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Phytochemical and Pharmacological Potential of *Hygrophila spinosa* T. Anders

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ABSTRACT

Hygrophila spinosa T. Anders (Acanthaceae) is described in Ayurvedic literature as Ikshura, Ikshugandha and Kokilasha "having eyes like Kokila or Indian cuckoo", common in moist places on the banks of tanks, ditches, paddy fields etc., widely distributed throughout India from Himalayas to Ceylon, Srilanka, Burma, Malaysia and Nepal. Seeds, whole plant, leaves, roots and ash of the plant are predominantly used for the treatment of various ailments. The compounds identified in *H. spinosa* are mainly phytosterols, fatty acids, minerals, polyphenols, proanthocyanins, mucilage, alkaloids, enzymes, amino acids, carbohydrates, hydrocarbons, flavonoids, terpenoids, vitamins and glycosides. Some of the reported phytoconstituents are lupeol, lupenone, 25-oxo-hentriacontanyl acetate, stigmasterol, betulin, β- carotene, hentriacontane, apigenin-7-O-glucuronide, apigenin-7-O-glucoside, 3-methylnonacosane, 23-ethylcholesta-11(12), 23(24)-dien-3β-ol, luteolin, asteracanthine, asteracanthicine, luteolin-7-rutinoside, methyl-8-n-hexyltetracosanoate, β-sitosterol, histidine, phenylalanine, lysine, ascorbic acid, nicotinic acid, n-triacontane, glucose, mannose, rhamnose, arabinose, xylose, maltose, myristic acid, oleic acid, palmitic acid, stearic acid, linoleic acid etc. Ethanolic extract of the fruits, hydroalcoholic extract of whole plant and crude petroleum ether extract of the plant are having anticancer activity. Antibacterial activity was exhibited by the chloroform and methanol extract of the whole plant, and methanolic extract of the leaves. Antifungal activity against *Aspergillus tamari*, *Rhizopus solani*, *Mucor mucedo* and *Aspergillus niger* is due to the proteins and peptides present in the plant. Potential in treating liver diseases of the aerial parts, roots and whole plant was studied by various models viz. carbon tetrachloride induced hepatotoxicity, paracetamol and thioacetamide intoxication, and galactosamine induced liver dysfunction in rats. Seeds, leaves, aerial parts and roots showed antinociceptive activity which was studied using both chemical and thermal methods of nociception in mice. Some Ayurvedic, Unani and Siddha formulations of the plant are claimed to have anabolic-cum androgenic like activity. The plant was also studied for haematopoeitic, hypoglycemic, anti-inflammatory, antioxidant, hypotensive, diuretic, macrofilaricidal activities etc. Apart from the above established studies the plant is traditionally used for the treatment of anasaraca, diseases of urinogenital tract, dropsy of chronic Bright's disease, hyperdipsia, vesical calculi, flatulence, diarrhea, dysentery, leucorrhoea, gonorrhoea, asthma, blood diseases, gastric diseases, painful micturition, menorrhagea etc. Therefore, these informations will help the scientists and researchers to screen the compounds responsible for different bioactivities and to elucidate the mechanism of action.

Keywords: Acanthaceae, Anticancer, Flavonoids, *Hygrophila spinosa*, Phytosterols

INTRODUCTION

Medicinal and aromatic plants constitute a major segment of the flora, which provides raw materials for use in the pharmaceuticals, cosmetics, and drug industries. The indigenous systems of medicines, developed in India for centuries, make use of many medicinal herbs. In one of the study of the World Health Organization, it is estimated that 80 per cent of the population of developing countries relies on traditional plant based medicines for their health requirements (1-4). Even in many of the modern medicines, the basic composition is derived from medicinal plants and has become acceptable for many reasons that include easy availability, least side effects, low prices, environmental friendliness and lasting curative property. The World Health Organization (WHO) has defined traditional medicine as "the sum total of all the knowledge and practices, whether explicable or not, used in diagnosis, prevention and elimination of physical, mental or social imbalance and relying exclusively on practical experience and observation handed down from generation to generation, whether verbally or in writing" (1). All traditional medicines have their roots in folk medicines and household remedies. WHO has listed 20,000 medicinal plants used in different parts of the world. Other estimates indicate the number to range between 35,000 and 70,000 worldwide (5, 6). Plant derived products are present in 14 of the 15 therapeutic categories of pharmaceutical preparations, which are currently recommended to medical practitioners in U. K. and they form an important part of

health care system in the western world (7). There are several factors for the continued popularity of traditional drugs and one is their ready availability as compared to the modern medicines besides the adverse effects of synthetic drugs (8).

Plants can, therefore, be described as the major source of medicine, not only as isolated active principles to be dispensed in standardized dosage forms but also as crude drugs for the population of developing countries. World Health Organization (WHO) has stressed the need to promote the indigenous systems of medicine among the rural population of the Third World Countries (9). This has led to an awareness of alternative systems of medicine, still practiced and found satisfactory by three-quarters of the world's population. On the other hand, the revival interest in herbal medicine as a system of natural cure has emerged as a new trend in the west.

Many drugs of modern medicine have had their origin in traditional medicine. Some common examples include the discovery of the alkaloid diosgenin in *Dioscorea deltoidea* used as source for the partial synthesis of cortisone and steroid hormones in the forties, the discovery of the hypotensive alkaloid reserpine in *Rauvolfia serpentina* and the analgesic alkaloid aspirin in *Filipendula ulmaria* in the fifties, the discovery of anti-asthmatic alkaloid ephedrine in *Ephedra sinica* and the anti-cancer alkaloid podophyllotoxin in *Podophyllum hexandrum* in the sixties, etc.

The genus Hygrophila is an angiospermic plant belonging to the family Acanthaceae. The family composes of a number of genus and species having medicinal value and they are usually perennial herbs or shrubs, rarely trees; some are lianes, xerophytes, aquatica, or mesophytes. From related families, the plants of Acanthaceae are distinguished by a number of characters, notably the presence of cystolith in vegetative organs, the presence and development of floral bracts and bracteoles, usually bilabiate corollas associated with the bilocular ovary, generally bivalvate elastically dehiscing capsules, and usually by the curved retinacula supporting the seeds. The anthers and stamens provide many diagnostic characters of the genera. Some species of Hygrophila are: *H. salicifolia, H. phlomoides, H. quadrivalvis* Nees, *H. serphyllum* T. Anders, *H. spinosa* T. Anders, *H. obovata, H. ringens, H. polysperma (Roxb.)* T. Anders, *H. difformis, H. erecta, H. megalantha, H. pogonocalyx, H. balsamica,* etc (10-14).

Hygrophila spinosa T. Anders contains various groups of phytoconstituents viz. phytosterols, fatty acids, minerals, polyphenols, proanthocyanins, mucilage, alkaloids, enzymes, amino acids, carbohydrates, hydrocarbons, flavonoids, terpenoids, vitamins, glycosides etc and is useful in the treatment of anasaraca, diseases of urinogenital tract, dropsy of chronic Bright's disease, hyperdipsia, vesical calculi, flatulence, diarrhea, dysentery, leucorrhoea, gonorrhoea, asthma, blood diseases, gastric diseases, painful micturition, menorrhagea etc (12, 15-18).

Description of *Hygrophila spinosa*

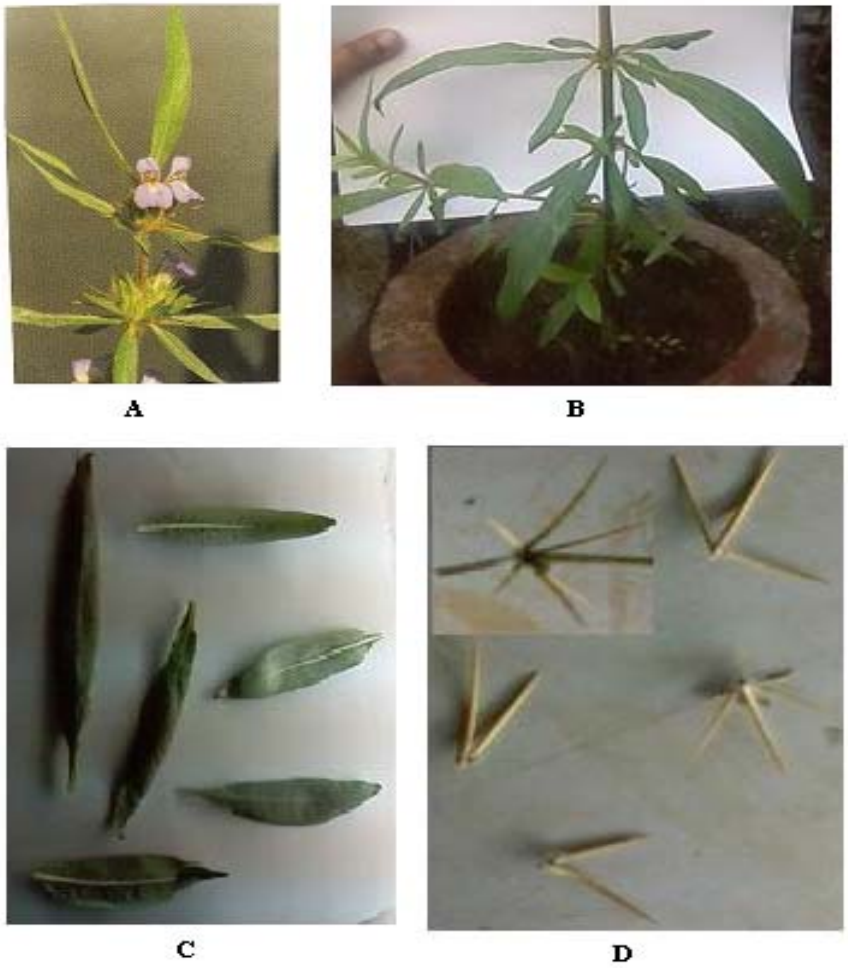
Hygrophila spinosa (Acanthaceae) is described in Ayurvedic literature as Ikshura, Ikshugandha and Kokilasha "having eyes like Kokila or Indian cuckoo", common in moist places on the banks of tanks, ditches, paddy fields etc., widely distributed throughout India from Himalayas to Ceylon, Srilanka, Burma, Malaysia and Nepal (15, 19-22). It is a stout herb with numerous fasciculate usually unbranched subquadrangular erect stems, 0.6-1.5 m high, thickened at the nodes, more or less hispid with long hairs, especially below each node. Leaves sparsely hispid on both sides, tapering at the base, sessile, in verticels of 6 at a node, the 2 outer leaves of the whorl larger, reaching 18 by 1.3-3.2 cm, oblong-lanceolate or oblanceolate, the 4 inner leaves (two on each side) reaching about 3.8 cm long, each of the 6 leaves with nearly straight sharp yellow spine, 2.5-4.5 cm long, in its axil. Flowers in whorl of 8 (in 4 pairs) at each node; bracts about 2.5 cm long, like the leaves, lanceolate, hairy and ciliate; bracteoles 2 cm long, linear-lanceolate, with hyaline margin in the lower part, hairy and ciliate with long white hairs. Calyx 4 partite; upper sepal 1.6-2 cm long, broader than the other 3, which are 1.3 cm long, all linear lanceolate, coarsely hairy on the back, and with hyaline ciliate margins. Corolla purple-blue, reaching 3.2 cm long, widely 2-lipped; tube 1.6 cm long, abruptly swollen at the top; lips subequal, 1.6 cm long, the upper lip 2-fid with oblong truncate lobes, the lower lip with 2 entire crest like longitudinal folds or callosities on the palate, deeply 3-lobed, the lobes oblong or slightly obovate, rounded or truncate. Filaments quite glabrous, one short and one long filament of each pair united at the base. Style slightly pubescent, filiform. Capsules 8 mm long, linear-oblong, pointed, 4-8 seeded, ovate-quadrate, black, compressed, hygroscopically hairy and 0.3 x 0.2 cm (Figure 1) (16-17, 22-27). The various common names/vernacular names of the plant are Kakilakshya, Ikshugandha, Ikshura, Kokilaksha, Kokilanayana, Kshura, Kshuraka, Vajra, Gokhulajanum, Katreiriki, Ikkiri, Tal-makhana, Talimakhana, Gokhulakanta, Gokshura, Talimkhana, Kuilirakha, Koillekha, Koilrekha, Kolista, Talimakhana, Kolsunda, Talimkhana, Kuliakhara, Kantakalika, Nirmalli, Vayalchulli, Nirmulli, Neremulli, Nirumalli, Kettu, Nirguvireru, Nerugobbi, Neerugubbi, Nirguviveru, Kokilaksamu, Kantakulika, Kalavankabija, Eyitror, Ekharo, Dayingiwa, Kolavalike, Kolavali, Kolarind, Soopadan, Long-leaved barleria etc (15-17, 19-22, 25-30).

The botanical classification of the plant is:

Kingdom	Plantae-Plants
Subkingdom	Tracheobionta-Vascular plants
Superdivision	Spermatophyta-Seed plants
Division	Magnoliophyta-Flowering plants
Class	Magnoliopsida-Dicotyledons
Subclass	Asteridae
Order	Scrophulariales
Family	Acanthaceae-Acanthus family

Genus	Hygrophila R. Br.-swamp weed
Species	*spinosa* T. Anders

Figure 1 : Morphological characters of Hygrophila spinosa



***A,** flowering shoot; **B,** Arrangement of leaves at node; **C,** Leaves; **D,** Spines of the plant and their arrangement at the node*

Table 1: Traditional Uses of Hygrophila spinosa

Part of the Plant	Used (as/in)	References
Roots	Diuretic, jaundice, dropsy, rheumatism, anasaraca, diseases of urinogenital tract, gonorrhoea, cooling, bitter tonic, demulcent, refrigerant, antitumour, snake bite, anti-inflammatory, dropsy of chronic Bright's disease, ascites, hyperdipsia, strangury, flatulence, dysentery, leucorrhoea	(15-17, 19, 25-27, 43-50)
Seeds	Gonorrhoea, spermatorrhoea, jaundice, dropsy, rheumatism, anasaraca, diseases of urinogenital tract, tonic, aphrodisiac, cooling, acrid, bitter, sedative, constipating, antipyretic, diseases of the blood, diuretic, impotence, general debility, demulcent, nutritive, aromatic, stimulant, asthma, diarrhea, leucorrhoea, refrigerant, liver tonic, rejuvenating, lithontriptic, nervine tonic, anaemia, dysentery, strangury, renal and vasical calculi, arresting abortion, lithiasis	(12, 15, 17, 19, 25-26, 29-30, 41, 47, 51-62)
Leaves	Diuretic, jaundice, dropsy, rheumatism, anasaraca, diseases of urinogenital tract, leucor, sweet, sour, bitter, tonic, oleaginous,	(12, 15, 17, 19, 22, 25, 27, 30, 47, 63-65)

	aphrodisiac, hypnotic, diarrhea, dysentery, urinary calculi, urinary discharge, anti-inflammatory, joint pain, biliousness, eye disease, ascites, abdominal troubles, anaemia, anuria, gleet, cough, demulcent, stomachic, lumbago, arthritis, gastric disorder, leucorrhoea	
Whole plant	Antibacterial, dysurea, painful micturition, tonic against debility, hepatopotective	(12, 15, 27, 41, 48-49)
Flower	Leucor	(12)
Aerial part	Body pain, jaundice, malaria	(56)
Fruits	Menorrhagea	(63)
The plant	Diuretic, cancer, tubercular fistula, anaemia, hepatoprotective, diabetes, dysentery, dropsy, rheumatism, anasaraca, diseases of urinogenital tract, aphrodisiac, haematinic, antifungal, spasmolytic, hypotensive, antidiabetic	(11-12, 19-20, 31, 41, 66-71)
Ashes of plant	Diuretic, dropsy, gravel	(15)

ETHNOMEDICINE

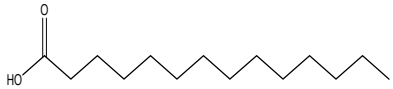
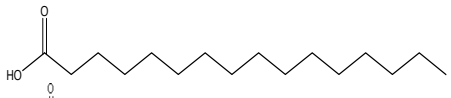
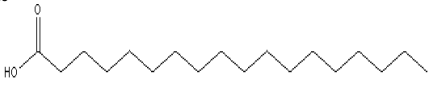
The various Ayurvedic properties of the drug are: Rasa- *Madhura, Amla, Tikta*; Guna- *Pichchhila, Snigdha*; Veerya- *Sheet*a; Vipaka- *Madhura*; Doshaghnata- *Vatapittashamaka*; Rogaghnata- *Nadidaurbalya, Vatarakta, Vatavyadhi, Kamala, Jalodara, Yakridudara, Anaha, Udararoga, Pittashmari, Shotha, Kasa, Shukradaurbalya, Klaibya, Mootrakrichchhra, Ashmari, Bastishotha, Daurbalya*; Karma- *Nadibalya, Santarpana, Yakriduttejaka, Ruchya, Anulomana, Shothahara, Stanyajanana, Mootrala, Vrishya, Vajikara, Shukrashodhana, Balya, Brinhana* (17). Its uses in Ayurveda and Siddha are: Mathura-amlarasa; diuretic, aphrodisiac, pandu, dropsy, scanty urine, ascites; seeds are premeham and athisaram (15, 20). In Unani system of medicine it is Hot 1^0, Dry 1^0; seeds are aphrodisiac, nutritive; leaves are diuretic, externally for lumbago and rheumatism (15). It is a source of the Ayurvedic drug 'Kokilaaksha' (31), Unani drug 'Talmakhana' (32) and Siddha drug 'Neermulli' that are claimed to have anabolic-androgenic activity (33). The plant is used as antitumour (34), hypoglycemic (35) antibacterial (36-37), hepatoprotective (38), low moluscicidal against Bulinus truncates (16), demulcent,

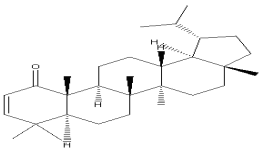
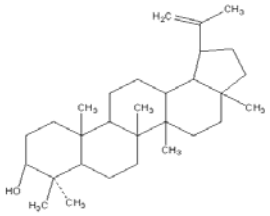
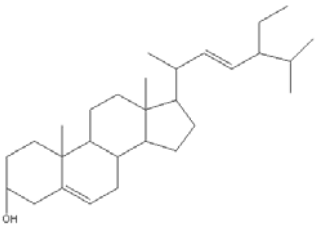
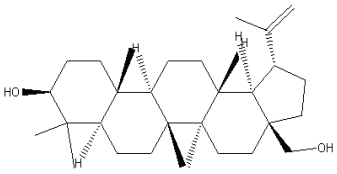
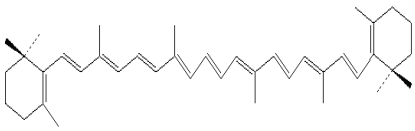
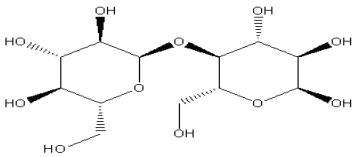
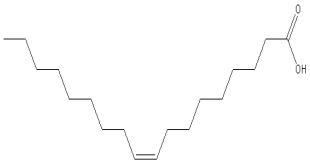
aphrodisiac and diuretic. The aerial part and root are used in herbal preparations (39-40). The dose of the plant used in powder form is 3 to 6 gm (28-29, 41) and various parts of the plant used are the whole plant, seeds, roots, leaves and ashes of the plant (15, 17, 28, 42). Different morphological parts of the plant used traditionally for the treatment of various ailments are listed below (Table 1).

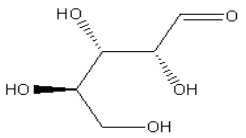
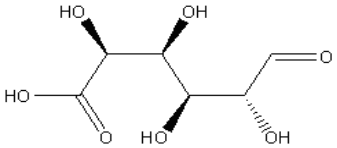
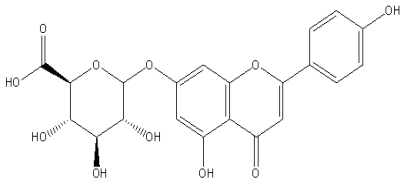
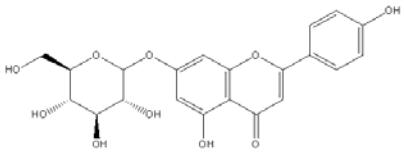
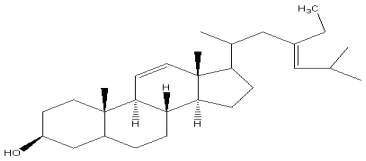
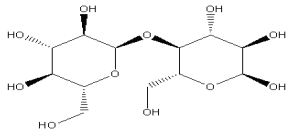
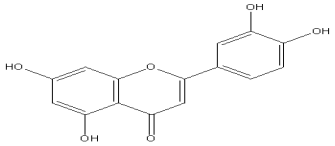
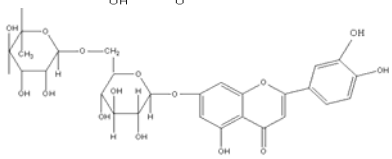
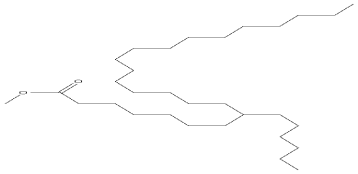
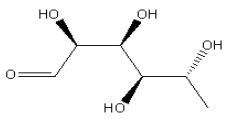
CHEMICAL CONSTITUENTS

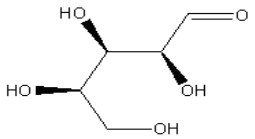
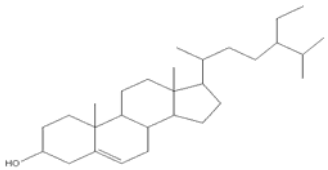
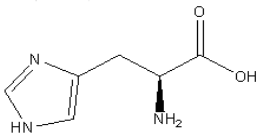
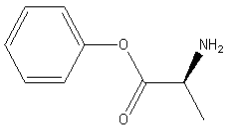
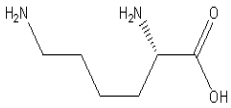
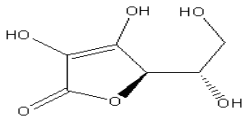
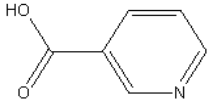
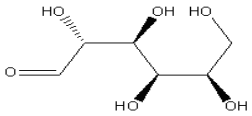
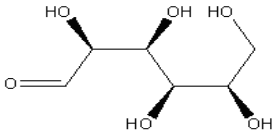
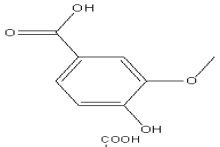
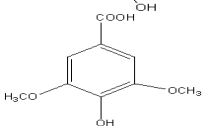
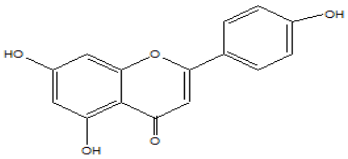
Root of the plant contains essential oils (17, 25, 28), alkaloids (15), waxy substances, gum (19), minerals as Ca, Mg, K, Fe, Cu, Zn, Mn, Co & Cr (72) and phytosterols (17); alkaloids and sterols are present in the aerial parts (12); Seeds contain mucilage, potassium salts, diastase, lipase, protease (15, 17, 25-28,73-74), sterols (12, 27, 29, 73,75-77), alkaloids, fixed oils (15), fatty acids (78) and minerals like Ca, Mg, K, Fe, Cu, Zn, Mn, Co & Cr (72); Whole plant contains essential oil (12), a straight chain ketone (79) and alkaloids (28); Leaf contains proteins, nitrogen, polyphenols (80), minerals as Ca, Mg, K, Fe, Cu, Zn, Mn, Co & Cr (72), glycosides, reducing sugars (81), acacetin, proanthocyanins, phenolic acid (27); hydrocarbons (12, 82-83), minerals as Ca, Mg, K, Fe, Cu, Zn, Mn, Co & Cr (16), alkaloids, mucilage, potassium salts, sugars, purine alkaloid (19, 75-76, 84), flavonoids, terpenoids (85), manganese salts, potassium chloride & sulphate, fixed oils (84) are reported in the plant without any specification of the morphological part of the plant and ash from the root contains potassium salts (19). Some of the phytoconstituents of the plant are summarized in Table 2.

Table 2: Chemical Constituents of Hygrophila spinosa

Constituent	Structure	Isolated from Part of Plant	References
Myristic acid		Seed	(15, 19, 29, 86-88)
Palmitic acid		Seed	(15, 17, 19, 29, 73, 83-84, 86-88)
Stearic acid		Seed	(15, 17, 19, 29, 73, 86-88)

Linoleic acid		Seed	(15-17, 19, 29, 83-84, 86-88)
Lupenone		Root	(89)
25-oxo-hentriacontanyl acetate		Plant, Aerial part	(17, 90-91)
Alkaloid (Hygrosterol)	---	Root	(92)
Lupeol		Aerial part, Root, Leaf, Stem, Whole plant, Seed	(17, 19, 27, 41, 75-76, 78- 79, 83-85, 89, 91, 93-96)
Stigmasterol		Aerial part, Whole plant, Leaf	(17, 27, 41, 78-79, 83-85, 93)
Betulin		Aerial part, Root	(17, 78, 83-84, 90, 93)
β- carotene		Leaf	(80, 97)
Phytosterol (Hygrosterol)	---	Root	(19)
Maltose		Root	(19)
Oleic acid		Seed	(17, 19, 29, 83-84, 86-88)
Hentriacontane		Leaf, Stem	(19, 76)

Xylose		Seed	(17, 29, 73, 84, 98)
Glucuronic acid		Seed	(17, 29, 73, 83)
Apigenin-7-O-glucuronide		Flower	(17, 27, 41, 79, 84)
Apigenin-7-O-glucoside		Flower	(17, 27, 41, 79, 84)
3-methylnonacosane		Aerial part	(17, 85, 91)
23-ethylcholesta-11(12), 23(24)-dien-3 β-ol		Aerial part	(17, 85, 91)
Maltose		Aerial part	(76)
Asteracanthine	---	Seed	(79, 99)]
Asteracanthicine	---	Seed	(17, 79, 99)
Luteolin		Leaf	(79)
Luteolin-7-rutinoside		Leaf	(79)
Methyl-8-n-hexyltetracosanoate		Plant, aerial part	(17, 90)
Rhamnose		Seed	(73)

Arabinose		Seed	(29, 73, 98)
β- sitosterol		Root, stem, leaf, seed	(29, 94-96)
Histidine		Seed	(17, 29, 86, 100)
Phenylalanine		Seed	(17, 29, 86, 100)
Lysine		Seed	(17, 29, 100)
Polysaccharides	---	Seed	(17)
Ascorbic acid		Leaf	(17, 97)
Nicotinic acid		Leaf	(17)
n-triacontane		Plant	(17)
Glucose		Seed	(29, 73, 98)
Mannose		Seed	(29, 98)
Vannilic acid		Leaf	(27)
Syringic acid		Leaf	(27)
Apigenin		Leaf	(27)

PHARMACOLOGICAL STUDIES

Hussein Ayoub *et al.* (101) studied the anticancer activity of ethanolic extract of the fruits of *Asteracantha longifolia* (L) Nees using the KB test system and the ED_{50} found was more than 1 µg/ml in the KB cell culture. Further the antitumor activity in Ehrlich ascites carcinoma and

sarcoma-180 bearing mice of the petroleum ether extract of the roots of *Hygrophila spinosa* T. Anders was also studied (102). The extract showed decrease in packed cell volume, increases life span of EAC/S-180 bearing mice in a day dependent manner and also inhibited the rapid increase of body weight of tumor bearing mice. Sub-acute toxicity study of the hydroalcoholic extract of the whole plant of *H. spinosa* showed no significant change in body weight, organ weight (heart, kidney, liver, lung and spleen) and serum biochemical parameters. The LD_{50} was found to be 3020 mg/kg body weight.The tumor reducing potency of the extract (300 mg/kg body weight) in DMBA (7, 12-Dimethylbenz (a) anthracene) induced mammary tumor in female rats was assessed by recording the reduction in tumor weight (103).

Chloroform extract of the whole plant of *A. longifolia* (L.) Nees is active against *Bacillus subtilis* NCTC 8236, *Staphyllococcus aureus* NCTC 6447, *Pseudomonas aeruginosa* NCTC 6750 and *Escherichia coli* NCTC 8196; methanol extract is active against *B. subtilis* and *S. aureus*, but aqueous extract is not active against the above four strains (104).

Petroleum ether extract of the roots of *H. spinosa* has no sedative-hypnotic action, but when administered i.p. to mice, significantly potentiated the sleeping time of chlorpromazine, diazepam, pentobarbitone, chlordiazepoxide and protected against strychnine-induced convulsions (105).

Ethanolic extract and its chloroform fraction of the aerial parts of *Asteracantha longifolia* (L) Nees shows promising hepatoprotective activity, but the aqueous extract and methanol fraction of the ethanolic extract were inactive (106). The ethanolic extract and its chloroform fraction significantly reduced different enzyme levels like serum glutamate oxaloacetate transaminase (SGOT), serum glutamate pyruvate transaminase (SGPT), alkaline phosphatase and serum bilirubin in carbon tetrachloride induced hepatotoxicity in rats; also reduced the morphological parameters in liver (liver weight and liver volume). Further Sen *et al* (107) reported that the leaf extract (3 teaspoon, twice daily for 7 days) of *H. auriculata* (K. Schum) Heine (Acanthaceae) commonly known as 'Kuilekha' is used for treatment of jaundice by the local people at Bargarh district, Orissa, India. The methanolic extract of *H. auriculata* also protects the liver against paracetamol and thioacetamide intoxication in rats (108).The acute toxicity of the aqueous extract of the roots of *H. auriculata* was evaluated by administering the extract orally to different groups at the dose level of 250, 500, 1000 and 2000 mg/kg body weight. All animals were observed for toxic symptoms and mortality for 72 hrs. No mortality was observed upto a dose level of 2000 mg/kg body weight. As per the ranking system European Economic Community (EEC) for acute oral toxicity, the LD_{50} dose of 2000 mg/kg and above is categorized as unclassified (EC Directive 83/467/EEC, 1983). The extract has significant hepatoprotective and antioxidant activities in CCl_4 induced liver toxicity in rats. The extract significantly decreased the alanine transaminase, aspartate transaminase, alkaline phosphatase, lactate dehydrogenase and total bilirubin in the treated groups as compared to the control. The *in vitro* antioxidant activity was studied using ferric thiocyanate (FTC) and thiobarbituric acid methods (109). Again Usha *et al* (110) have reported the hepatoprotective activity of the aqueous extract of the roots of *H. spinosa* at a dose of 200 mg/kg body weight, orally in CCl_4 induced liver damage in rats. They analysed the levels of some known antioxidant (both enzymic and non enzymic) activities and histopathological studies to find out the hepatoprotective activity.

The anti-nociceptive activity of the aqueous extract of leaves, aerial parts and roots of *H. auriculata* was studied using both chemical and thermal methods of nociception in mice. The extracts at 100 and 200 mg/kg body weight doses inhibited the abdominal constrictions induced by acetic acid and also increased the pain threshold of mice towards the thermal source. The activity was comparable to standard drug aspirin (111-112).

Petroleum ether extract of the roots of *H. spinosa* at a dose of 40 mg/kg body weight (i.p.) once weekly for four weeks has changed serum aminotransferase, alkaline phosphatase and cholesterol. Higher dose (80 mg/kg body weight) changed all the above parameters in mice including total bilirubin, nonprotein nitrogen, blood urea, plasma protein and WBC count, but low dose (20 mg/kg body weight) does not exhibit appreciable action. In daily treatment for one month, high dose (8 mg/kg body weight) slightly affects liver and kidney functions and metabolism (alteration takes place in case of transaminase, alkaline phosphatase and serum cholesterol) and hematological parameters (only WBC). Low (2 mg/kg) and moderate (4 mg/kg) doses do not produce any significant toxic action (113).

Ethanolic extract of the aerial parts of *H. spinosa* at 100 and 200 mg/kg body weight orally increases the haemoglobin, haematocrit, RBC and total WBC as compared with vehicle treated control rat haemogram. In anemic rats, the extract increases haemoglobin, haematocrit, and RBC count, but decreases serum iron and serum total iron binding capacity as compared with vehicle treated anemic control rats (114). Pawar *et al* reported the LD_{50} and haematopoietic activity of the petroleum ether extract of the leaves of *A. longifolia* in rats (115). For LD_{50} study the extract was administered i.p., in doses of 250, 500, 750, 1000, 1250, 1500 mg/kg of body weight in different groups of animals. The LD_{50} studies revealed that albimo rats tolerated a considerable high dose of the extract (1000mg/kg body weight, i.p.), without any manifestations. Haematological parameters were evaluated in the anemic animal model and it was found that the extract significantly increases the haematological parameters (erythrocyte count, leukocyte count, haemoglobin and haematocrit value).

Indigenous drug (Speman) of Himalaya Drug Company in which *H. spinosa* is an ingredient increases the maltase activity of dorsolateral prostate, fructose content of seminal vesicles along with coagulating glands, which confirms it's anabolic-cum-androgenic like activity (33). One formulation of *H. spinosa* alone and also in combination with other two herbomineral formulations showed beneficial effects of various degrees in alcohol-exposed and normal rats with respect to the sexual behaviour of animals. There was also improvement in the number of LH-FSH-producing basophil cells in the pituitary and raised level of circulating testosterone. The mean sperm count was also higher in the drug treated animals (116).

Treatment of diabetic rats with the hydroalcoholic extract of the aerial parts of *H. auriculata* (100 and 300 mg/kg body weight) for three weeks showed reduction in blood glucose, thiobarbituric acid reactive substances (TBARS) and hydroperoxide in both liver and kidney. The extract increased the glutathione (GSH), glutathione peroxidase (GP_X), glutathione s-transferase (GST) and catalase in the treated groups. Treatment with the extract also reduced lipid peroxidation that is associated with increased activity of superoxide dismutase (SOD) and catalase. Hence the extract possesses antidiabetic and antioxidant activities (117). Further the antioxidant property of the plant was also reported (118-120). Administration of an aqueous extract of *H. longifolia* prior to glucose loading resulted in a significant increase in the glycogen content of liver and muscle, and a significant increase in triacylglycerol content of adipose tissue in comparison with control rats. However, the plant extract had no effect on the gluconeogenic absorption. It has been suggested to exert hypoglycemic action by mechanisms similar to those of sulphonylureas (121).

Decoction of the whole plant and aqueous extract of ashes of *H. spinosa* showed diuretic action in rats, which was attributed to presence of potassium salts in high concentration (18, 122). Diuretic activity of *A. longifolia* is attributed to lupeol (123). Lupeol also controls arthritis (124) and acts as chemopreventive and immunomodulatory (125). Lupeol and β- sitosterol are having antipyretic (73), hepatoprotective (38, 108), antioxidant, anticancer (34) and macrofilaricidal (126) activities.

The choloroform soluble alkaloidal fraction from the aerial parts of *A. longifolia* relaxes smooth muscles, lowers blood pressure of anaesthetized dog, possibly by vasodilation, stimulates respiration and has diuretic action on rabbits. Also the essential oil from the roots and aerial parts of the plant showed antibacterial activity against Gram-positive and Gram-negative organisms (75). Administration of aqueous extract of whole plant causes a continuous rise of blood pressure of anaesthetized cat and restores failing heart to normal in perfusion of frog's heart (84).

The plant is having anti-convulsant, antineoplastic, hepatoprotective, antifungal, antispasmodic, anti-inflammatory, diuretic, moderate antipyretic, hypotensive, vasodilatory, anabolic cum androgen like activity, bronchodilatory, antitumor promoting activity against chemically induced hepatocarcinogenesis in wistar rats. Administration of Kokilasha (*A. longifolia*), 8-10 gm (in divide doses) orally with milk or sugar for 3 months to fifty infertile couples with males suffering from oligospermia, necrospermia, less motile and unhealthy sperms showed appreciable change in viability after one month of treatment, including some change in morphological character of the sperm. In the 2nd month the semen analysis showed considerable improvement in number and motility and immaturity reduced. After three months of treatment normospermia developed in 80% of patients (17).

Methanolic extract of the seeds of *H. auriculata* showed potent inhibitory action against leukotriene B_4 biosynthesis in isolated bovine polymorphonulear leukocytes (127). Ethanol and distilled water extract of the plant exhibited significant anti-inflammatory activity, whereas significant analgesic activity was shown by petroleum ether and ethanol extract, when compared with respective controls and were comparable with those of standard drugs diclofenac sodium and analgin in albino rats and mice at a dose of 400 mg/kg body weight, orally (128).

The crude petroleum ether extract of *H. spinosa* was found to possess low toxicity (LD_{50} 1gm/kg in mice) and effectively arrested neoplastic growth in swiss mice. The associated pathologic changes in blood cell counts and haemoglobin content due to oncogenesis in the host returned to almost normal by drug treatment. Treatment of the test animals with the drug, previously inoculated with 3 different strains of tumour cells in mice, resulted in the inhibition of tumour growth in all three cases. The drug significantly increased the life span in Daton's lymphoma treated mice (129). The plant is also used for the treatment of urticaria (130) and one homeopathic medicine of the plant administered @ 3X twice a day cured a patient suffering from Hairy Cell Leukemia. The recovery was rapid and blood count stabilized; also there was relief from headache, red nodular urticarial eruption and insomnia (131).

The antifungal activity of *H. auriculata* extract against *Aspergillus tamari*, *Rhizopus solani*, *Mucor mucedo* and *Aspergillus nig*er is due to the proteins and peptides present (132). The methanolic extract at 30 μg/ml dose is effective against *Enterobacter aerogenes*, *Staphylococcus aureus* and *Burkholderia pseudomallei* (81). The aqueous and ethanolic extract of the whole plant of *A. longifolia* shows hepatoprotective activity against galactosamine induced liver dysfunction in rats. The activity was assessed by examination of blood biochemistry and histopathological studies of liver (133). Also the methanolic extract of the plant is an effective inhibitor of oxidative stress and

oxidant induced post necrotic proliferation in rat liver (134).

CONCLUSION

H. spinosa is widely distributed throughout India and is used for the treatment of cancer, arthritis, hepatotoxicity, inflammation, blood diseases, diabetes, fever, constipation, bacterial infection etc. The plant is also used as antioxidant, diuretic, hypotensive and macrofilaricidal, but the mode of action of for different bioactivities are not studied in detail. *H. spinosa* contains various phytoconstituents viz. alkaloids, glycosides, steroids, flavonoids, terpenoids, mucilage etc. which may be responsible for the different pharmacological activities. Hence, we can isolate some pure phytopharmaceuticals which in turn can be used as lead molecules for synthesizing novel agents having good therapeutic activity.

With regard to the development of quality herbal medicine the standardization of extracts, phytopharmacology of different extracts, isolation and characterization of active phytopharmaceuticals, elucidation of mechanism of action of the isolated compounds and clinical trial of the compounds are much needed. In the changing global scenario the interest towards plants with medicinal value is increasing substantially in the primary healthcare system both in the developed and developing countries. Therefore, the informations will help the scientists and researchers to screen the compounds responsible for different bioactivities, and to elucidate the molecular mechanism of action.

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