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Phyto-pharmacology of *Achyranthes aspera* : A Review

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ABSTRACT
Plants have been one of the important sources of medicines since the beginning of human civilization. There is a growing demand for plant based medicines, health products, pharmaceuticals, food supplements, cosmetics etc. *Achyranthes aspera* Linn. (*A. aspera*) is used as an emmenagogue, antiarthritic, purgative, diuretic, antimalarial, oestrogenic, antileprotic, antispasmodic, cardiotonic, antibacterial and antiviral agent. It is reported to contain alkaloids, flavonoids, saponins, steroids and terpenoids. A review of chemical constituents present in various parts *A. aspera* and their pharmacological actions is given in the present article.

KEY WORDS: *Achyranthes aspera*, phytochemical constituents, pharmacological actions, toxicity

INTRODUCTION

There exists a plethora of knowledge and information and benefits of herbal drugs in our ancient literature of Ayurvedic and Unani medicine. One of the earliest treatises of Indian medicine, the *Charaka Samhita* (1000 B.C.) mentions the use of over 2000 herbs for medicinal purpose. 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 (1,2). 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 0.9m high and found commonly as a weed throughout India. This article intends to provide an overview of the chemical constituents present in various parts of *A. aspera* and their pharmacological actions.

GENERAL INFORMATION

Achyranthes aspera Linn., belonging to family *Amaranthaceae*, is commonly found as a weed on way side and at waste places throughout India. It is known as Apamarg in Sanskrit, Aghedo and Aghedi in Gujarati, Chirchira and Chirchitta in Hindi and Prickly chaff flower in English. It is widely used for asthmatic cough, snakebite, hydrophobia, urinary calculi, rabies, influenza, piles, bronchitis, diarrhea, renal dropsy, gonorrhea and abdominal pain (3, 4, 5, 6, 7). A powder of dried leaf mixed with honey is useful in the early stages of asthma (8). 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 (9).

THERAPEUTIC USES MENTIONED IN AYURVEDIC PHARMACOPOEIA

The dried plant is used in sula (colic), udararoga (diseases of the abdomen), apaci (lymphadenitis-cervical), arsa (haemorrhoids), kandu (itching), medroga (obesity). The dried root of the plant is used in chardi (vomiting), adhmana (tympanitis), kandu (itching), sula (colic), apaci (lymphadenitis), granthi (tumor), bhagandara (fistula-in-ano), hrdaroga (disease of heart), jwara (pyrexia), switra (leucoderma), vadhirya (deafness), udararoga (diseases of the abdomen), yakrtroga (disorders of the liver), dantaroga (disease of tooth) and raktavikara (blood disorders).

THERAPEUTIC USES AS DEPICTED BY ETHNOBOTANICAL STUDIES

The plant is used in dropsy, piles, skin eruptions, colic, as a diuretic, astringent and purgative (10, 11, 12); as an antidote to snake bite (13); in fractured bones (14, 15, 16); whooping cough, respiratory troubles (17); for asthma (7, 18); as a laxative (4) and in leucoderma (19). The inflorescence is used in cough (20) and in hydrophobia (16). Fruit is used in hydrophobia (4). The seeds are employed as an emetic, purgative, and cathartic, in gonorrhoea, for insect bite and in hydrophobia (7, 10, 11, 18, 21), cough including whooping cough (21), as an anti-asthmatic (21). The leaves are used in wounds, injuries (22); in intermittent fever, as an anti-asthmatic, for urination, dog bite (14, 16) and in typhoid (23). The root is used in whooping cough, tonsilitis (14, 16), haemorrhage (19), cough and hydrophobia, as an anti-asthmatic (21), diuretic, diaphoretic, and antisyphilitic (10).

PHARMACOGNOSTICAL STUDIES

The T.S. of young stem shows 6-10 prominent ridges and collenchyma is present under each ridge. The epidermis is single layered, covered with thick cuticle. Trichomes arising from the epidermis are simple, covering, multicellular straight or somewhat spirally running, highly warty. The cortex is composed of 6 to 8 layers of parenchymatous cells containing cluster and rosette crystals of calcium oxalate. Xylem is composed of annular, spiral and pitted vessel,

tracheids, fibres and parenchyma. The diagrammatic T.S. of the young root shows a layer of epiblema with long unicellular hairs. Cortex is 5-6 layered, parenchymatous and narrow. The stelar region shows anamolous growth. Upper epidermal cells of leaf are more or less straight walled while the lower ones are wavy walled. Both the upper and lower epidermal cells are traversed with anomocytic and few anisocytic stomata. Trichomes are simple, covering, uniseriate, multi-cellular and many, arising from the lower epidermis. Rosette crystals of calcium oxalate measuring 20-45 µin diameters are embedded through out the parenchymatous cells of the mesophylls and the ground tissue of the mid rib (24).

PHYTOCHEMISTRY

The **plant** is reported to yield a water-soluble base and a chloroform soluble base. The former was earlier designated as achyranthine (25) and was characterized as a betaine derivative of N-methylpyrrolidine-3-carboxylic acid (26). Later studies by Kapoor and Singh (27) showed that the water-soluble base was betaine and not achyranthine. The chloroform soluble basic fraction was shown to be a mixer of two uncharacterized alkaloidal entities (28).The ethanol extract of the plant contained alkaloids and saponins while flavonoids and tannins were found absent (29).

The **shoot** yielded a new aliphatic dihydroxyketone, characterized as 36,47- dihydroxyhenpentacontan-4-one together with tritriacontanol (30); an essential oil; a new long chain alcohol characterized as 17-pentatriacontanol (31); four new compounds characterized as 27-cyclohexylheptacosan-7-ol, 16-hydroxy-26-methylheptacosan-2-one (32), 4-methylheptatriacont-1-en-10-ol and tetracontanol-2 (33).

Various parts of the plant, viz., seeds, stem, leaves (34) and root (35) are reported to contain ecdysterone. The chloroform extract of the stem led to the isolation of pentatriacontan, 6-pentatriacontanone, hexatriacontane and triacontane (36). The inflorescence is reported to contain flavonoids and alkaloids (37).

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 hydrolysate contains the usual amino acids. The values obtained for ten essential amino acids and cystine shows that the seed protein can be compared favorably 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 (38).

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 (39, 40). Khastgir and associates (41) isolated a crude sapogenin fraction from the seeds, which yielded oleanolic acid. Later, investigation led to the isolation of two oleanolic acid based saponins, saponin A and saponin B which were characterized as α -L-rhamnopyranosyl (1→4)-ß-D-glucopyranosyl (1→4)-ß-D-glucuronopyranosyl(1→3)-oleanolic acid and ß-D-galactoyranosyl (1→28) ester of saponin A, respectively (42). In another study, the total saponins were hydrolysed with acid and the genin was identified as oleanolic acid (43). A rapid procedure for the separation of triterpenoid saponin based on partition chromatography from the plant has been described (44). The seeds are reported to contain hexatriacontane, 10-octacosanone, 10-triacosanone and 4-triacontanone (36).

The unripe **fruit** is reported to yield two new saponins (C and D), which were identified as ß -D-glucopyranosyl ester of α-L-rhamnopyranosyl (1→4)- ß -D-glucuronopyranosyl (1→3)-oleanolic acid and ß-D-glucopyranosyl ester of α -L-rhamnopyranosyl (1→4)- ß -D-glucopyranosyl (1→4) ß -D-glucuronopyranosyl (1→3)- oleanolic acid (45).

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 (41). Both root and shoot of the plant were found to contain saponin and alkaloids but no flavonoids (37). In another study, the root of the plant was found to contain alkaloids but indicated absence of saponin and tannins (46). In yet another preliminary chemical study, the **root** was reported to contain alkaloids, flavonoids, saponins, steroids and terpenoids. Glycosides were found to be absent (47). Isolation of ß-sitosterol was also reported from the root (32).

PHARMACOLOGY

Anti inflammatory activity

An alcohol extract of *Achyranthes aspera* showed the anti-inflammatory activity on carrageenin-induced hind paw oedema and cotton pellet granuloma models in albino male rats (48). 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 (49). The water-soluble alkaloid achyranthine isolated from *A. aspera* was screened for its anti inflammatory and antiarthritic 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 (22).

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*, *Streptococuss heamolyticus* and *Bacillus typhosus* (50). While the alcoholic and the aqueous extract of the leaves showed antibacterial activity against *S. aureus* and *E. coli* (51)

The seeds growing on cattle dung revealed antibacterial activity against bacterial strains of *B. subtilis, Pseudomonas cichorii* and *Salmonella typhimurium* (52). 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 (53).

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 (anti-implantation and abortifacient) activity of ethanol extract was 100%. The ethanol extract also exhibited estrogenic activity tested in immature ovariectomised female albino rats (54). 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). 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 (56). The methanolic leaves extract of *Achyranthes aspera* on some indicators for anti-fertility activities such as abortifacient, estrogenesity, 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 ovarectimized rats. The extract, however, did not significantly influence serum concentration of the ovarian hormones and various lipids except lowering HDL at doses tested (57).

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 (58). The crude benzene extract of the stem was found to have potent abortifacient effect in mice (59). In an attempt to locate the active principle, 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 (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 (61). The n-butanol fraction of the aerial parts prevented pregnancy in adult female rats when administered orally at a daily dose of 75 mg/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 a marked stimulation in uterine weight. Marked uterotrophic effect was discerned even at a dose of 3.75 mg/kg (62). In another study, 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 (63).

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 (64). A benzene fraction of the benzene extract of the whole plant showed abortificient activity in rabbit at a single dose of 50 mg/kg (64).

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 titers 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 (65). Catla catla, 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 ip injection with chicken erythrocytes. Hemagglutination 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 (66).

Immunomodulatory activity of *Achyranthes aspera* seed was studied by incorporating it in the diets of Labeo rohita, rohu fingerlings. Superoxide 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 (67). In another study, *Achyranthes aspera* was incorporated in artificial fish diet, and fed to Catla 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* (68).

Anti-hyperlipidemic activity

The alcoholic extract of the plant *A. aspera* at 100mg/kg dose lowered total serum cholesterol (TC) and phospholipid (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 (69).

Anti-diabetic activity

The 50% ethanolic extract of entire plant (70) 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 bw orally in mice (70). In another study, 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 (71).

Diuretic activity

The saponin isolated from the seeds 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 (72).

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 µg) 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 hypodynamic 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 (72). The effect of saponin on the phosphorylase activity of the perfused 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 (73).

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's heart the extracts had a temporary negative inotropic and chronotropic effects. The extracts produced spasm of isolated rabbit's ileum, increased the tone and amplitute 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 (74). The total chloroform soluble basic fraction (alkaloidal 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 (28). 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 and amplitude of respiration anaesthetized dogs (50, 75).

Anti-carcinogenic activity

Achyranthes aspera leaves have been assessed for chemopreventive activity. The methanolic extract, alkaloid, non-alkaloid and saponin fractions exhibited significant inhibitory effects (concentration 100 µg) on the Epstein-Barr virus early antigen activation induced by the tumor promotor 12-O-tetradecanoylphorbol-13-acetate in Raji cells. In this *in vitro* assay the non-alkaloid fraction containing mainly non-polar 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%) (76).

Miscellaneous

The effects of *Achyranthes aspera* leaf extract on body weight, hepatic protein content, 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 (77). Fresh leaf extracts of *Achyranthes aspera* were tested against Alternatia alternate causing leaf spot disease of Vicia faba. Inhibition of growth was recorded (78). The alkaloidal fraction obtain from the alcoholic extract of the root bark of *A. aspera* inhibited the response of oxytocin in isolated rat uterus. This fraction did not inhibit

Table 1: Differenct parts of Achyranthes aspera with the pharmacological activity

Part Used/Extract/ Compound	Pharmacological Activity	Reference
Oil from root	Anti-asthmatic	9
Total chloroform soluble basic fraction of whole plant	Hypertensive, positive ionotropic action, spasmolytic	28
Alcoholic Extract of whole plant	Anti-inflammatory	48
Ethanolic Extract of whole plant	Anti-inflammatory	49
Achyranthine	Anti-inflammatory	22
Aqueous solution of entire plant	Anti-microbial	50
Aqueous and alcoholic extract of leaves	Anti-microbial	51
Seeds	Anti-microbial	52
Ethanolic extract of leaves and stem	Anti-microbial	53
Ethanolic extract of root	Anti-fertility	54
Methanolic extract of root	Anti-fertility	55
Composite plant extract	Anti-fertility	56
Methanolic extract of leaves	Anti-fertility	57
Benzene extract of stem bark	Anti-fertility	58
Benzene extract of the stem	Anti-fertility	59
Ethanolic extract of aerial parts	Anti-fertility	61
n-butanol fraction of the aerial parts	Anti-fertility	62
Ethanolic extract of whole plant	Anti-fertility	63
Extracts of the whole plant	Anti-fertility	64
Plant extract of whole plant	Immunomodulatory	65
Seeds	Immunomodulatory	66, 67
Alcoholic extract of whole plant	Anti-hyperlipidemic	69
Ethanolic extract of entire plant	Anti-diabetic	70
Whole plant powder, aqueous and methyl alcohol extracts	Anti-diabetic	71
Saponin mixture from seeds	Diuretic	72
Saponin from seeds	Diuretic, Positive ionotropic action	73
Saponin from seeds	Stimulation of phosphorylase	74
Aqueous and alcoholic extracts of the roots	Diuretic, hypotension	75
Achyranthine	Anti-hypertensive, spasmogenic	50, 76
Methanolic extract, alkaloid, non-alkaloid and saponin fractions of leaves	Anti-carcinogenic	77
Leaf extract	Pro-thyroidic	78
Alkaloidal fraction obtain from the alcoholic extract of the root bark	Anti-spasmodic	80
Oral decoction	Anti-leprotic	82, 83, 84
Kshaarasootra	Treatment of Fistula-in-ano	85, 86, 87, 88, 89, 90, 91, 92

the response to serotonin and acetylcholine in rat uterus and to histamine in guinea pig uterus (79). The total chloroform soluble basic fraction (alkaloidal residue) obtained from the plant *A. aspera* showed spasmolytic action against various spasmogens on intestine and uterine muscles of guinea pigs and a slight anti-diuretic action in rats. No specific CNS effects were observed in mice. The fraction did not possess analgesic activity in rats (28). The water-soluble alkaloid, achyranthine isolated from the plant showed spasmogenic effect on frog's 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 (50, 75).

The ethanolic extracts of leaves (80) 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 LD_{50} of the latter extract was >1000 mg/kg *i.p.* in mice (80).

CLINICAL STUDIES

The plant was subjected to wide clinical evaluation with special reference to its use in leprosy, bronchial asthma and fistula-in-ano. Diuretic activity could not be confirmed.

7eprosy

The effect of oral decoction of *A. aspera* in the treatment of leprosy was studied (uncontrolled) in 19 patients who were found to have positive stain smears at the S. S. Hospital, Varanasi. Fourteen patients were in stage of reaction and rest of them had active lesions but none of them was in quiescent stage. The study revealed encouraging results in both lepra reaction as well as the quiescent stage of lepromatous leprosy (81).

In an attempt to get additional data on the efficacy of the decoction of *A.aspera*, it was observed that the decoction was useful in the treatment of reaction in leprosy particularly in subacute and mild type. When administered in conjunction with the antileprosy drug diaminodiphenylsulphone (DDS), it was found that the chance of reaction became less and rate of improvement was faster. No toxic manifestation, which could be attributed to *A. aspera* was noted during the trial (82, 83).

Fistula-in-ano

The studies revealed that the longterm use of 'Kshaarasootra' (a medical thread prepared by coating the latex of *Euphorbia neriifolia*, alkaline powder of *A. aspera* and *Curcuma longa*) was quite effective in treatment of various fistulous tracks (84, 85, 86, 87, 88, 89, 90).

The Indian Council of Medical Research has carried out a multicentric randomized controlled trial to evaluate the efficacy of 'Kshaarasootra' in the management of fistula-in-ano (265 patients) in comparison with the conventional surgery (237 patients). The results have revealed that the long-term outcome with 'kshaarasootra' (recurrence 4 percent) was better than with the surgery (recurrence 11 percent), although the initial healing time was longer (8 wk with thread and 4 wk with surgery). "Kshaarasootra' offered an effective, ambulatory and safe alternative treatment for patient with fistula-in-ano.

"Kshaarasootra' has also been found to give encouraging results in 5 patients of chronic non healing milk-fistula 'stannadi-vrana' with additional local application of 'jatyaditaila' and oral administration of ' shigru guggulu' (two tablets t.i.d.) during the course of treatment (91).

Bronchial Asthma

A pilot study was carried out at the Central Research Institute for Siddha in Madras on 15 cases of bronchial asthma. The oil obtained from the root of *A. aspera* soaked in cow urine was smeared on betel leaf and administered thrice a day to these patients. In most of the cases symptoms like wheezing, gasping, dyspnoea, sneezing and cough disappeared. A fall in total WBC, eosinophil counts and ESR was observed (9).

TOXICITY

A 7 day acute toxicity study of whole plant powder didnot reveal any adverse or side effect upto a dosage of 8g/kg, orally (92). The alkaloid isolated from the plant was tested for its acute, subacute and chronic toxicity in rats. During acute toxicity test, there was a slight increase in sedation and slight loss in righting region at 6.0mg/kg dose level, which became prominent at 7.0mg/kg dose level. At higher doses, significant depletion in righting region, depression in respiration, remarkable increase in sedation and diarrhoea was observed. Subacute toxicity test revealed (5.0 and 6.0 mg/kg) a significant increase in sedation and hypnosis, depletion in respiration and loss of righting reflexes. At 6.0 mg/kg dose, it also caused remarkable increase in salivation and diarrhoea. Chronic toxicity showed (3.0 mg/kg) an increase in sedation, hypnosis, salivation and diarrhoea. There was a significant depression of respiration and loss of body weight (93).

CONCLUSIONS

A. aspera is commonly found as a weed on way side and at waste places throughout India. The plant is used in dropsy, piles, skin eruptions, colic, as a diuretic, astringent and purgative, as an antidote to snake bite, in fractured bones, whooping cough, respiratory troubles, for asthma, as a laxative and in leucoderma. It is reported to contain alkaloids, flavonoids, saponins, steroids and terpenoids. The pharmacological and clinical studies reported in the present review confirm the therapeutic value of *A.aspera*.

Presence of wide range of chemical compounds indicates that plants could serve as "lead" for the development of novel agents having good efficacy in various pathological disorders in the coming years. Sodium chromoglycate is one of the examples of the "lead" prepared from the analogs of the naturally occurring furanochromone khellin (visammin), found in *Ami visnaga*. Exploration of the chemical constituents of the plants and pharmacological screening will thus provide us the basis for developing such leads. However, less information is available regarding the chemical constituents of this plant. There are lack phyto-chemical and phyto-analytical studies of this plant. With the availability of primary information, further studies can be carried out like phyto-pharmacology of different extracts, standardization of the extracts, identification and isolation of active principles and pharmacological studies of isolated compound. These may be followed by development of lead molecules as well as it may serve for the purpose of use of specific extract in specific herbal formulation.

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