowers and fruits has been used for medicinal purpose ¹³.

ethanol extract of whole plant on various Hematological (i.e. RBC, WBC count, Hb%, clotting time, O₂ carrying capacity) and biochemical parameters (i.e. blood sugar level, lipid profile) in alloxan induced diabetic rats and concluded that Achyranthes aspera has haematinic, hypoglycemic antihyperlipidemic activity which complement in treatment of diabetic complications ¹⁹. Ethyl acetate extracts of whole plant (dried leaf, flower and seed extract) showed antiparasitic activity against the larvae of cattle tick Rhipicephalus microplus, sheep internal parasite Paramphistomum cervi 35. The methanolic extract of the whole plant showed nephroprotective activity against lead acetate induced nephrotoxicity in male albino rats ³⁶. The juice of the plant is used to treat opthalmia and dysentery ²².

Uma et al, 2010 37 evaluated the antinociceptive activity of ethanolic extract of A. Aspera (EEAA) and to find the phytochemical responsible for this activity with possible mode of its activity. The extract of the entire aqueous plant hepatoprotective ³⁸. The hydroalcohalic extract stimulates cell mediated immune system by increasing phagocytic function ³⁹. Krishnakumari and Priya, 2006 40 evaluated the antihyperlipidemic effect of aqueous extract of Achyranthes aspera in experimental rats fed with diet containing sesame oil. Sandhyakumari, et al, 2002 41 reported ethanolic extract of A.aspera caused induction of reproduction in male rat. Extracts of A. aspera possess antioxidant properties and could serve as free radical inhibitors or scavenger or acting possibly as primary antioxidants. The decline in the hepatic marker shows the hepatoprotective properties chemically (NDEA and CCl₄) induced hepatocellular carcinoma 42.

Prasad and Pathak, 2011 43 studied Achyranthes aspera (Ash) on reproductive fitness on Drosophila melanogaster using larval and adult feeding. Goyal et al, 2008 44 studied the bronchoprotective effect of ethanolic extract in toluene diisocyanate (TDI) induced occupational asthma in wistar rats. Apart from this whole plant also used for the treatment of bronchial infection, blindness, rheumatism, cough, diuretic in renal dropsy, beriberi, pneumonia 45, 46, 47.

Whole Plant: Mandar et al, 2011¹⁹ showed the Stem/aerial part: Bhattarai, 1994 ⁴⁸ observed abortifacient activity of benzene extract of the stem bark in the rat. The ethanolic extract of stem inhibited the growth of Bacillus subtilis and Staphylococcus aureus bacterial strains ⁴⁹. Aziz et al, isolated 3-Acetoxy-6-benzoyloxyapangamide from an ethyl acetate extract of the stem of Achyranthes aspera. The extract was found to show antibacterial activity against Bacillus cereus. Bafna and Mishra, 2004 50 reported hepatoprotective activity of methanolic extract of the aerial parts on rifampicin induced hepatotoxicity in albino rats which decreases levels of serum glutamic pyruvic transaminase (SGPT), serum glutamic oxaloacetic transaminase (SGOT), Alkaline phosphatase (ALP) and total bilirubin.

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Misra et al, 1992 51 reported antifungal activity of shoots against Asperigillus carneus which is due to 17-pentatriacontanol as a chief constituent isolated from essential oil of the shoots of plant ⁵¹. Patil *et al*, 2012 ⁵² studied *in-vitro* antibacterial potential of dry stem extracts against dental caries causing microbes. The ethanol and methanol extract of stem showed antimicrobial activity against Escherichia coli and also reported secondary metabolites as flavonoid and glucoside 53. Shendkar et al, 2012 54 has been prepared activated carbon from stem of Achyranthes aspera by chemical treatment (by X-ray fluorescence spectroscopy). Activated carbon is used in gas purification, gold purification, metal extraction, water purification, medicine, sewage treatment, air filters, as an efficient catalyst and many other applications.

Leaf: The leaves are used for the treatment of ophthalmic and other eye infections, it also has nephroprotective, post-coital antifertility, nephroprotective and immunomodulatory activities 55. Shendkar et al, 2012 56 showed the presence of total thirteen amino acids in different mobile phases. Elumalai et al, 2009 ² evaluated antifungal activities from aqueous, ethanol and methanol extracts. The the methanolic extract of the leaves showed antifertility activities such as abortifacient. estrogenesity, pituitary weight, ovarian hormone level and lipids profile in female rats, hypoglycaemic effect, analgesic antipyretic and diuretic activities ^{58,} , anti-depressant effects ⁶⁰ and anti-tumor activity

Bagavan et al, 2008 62 first reported mosquito antifertility and estrogenicity 82, anti-inflammatory activity 68, 83, antilithiatic activity or effective antiurolithiatic agent ²⁷, infantile diarrhea and cold ⁵², anti-fertility drug ²², induce labor pains ⁸⁴ and against larvae of Aedes aegypti and Culex inhibited the growth of Bacillus cereus and Staphylococcus aureus bacterial strains 84, 85.

larvicidal activity of the saponin from the ethyl acetate extract and studied the acetone, chloroform, ethyl acetate, hexane and methanol leaf extracts quinquefasciatus. The ethanol crude extract inhibited the growth of Bacillus subtilis and Staphylococcus aureus bacterial strains 49.

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, antiperoxidative properties 63, anti-oxidant activity 64, anti-inflammatory and anti-nociceptive ⁶⁵, antimicrobial activity ^{66, 67}, analgesic activity ^{65, 68}, antibacterial and antifungal activities against E. coli, P. aeruginosa, P. vulgaris, Staphylococcus aureus, Klebsiella species ⁶⁹, wound healing activity ⁷⁰, anti-inflammatory activity ^{71, 72}, antimicrobial activity against Escherichia coli ⁵³, in vitro anti-cataract and antioxidant activities against glucose-induced cataractogenesis using goat lenses 31, hypolipidemic effect on high fat diet induced atherogenic rats ²⁰.

Adnyana et al, 2008 73 reported that the alkaloid fraction of Achyranthes aspera leaf induced apoptosis breast cancer cell through p⁵³ pathways i.e leaf is used to treat cancer, particularly breast and cervix cancer. Apart from this leaves are also used for the treatment of syphilitic sores, bowel complaint, pile, stomache, skin eruption, early stages of diarrhea, dysentery, antiperiodic, Gonorrhoea, asthma, cure strained back, mitigate pain from bite of wasps and also recommended in several Women's diseases 15,45,47,74,75

ROOT: Roots or its different extracts are used as astringents to wounds, in abdominal tumor and stomach pain, pneumonia, stomachic, menstrual disorders, antifertility, mild astringent, cough, ascites and anasarca 45, 76, bleeding in delivery nephrolithiasis and prevented urolithiasis induced with ethylene glycol and reduced the growth of calcium oxalate stones ⁷⁸, Spermatotoxicity ⁷⁹, snake bites, tooth brush, ophthalmia and opacities of the cornea 74, spermicidal activity in human and rat sperm, sperm immobilization, sperm viability, acrosome status, 5'-nucleotidase activity and nuclear chromatin decondensation 80, 81, 15, post coital

Pharmacognostic, preliminary phyto-chemical and pharmacological studies showed its anti-cancer, antidiabetic, anti-inflammatory, anti-spasmodic, antibacterial, diuretic and antileprotic activities 85, 86.

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Seed: Achyranthes aspera is well documented for the presence of phytoactive constituents. Reduction in rate of lipid peroxidation and enhancement in free radical scavenging activity of the herbal seed powder is due to presence of phytoactive constituent. Seeds are rich in protein, and used in night blindness and cutaneous diseases, antipyretic activity, expectorants, hepatoprotective potency or treatment of Jaundice and antioxidant activity 16, 45, 86, 87.

Ethanol and chloroform extracts of seeds of Achyranthes aspera shows mild to moderate antibiotic activity against B. subtilis, E. coli and P. ⁸⁸. Achyranthine, a water-soluble aeruginosa from alkaloid isolated Achyranthes decreased blood pressure and heart rate, dilated blood vessels, it also possess antipyretic activity and anti-inflammatory activity 71. Oleanolic acid present in A. aspera, A. bidentata extract can promote neuronal growth, protect hippocampal neurons against toxicity, and also has anti-stress and antiapoptosis activities ^{89, 90, 91}.

Different proportion (0.25%, 0.5%, and 1.0%) of raw seed and its different fraction (alcohol, petroleum ether and 50% aqueous alcohol extracts) have shown growth stimulating and immunostimulatory properties in Indian major carps ^{92, 93, 94}. Dietary supplementation of seed enhanced the growth of fish, provided protection against oxidative stress, prevented tissue damage and also enhanced the resistance of larvae against the pathogen A. hydrophila i.e. seeds improved the overall health status of the fish.

Plant ingredient plays dual role - directly enhances the immunity of fish, indirectly fastens the growth rate and helps fish to overcome vulnerable early developmental stages.

aspera seed is ecdysterone, whereas immune stimulating effect is primarily due to essential fatty acids (EFAs). The immune stimulation is higher when EFAs (linolenic acid and oleic acid) 95 are given in combination with other constituents of the seed. This synergetic effect may be due to the nutrients present in the whole seed or it may be due to some coexisting components, which possibly increase the bioavailability of EFAs. Seeds at the 0.50% level provided protection against oxidative prevented tissue damage, stress. increased activity. myelperoxidase lysozyme activity, hemmaglutinetion antibody titre, total serum and protein, albumin and globulin levels ⁹⁵. Therefore, the seeds can be made available to the aquaculture industry on a commercial scale.

FLOWER AND FRUIT: Flowers and fruits of *achyranthes aspera* are used for the treatment of menorrhagia and respiratory disease⁴⁷, snakes and reptiles bites⁴⁵.

CONCLUSION: Natural products are having a great importance in ancient traditional medicine systems. Herbs are the natural drugs used to regain the alterations made in normal physiological system by foreign organisms or by any malfunctioning of the body. From different literature and review it has been seen that plant Achyranthes aspera is a resuscitative plant due to its large number of medicinal properties and having medicinally important chemicals like ecdysterone, n-hexacos-17achyranthine, enoic, spinasterol, betaine, pentatriaontane, hexatriacontane, tritriacontane, Hydroquinone, p-benzoquinone, spathulenol, nerol, asarone, and essential fatty acids (EFAs).

The plant shows many pharmacological activities anti-allergic, cardiovascular, like spermicidal, nephroprotective, antiparasitic, anti-inflammatory, hypoglyceamic, analgesic, hepatoprotective potency, inhibit leukocyte infiltration (particularly eosinophils neutrophils), antiperiodic, antimicrobial, purgative, antipyretic and are used in various types of gastric disorders. Thus, Achyranthes aspera is quite promising as a multipurpose medicinal agent and further clinical trials should be performed to efficacy. prove its So the present review substantiates the long standing believe that Achyranthes aspera has medicinal properties.

The growth-stimulating component of *Achyranthes* Being a weed this can prove to be an elixir to the *aspera* seed is ecdysterone, whereas immune common man. Further research can be directed at stimulating effect is primarily due to essential fatty elucidating the active components as well as the acids (EFAs). The immune stimulation is higher pathways threw which they act.

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