



A REVIEW ON HELIOTROPIUM INDICUM

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RACT

It is a fetid herb grown in the tropical and temperate regions of the world. The plant is native to Asia and found in India, Bangladesh, Philippines. *H. indicum* has been used in different traditional and folklore systems of medicine for curing various ailments. An ethno-pharmacological survey revealed that, the traditional healers in Kancheepuram district of Tamil Nadu, India use *H. indicum* to cure skin diseases, poison bites, stomach ache and nervous disorders. It is used topically for ulcers, sores, wounds, gum boils, skin infections and rheumatism. A decoction of the leaves is used in fevers and that of roots in cough and fevers. It possesses wound healing property, fertility control, antitumor activity and anti-inflammatory effect. Seeds are stomachic. The flowers are considered emmenagogue in small doses and abortifacient in large doses. This review throws light on botany, phytochemistry, its traditional and scientific uses and glimpses of elaborative study of research carried out on *Heliotropium indicum*.

KEYWORDS: *Heliotropium indicum*, ethnopharmacology, anti-inflammatory activity, emmenagogue.

INTRODUCTION

It is a fetid herb grown in the tropical and temperate regions of the world. The plant is native to Asia and found in India, Bangladesh and Philippines. In India it is found in sunny localities, on waste lands, weeds, and anthropogenic habitats, widely considered as a weed of fields.^[1] The name "heliotrope" originates from the traditional idea that the inflorescence of these plants turned their rows of flowers to the sun.

Botanical Description^[2]

Indian Heliotrope is a herb, slightly woody, with a long taproot, erect stem, sometimes unbranched and sometimes branched; leaves alternate or sometimes sub opposite, distinctly petiolate, blade long-decurrent on petiole from a sub truncate base, ovate-deltoid, margin slightly wavy-cripsed, acute, lateral veins 4-7 pairs. Inflorescence terminal, tip coiled. The inflorescence uncoils after the central flowers, which are the oldest ones. The flowers are arranged on one side of the inflorescence. Flowers are pale violet with a yellow throat, but fading to dull white, calyx-lobes linear-lanceolate, ciliate; petals rounded. Fruit is 3.5 mm long, ovoid, ribbed, separating into 2 nutlets each 2-celled.

The name "heliotrope" originates from the traditional idea that the inflorescence of these plants turned their

rows of flowers to the sun. The meaning of 'helios' in Greek is 'sun' and 'tropein' from where the word 'tropium' is derived means 'to turn'.^[3] *Heliotropium indicum* Linn belongs to family Boraginaceae. A majority of the plants in the family are herbs. Several heliotropes are popular garden plants and some others found as weeds.

H. indicum may flower whole year; the flowering season is too long. The flowers are white or violet coloured, regular, sessile. Sepals - green, linear lanceolate and unequal. Numerous branched, more or less densely hirsute with spreading hairs are found in the stem and the root system is tap root and branched.^[4,5,6]

Ethno-pharmacology: *H. indicum* has been used in different traditional and folklore systems of medicine for curing various ailments. An ethno-pharmacological survey revealed that, the traditional healers in Kancheepuram district of Tamil Nadu, India use *H. indicum* to cure skin diseases, poison bites, stomach ache and nervous disorders.^[7] In some African countries, another ethno-pharmacological survey reports that *H. indicum* is believed to be useful in treating malaria, abdominal pain and dermatitis. It is mostly reported to be used in the treatment of malaria.^[8] In Jamaica, the decoction of the entire plant is taken orally for treatment

of intractable fever, ulcers, venereal diseases and sore throat and used externally in vaginal cavity to induce abortion in pregnant women and administered rectally to treat local sores in the rectum,^[9] while in Philippines⁷ and Senegal, it is used orally as diuretic and for the treatment of kidney stones.^[10,11]

The infusion of the flower is taken orally for the treatment of menorrhagia by females in Jamaica.^[9] The decoction of the entire plant is used externally for treating herpes and the paste of fresh plant is used externally for cleansing and dressing of wounds and ulcers in Rodrigues. The sap of the stem is used by females orally for treating dysmenorrhoea.^[12] The decoction of the flower is taken orally as an emmenagogue in small dose and abortive in large dose by the females while a paste of fresh entire plant is used externally to get rid from head lice in the West Indies.^[13]

In Thailand, the dried inflorescence is believed to produce permanent sterilization when used orally in women. One gram of the dried and powdered inflorescence mixed with milk is used for three days beginning with the fourth day of menses to achieve the desired effect.^[14] Other folk remedies include use of



Traditional Uses

It is used topically for ulcers, sores, wounds, gum boils, skin infections and rheumatism. A decoction of the leaves is used in fevers and that of roots in cough and fevers. It possesses wound healing property,^[23] fertility control,^[24] antitumor activity,^[25,26] and anti-inflammatory effect.^[27] Seeds are stomachic. The flowers are considered emmenagogue in small doses and abortifacient in large doses.

Uses

Heliotropium indicum has been used widely on warts and to treat inflammations and tumours.^[28] Throughout tropical Africa, it is used as an analgesic, diuretic and for numerous skin problems. In Nigeria, an infusion of the plant is used as an eye-lotion and to clean ulcers. In Gabon, the powdered leaves are used to treat infected gums. The Ngoni of Tanzania, use an extract made from the roots to treat yaws. In Madagascar, a plant infusion is used as a diuretic. In the Seychelles, the leaves are applied as an analgesic to treat stomach-ache in adult patients after operations. In Mauritius, a leaf infusion is

decoction of the leaves for treatment of fever,^[1] insect bites, stings, diarrhoea, skin rashes, menstrual disorders and urticaria.^[16] The decoction of the leaves is also credited to be useful in curing insect stings, scorpion stings,^[11] as abortive agents in large dose and emmenagogue in small dose.^[16]

The leaf paste is applied topically to cure rheumatism in Rayal Seema in Andhra Pradesh, India,^[17] and skin infection in Nicaragua.^[18] The decoction of both leaf and root mixture is used for treating whooping cough in children in Eastern Nicaragua.^[19] In Amazon, the paste of both leaf and root mixture is applied externally in scorpion stings, bug bites,^[20] while the paste is recommended for treating sores and warts in Taiwan.^[21]

In Malaysia, a paste made from the plant is applied to counteract putrefaction and ringworm infection. In Burma, a decoction of the whole plant is used to treat gonorrhoea while in Indonesia, an infusion of the leaves is used to soothe mouth ulcer. A decoction of the dried roots is used in the Philippines to promote menses, while the seeds are used to treat cholera, malaria and wounds.^[22]

taken against kidney infections and as a diuretic. A poultice made from the leaves is applied to rheumatic limbs, to wounds and insect bites. A flower decoction is an emmenagogue in small doses and an abortifacient in large doses.

In Gambia the whole plant is buried and after the fleshy tissue has rotted away the remaining fibre is used to make false hair for women.

Phytochemical Constituents

The major constituents of the extract of *Heliotropium indicum* are tannins and alkaloids.^[29,30] Aerial parts contain pyrrolizidine alkaloids, indicine (principal), echinitine, supinine, heleurine, heliotrine, lasiocarpine, its N-oxide, acetyl indicine, indicinine and anti-tumour alkaloid, indicine-N-oxide. The plant also contains rapanone and lupeol and an ester of retronecine. Volatile oil from aerial parts of *H.indicum* contains phytol, 1-dodecanol and β -linalool.^[31] Root contain Estodiol and seeds contain Heliotrine as chemical constituents.^[32] João Sammy N. Souza et al.,^[33] isolated a new

pyrrolizidine alkaloid with unusual structural features Helindicine, together with the known lycopsamine, from the roots of *Heliotropium indicum*.

Research on *Heliotropium indicum*

Anti-inflammatory activity

K. Srinivas *et al.*^[34] studied the anti-inflammatory effect of *Heliotropium indicum* and *Leucas aspera* on carrageenin induced hind paw oedema and cotton pellet granuloma in rats. Hind paw oedema was produced by subplantar injection of carrageenin and paw volume was measured by plethysmometer at '0' and '3' hours intervals after injection. Cotton pellet granuloma was produced by implantation of 50 + 1 mg sterile cotton in each axilla under ether anaesthesia. The animals were treated with *H. indicum* and *L. aspera* and the standard drugs viz., acetylsalicylic acid and phenylbutazone. Both the plants have produced significant anti-inflammatory effect in both acute and subacute models of inflammation.

Kalyan S Betanabhatla *et al.*^[35] investigated for anti-inflammatory and anti-nociceptive activities of Chloroform extract of *Heliotropium indicum* in experimental animal models. Anti-inflammatory activity was evaluated by carrageenan induced paw edema model in and compared to a standard drug, Diclofenac sodium. The extract of *H. indicum* at a dose of 150 mg/kg b.w. showed maximum (80.0%) inhibition on carrageenan induced rat paw edema. Anti-nociceptive activity was evaluated with hot plate model in male Swiss albino mice and compared to a control drug, Pentazocine. The extract of *H. indicum* with a concentration of 150 mg/kg b.w. showed maximum (82.79%) anti-nociception in the hot-plate test.

Anti-ulcer activity

Akinlolu Abdulazeez Adelaja *et al.*^[36] aimed to study ulceration of the gastric mucosa in Wistar rats induced through oral administration of 80mg/kg/b.w of Indomethacin. Histological analyses of the stomach body wall in the rats of Groups 2 and 4 (which were given 100mg/kg/ b.w of extract before oral administration of 80mg/kg/b.w Indomethacin and 80mg/kg/ b.w Indomethacin only respectively) showed erosion of the mucus-secreting cells, gastric pit, upper and middle parts of gastric glands and some of the parietal cells. Histological studies of the stomach body wall in rats of Group 5 (which were given 200mg/kg/ b.w of extract before oral administration of 80mg/kg/ b.w of Indomethacin) showed erosion of the mucus-secreting cells, gastric pit and the upper part of the gastric gland. Histological studies of the stomach body wall in rats of Groups 1, 6 and 3 (which were given 50mg/kg/ b.w of Ranitidine and 400mg/kg/ b.w of extract before oral administration of 80mg/kg/ b.w Indomethacin; and only 80mg/kg/ b.w of Normal Saline respectively) showed normal morphological appearance of mucosa layer.

Shenoy *et al.*^[37] evaluated the anti ulcer activity of ethanol extract of leaves of *Heliotropium indicum*. The

ethanol extract of *H. indicum* was investigated for its anti ulcer activity against Aspirin plus pylorus ligation induced gastric ulcer in rats, HCl –Ethanol induced ulcer in mice and water immersion stress induced ulcer in rats. The antiulcer activity was assessed by determination and comparison of gastric volume, free acidity and ulcer inhibition in aspirin- pylorus ligation induced gastric ulcer model. The number of lesions in HCl-Ethanol induced peptic ulcer model and mean score value of ulcer inhibition in water immersion stress induced ulcer model. A significant antiulcer activity of plant extract was observed in all the models. Pylorus ligation model showed significant reduction in gastric volume, free acidity and ulcer index as compared to control. Also extract showed significant ulcer inhibition in HCl-Ethanol induced ulcer and ulcer protection index in stress induced ulcer.

Janardhanan *et al.*^[38] studied about anti-ulcer activity of hydro alcoholic extract of *Heliotropium indicum* on four different models of antiulcer activity. The anti-secretory, acetic acid induced ulcer and cystamine induced duodenal ulcer data have been expressed. These results showed that the crude hydro alcoholic extract of *Heliotropium indicum* at dose levels 200 and 400mg/kg were dose dependent and decreased in the ulcer index and ulcer scoring when compared to control and positive control. The physicochemical studies have revealed that the extract of *Heliotropium indicum* on offensive and defensive factors were indicated, antiulcer activity when compared to control and positive control. The biochemical parameters results have shown that the extract of *Heliotropium indicum* dose levels 200 and 400 mg/kg, offensive and defensive factors were indicated antiulcer activity when compared to control and positive control.

S.Nethaji *et al.*^[39] performed phytochemical screening and anti-ulcer activity of leaves and root extracts of *Heliotropium indicum* Linn. The preliminary phytochemical screening was done by *in vitro* method and anti-ulcer activity was conducted by *in vivo* method. The phytochemical analysis showed the presence of alkaloids, carbohydrates, glycosides, phytosterols, fixed oils, fats, phenolic compounds, tannins, flavonoids, terpenoids, proteins and amino acids. The ethanolic extract of *Heliotropium indicum* leaf and root was evaluated for its anti-ulcer activity against pylorus ligation induced gastric ulcer in rats. It showed significant reduction in gastric volume, free acidity, total acidity and ulcer index.

M.D. Ayoola *et al.*^[40] evaluated the gastroprotective properties of the non-polar (n-hexane) fraction of *H. indicum* to establish its anti-ulcer activities. Rats of Groups I and II received normal saline and 80 mg/kg/bw of Indomethacin respectively. Rats of Groups III– VI given orally 100, 200 and 400 mg/kg/b w of the n – hexane fraction of methanolic extracts of dried leaves of *H. indicum* and 50 mg/kg/bw of Ranitidine respectively

before the induction of gastric ulceration. One hour after administration of extract and Ranitidine, 80 mg/kg/bw of Indomethacin was administered orally to rats of Groups III – VI. Morphological analyses show that administration of 100, 200 and 400 mg/kg/bw of extract and Ranitidine showed percentage ulcer reductions of 45%, 50%, 75% and 95% respectively. Histological analyses of the stomach in rats of Groups II and III show erosion of mucus-secreting cells, parietal cells, gastric pit and glands. Erosion of few mucus-secreting cells, gastric pit and parietal cells were observed in rats of Group IV. Normal cytoarchitectures of the mucosa layer were observed in rats of Groups I, V and VI. Final results show that the n-hexane fraction of *H. indicum* possessed gastroprotective properties.

Wound healing activity

Dodehe Yeo *et al.*^[41] evaluated *in vitro* wound healing activity of the butanol, ethyl acetate extracts from *H.indicum*. Wound healing activity was studied using incision wound models in cell culture (H292). All the fractions proved to have a wound healing effect. But n-butanol and ethyl acetate extracts showed significant wound healing activity. The activity was when compared to residue extract ($p < 0.5$). There was no much difference between the wound healing effect of butanol and ethyl acetate ($p < 0.5$). *H.indicum* possesses significant *in vitro* dose-dependent wound healing; this supported *in vivo* study and traditional claims for the plant as a wound healer.

Dodehe Yeo *et al.*^[42] studied wound healing effect of n-butanol fractions in H292- cells. Fractions which possessed potent wound healing activity were fractionated on Sephadex LH20 column chromatography. Two compounds have been isolated which were responsible for this wound healing effect. Their structures were established as Pestalamide B (1) and Glycinamide, N-(1-oxooctadecyl) glycyl-L-alanyl-glycyl-L-histidyl (2) on the basis of spectral analysis. Both compound 1 and 2 showed significant wound healing effect compared with the control ($P < 0.05$).

G. K. Dash *et al.*^[43] studied review of *Heliotropium Indicum*. The plant is reported to possess antibacterial, antitumor, uterine stimulant effect, anti-fertility, wound healing, anti-inflammatory, anti-nociceptive and diuretic activities. Several pyrrolizidine alkaloids have been isolated from this species. The active principle Indicine-N-oxide has reached Phase 1 clinical trials in advanced cancer patients. But severe toxic side-effects showed that a therapy with indicine-N-oxide was not advisable. Most of the alkaloids are hepatotoxic and therefore internal use of *Heliotropium* species is not recommended. External application to promote wound healing and to fight infections seems to be less toxic, but still more extensive research is needed.

B.Sangeetha *et al.*^[44] evaluated the wound healing activity of ethanolic leaf extract of *Heliotropium indicum* in rabbit by excision wound model. In this study, the wound was made by excising the skin, within the border of the template to the level of loose subcutaneous tissue, using a size No.15 scalpel blade and a forceps. The wound closure time was lesser, as well as the percentage of wound contraction was much more with dose of extract and 100% *Heliotropium indicum* contraction was observed in (15.7 ± 0.14) days, which was close to betadine treated (14.8 ± 0.6) days. The 5% extract group of animals showed significant wound contraction from 6th day onwards and achieved 100% wound closure in 18.9 ± 38 days. The study provides scientific evidence for further evaluation of *Heliotropium indicum* in the topical treatment of wounds.

Anti-oxidant activity

Nusrat Ahmed Mourin *et al.*^[45] Performed screening for antioxidant, cytotoxic, thrombolytic, membrane stabilizing and antimicrobial activities on methanolic extracts of whole herb of *Heliotropium indicum*. In free radical scavenging activity assay, the carbon tetrachloride soluble fraction showed the highest free radical scavenging activity ($IC_{50} = 37.88 \pm 0.51$ $\mu\text{g/ml}$) which can be correlated to total phenolic content (40.35 ± 0.17 mg of GAE/g of extractives). In brine shrimp lethality bioassay, the crude methanol extract ($LC_{50} = 2.57 \pm 0.22$ $\mu\text{g/ml}$) showed the presence of the highest amount of considerable bioactive principles. During assay for thrombolytic activity, the carbon tetrachloride soluble materials showed 36.90 ± 0.75 % of clot lysis compared to 66.77% by standard streptokinase. In hypotonic solution and heat induced conditions, the carbon tetrachloride soluble fraction inhibited haemolysis of human erythrocyte by 41.47 ± 1.12 % and 37.97 ± 0.14 % resp. The carbon tetrachloride soluble materials showed activity against microbial growth with zone of inhibition ranging from 7.0mm to 20.0 mm.

R. Meenatchi Ammal *et al.*^[46] studied scavenging activity of ethanolic extract of *Heliotropium indicum* leaves in free radical mediated diseases including diabetes, cardiovascular diseases, cancer etc. The ethanolic extract was evaluated for *in vitro* antioxidant activity by radical scavenging such as DPPH scavenging, superoxide anion radical scavenging, metal chelation, reducing power activity and total antioxidant assay at different concentrations. In this study, leaf extract showed marked antioxidant activity probably due to the phytochemicals present in it. The antioxidant activity was found to be concentration dependent and may be attributed to the presence of bioactive compounds in the leaves of *Heliotropium indicum*. The results conclude that the plant extract is a source of natural antioxidants which might be helpful in preventing the progress of various oxidative stress mediated diseases.

Jitpisute Chunthong *et al.*^[47] investigated anti-inflammatory and antioxidant activities of *Heliotropium*

indicum extracts. Dried plant materials were extracted by maceration in 95% ethanol and boiling in water. For anti-inflammation activity, both extracts were tested for suppression of nitric oxide (NO) production in LPS-induced RAW 264.7 cells. They were also assessed for antioxidant activity by DPPH method. Results showed that ethanolic extract of *Heliotropium indicum* exhibited higher inhibitory activity of NO release than Indomethacin as a positive control (IC₅₀ value of 24.17±2.12 and 34.67±6.23 µg/mL, respectively). For DPPH radical scavenging assay, the ethanolic extract also exhibited antioxidant activity but less than BHT as an antioxidant compound (EC₅₀ values = 28.91±4.26 and 13.08±0.29 µg/mL, respectively). In contrast, its aqueous extract had no inhibitory activity on NO release (IC₅₀ > 100 µg/mL) and no inhibitory activity on DPPH radicals (EC₅₀ values > 100 µg/mL). The results showed correlation between anti-inflammation and antioxidant activity and these results also support usage of the plant in cancer patients.

Kabita Mahato *et al.*^[48] explored anti-oxidant activity of three ethnomedicinal plants of Assam viz., *Calamus leptospadix* Griff., *Heliotropium indicum* Linn., *Lasia spinosa* Lour. The methanolic extracts of aerial parts were studied for phytochemical screening and anti-oxidative activity by different *in vitro* assays: DPPH radical scavenging method, Nitric oxide radical scavenging activity, Hydrogen peroxide radical scavenging activity, Total phenolic content and Total flavonoid content. The percentage of inhibition was calculated by comparing the absorbance values of the control and test samples. The study revealed that methanolic extract of *Calamus leptospadix* (CL) exhibited the highest DPPH radical scavenging activity (IC₅₀ value of 29 ± 3.24 µg/ml), Nitric oxide radical scavenging activity (233.33 ± 3.54 µg/ml), Total phenolic content (8.02 ± 0.32 µg/ml expressed as gallic acid equivalents) and Total flavonoid contents (61.71 ± 1.16 µg/ml expressed as quercetin equivalents). Methanolic extract of *Lasia spinosa* (LS) showed highest hydrogen peroxide radical scavenging activity (IC₅₀ value of 221.89 ± 2.14 µg/ml). The results indicate that aerial parts of *Calamus leptospadix* have potent, *Lasia spinosa* have moderate and *Heliotropium indicum* (HI) have mild antioxidant and free radical scavenging activity.

Anti-Diabetic activity

Monteomo Gnate François *et al.*^[49] have compared Antihyperglycemic Activity of *Sclerocarya Birrea*, *Khaya Senegalensis*, *Heliotropium Indicum* and *Ocimum Gratissimum* in albino wistar Rats. The rats were given oral load of glucose (4g/kg) after receiving one single dose of plant extract. The result showed that, rats who were administered the aqueous extract of *Sclerocarya birrea*, *Khaya senegalensis* and the aqueous extract of *Khaya senegalensis* had significant antihyperglycemic effects respectively 30% and 20% (p<0,05; n= 8) after 2 hours. These reductions of blood glucose reached 40%

and 26% at the 4 hour. The aqueous extract of *Ocimum gratissimum* didn't show any remarkable effect on the blood glucose of the rats, the decrease was 4, 5 % (p<0,05; n= 8). The aqueous extract of *Heliotropium indicum*, showed insignificant antihyperglycemic effect on the blood of the rats tested. The phytochemical analysis showed the presence of alkaloids, coumarins and tannins to *Sclerocarya birrea*. *Khaya senegalensis* contained alkaloids and coumarins and polyphenols to *Heliotropium indicum*. The aqueous extract of *Ocimum gratissimum* contained flavonoid and tannins. The antihyperglycemic effect of the traditional preparation could be due of antidiabetic activities of *Sclerocarya birrea* and *Khaya senegalensis*. However, the aqueous extract of *Heliotropium indicum* and *Ocimum gratissimum* hadn't shown anti-diabetic effect so, its can be considered as additives in this traditional preparation.

Similarly Rasheed B *et al.*^[50] assessed the anti-diabetic potentials of *Heliotropium indicum* L. leaf aqueous (HILA) extract which was used by Traditional Medicinal Practitioners (TMPs) in Nigeria. Alloxan (ALX)-induced hyperglycaemic rats were orally administered with known folkloric dosage of 30 and 75 mg/kg b. w. of HILA extract once a day for 14 days. Fasting blood glucose (FBG) levels were recorded and pancreatic histology was examined. Net hepatic glycogen (GLY) concentration and lipid profiles were also recorded. Prior to treatment, ALX-induced hyperglycaemia (>250 mg/dL) was induced in rats. Oral administration of 30 and 75 mg/kg b. w. HILA extract to diabetic rats for 14 days reduced FBG significantly to normal values in non-diabetic conditions. Treatment with HILA extract also showed improvement in lipid abnormalities observed in hyperglycaemic condition, levels of triglyceride, total cholesterol and LDL cholesterol were significantly reduced and HDL-cholesterol increased resulting in improved atherogenic index. Hepatic GLY concentration was increased in diabetic rat treated with the extract. Histological examinations revealed degenerated pancreatic islets cells in non-diabetic rat, whereas microscopy of treated rats showed mild to normal structure. Results showed that the aqueous leaf extract of *H. indicum* possesses antihyperglycaemic along with antidyslipidemic activities.

Anti-cancer activity

V. Sivajothi *et al.*^[51] aimed to provide scientific validation to the traditional use of *Heliotropium indicum* in *in vitro* cytotoxic effect on HeLa cell lines. The study was done using methanolic extracts against human cancer cell line (HeLa) using MTT assay to analyze the cell growth inhibition. The results showed that the methanolic extracts of stem and leaf of *Heliotropium indicum* possessed potent anticancer activity and IC₅₀ for both the extracts found to be 200 µg/ml. whereas stem extracts exhibited significant activity up to 64.5% at 200 µg/ml and followed by leaf extract up to 49.67% at 200 µg/ml. The results support the traditional claim of the plant.

Neuroprotective activity

Dasarapu Santhosha *et al.*^[52] investigated the protective effects of ethanolic extract of whole herb of *Heliotropium indicum* on cerebral ischemia/reperfusion induced brain damage in rats. Cerebral ischemia was induced by occluding bilateral common carotid arteries for 60 min followed by 3h of reperfusion. Ischemia/reperfusion-induced neuronal injury was assessed by measurement of brain infarct area, biochemical estimations and histopathological studies. Pretreatment of *Heliotropium indicum* extract (200, 280 and 400 mg/kg, p.o.) significantly reduced the lipid peroxidation, increased the total thiol content, Catalase and glutathione-S-transferase activity in brain homogenates. The diminished cerebral infarct area in Extract-treated groups and histopathological sections confirmed the above results.

Micellaneous activities

Saguna Datta Gupta *et al.*^[53] studied Pharmacognosy of leaf of *Heliotropium indicum* Linn. (Fam. Boraginaceae). The plant has pubescent, exstipulate, ovate-elongate leaves with ranunculaceous stomata on both surfaces, near 2I stornatal index, different types of non-glandular and glandular hairs, about 6palisade ratio, lacunar collenchyma in mid-veins, suberin at trichome bases and alkaloids in leaf extracts.

P. R. Rao *et al.*^[54] investigated the antimicrobial activity of alcoholic extract of *Heliotropium indicum*. Study was carried out at the concentrations of 1 fYg/ml, 100fYg/ml, 1 mg/ml, 50mg/ml and 100 mg/ml of the extract dissolved in propylene glycol against four strains each of Gram positive and Gram negative bacteria, three strains of fungi and two yeast by agar cup plate diffusion method. The alcoholic extract of *Heliotropium indicum* was found to possess dose dependent antimicrobial activity in all the test organisms. The study supports use of the plant as folklore medicine for the treatment of infectious diseases.

Joanne Beroa *et al.*^[55] evaluated *in vitro* anti-plasmodial activity of crude extracts of 12 plant species traditionally used in Benin for the treatment of malaria. For each species, dichloromethane, methanol and total aqueous extracts were tested. The antiplasmodial activity of extracts was evaluated using the measurement of the plasmodial lactate dehydrogenase activity on chloroquine-sensitive (3D7) and resistant (W2) strains of *Plasmodium falciparum*. The selectivity of the different extracts was done by using the MTT test on J774 macrophage like murine cells and WI38 human normal fibroblasts. The potent growth inhibition of both strains of *Plasmodium falciparum* was observed with the dichloromethane extracts of *Acanthospermum hispidum* DC. (Asteraceae) (IC50 = 7.5g/ml on 3D7 and 4.8g/ml on W2), *Keetia leucantha* (K. Krause) Bridson (syn. *Plectronia leucantha* Krause) (Rubiaceae) leaves and twigs (IC50 = 13.8 and 11.3g/ml on 3D7 and IC50 =

26.5 and 15.8g/ml on W2, respectively), *Carpolobia lutea* G. Don. (Polygalaceae) (IC50 = 19.4mg/ml on 3D7 and 8.1mg/ml on W2) and *Strychnos spinosa* Lam. (Loganiaceae) leaves (IC50 = 15.6mg/ml on 3D7 and 8.9mg/ml on W2). All these extract had low cytotoxicity.

R. V. Savadi *et al.*^[56] explored antifertility activity of *Heliotropium indicum* leaves on Albino rats. Acute toxicity studies carried out according to OECD guidelines no.423 and oral doses of 200 and 400 mg/kg body weight were fixed. Ethanolic extract and its fractions were subjected for contraceptive studies using the models like Anti-implantation, Abortifacient. Sperm motility an *in vitro* study was carried out using 1%, 2.5%, 5% and 10% concentrations of extract and its fractions at various time intervals like 0, 15, 30, 60, 90, 120 and 150 seconds respectively. This study has shown better anti implantation activity with n-hexane rather than benzene fraction and ethanolic extract. In case of abortifacient model, higher dose of 400mg/kg body weight shown potent activity. Similarly in sperm motility an *in-vitro* study, potent activity was observed at 10% concentration. Study confirms the use of plant as abortifacient and has moderate antiimplantation and sperm motility.

R. C. Gupta *et al.*^[57] made an attempt to add new or varied cytotypes by Cytomorphological studies in some gamopetalous species of Western Himalaya. The cytological studies made on 30 populations of 26 species of the Gamopetalae from selected localities of Western Himalaya. The chromosome counts in *Strobilanthes alatus* (2n=16), *Artemisia vestita* (2n=36) and *Ainsliaea latifolia* (2n=16) were first ever cytological reports for the species. While, *Bidens pilosa* (2n=96) and *Coreopsis lanceolata* (2n=26) are new reports from India.

Asha N Bagadekar *et al.*^[58] performed *In vitro* callogenesis and rhizogenesis from different explants in stem and leaf of *Heliotropium indicum*, L. Explants were incubated on Murashige and Skoog (MS) medium supplemented with different concentrations and compositions of auxins like 2,4-D, NAA and IBA at 1.0mg/L-3mg/L and cytokinins like Kn and BAP at 2mg/L. In the present study on *Heliotropium indicum*, L indicated that there is a strong ability for *in vitro* rhizogenesis than caulogenesis. Ethanolic crude extracts of roots of *Heliotropium indicum* L., showed the presence of alkaloids, steroids and carbohydrates. This provides a basis for germplasm conservation and for further investigations of bioactive constituents of the plant.

Fayemi Scott O *et al.*^[59] compared Antimicrobial Effects of *Mezoneuron benthamianum*, *Heliotropium indicum* and *Flabellaria paniculata* on *Candida* species. Antimicrobial activities, minimum inhibition concentrations (MIC) and phytochemical tests of *Mezoneuron benthamianum*, *Heliotropium indicum* and

Flabellaria paniculata ethanolic plant extracts were investigated against characterized *Candida albicans*, *Candida torulopsis*, *Candida krusei*, *Candida glabrata* and *Candida stellatoidea* isolated from human buccal cavity. The zones of inhibition for the whole plant extract of *F. paniculata* range from 12.8 ± 0.30 mm against *C. krusei* to 14.5 ± 0.50 mm observed against *C. albicans* while that of *H. indicum* range between 8.6 ± 0.50 mm against *C. torulopsis* to 13.4 ± 0.50 mm observed against *C. glabrata*, and *M. benthamianum* was from 7.8 ± 0.60 mm against *C. glabrata* to 12.8 ± 0.20 mm against *C. krusei*. Phytochemical tests revealed saponins, alkaloids, anthraquinones, flavonoids and tannins in *F. paniculata* extracts and *M. benthamianum* extracts is positive for saponins, anthraquinones, flavonoids and tannins. But, *H. indicum* contained saponins and tannins only. Between 5mg/ml and 8mg/ml was recorded as MIC for *Candida* species against *F. paniculata*. *M. benthamianum* recorded 6-15mg/ml while, *H. indicum* indicated 6-8mg/ml. The highest zone of inhibition in this study was obtained in *F. paniculata* followed by *H. indicum* and *M. benthamianum* consecutively. The conclusion was that there is the need to further investigate and characterize individual phytochemical compounds in these plants and their anti-candidal effect determined.

George Asumeng Koffuor *et al.*^[60] studied Hypotensive effect of an aqueous extract of *Heliotropium indicum* Linn (Boraginaceae). This study was aimed at investigating the effects of an aqueous extract of *H. indicum* Linn on the heart and blood pressure of some animals. The extract was applied *in vitro* to an isolated frog and rabbit heart to check its effect on the force and rate of cardiac contraction, and administered to an anaesthetized cat to establish its effect on blood pressure. The extract had a dose-dependent negative inotropic and chronotropic effect on the frog and rabbit hearts similar to that of acetylcholine and histamine. These effects were inhibited by atropine but not mepyramine suggesting a muscarinic-receptor mediated effect. *In vivo*, the *H. indicum* aqueous extract produced a dose-related reduction in blood pressure of the anaesthetized cat. Findings confirm that *H. indicum* has hypotensive effect supporting its use in the treatment/ of hypertension and cardiovascular diseases.

V.Ramamurthy *et al.*^[61] studied the effect of plant extract, *Heliotropium indicum* and *Mukia maderaspatana*, on different larval instars and pupae of mosquito vector of *A. aegypti*. A Bio-assay was performed using the solvent acetone to find out the median lethal concentration. The study indicated that essential compounds were used for the control of mosquito larvae while extract was used to control adult mosquitoes. The results suggest a potential use of the extracts of these two plant species for the control of *A. aegypti*.

Ramamurthy V. *et al.*^[62] investigated for *in vitro* antimicrobial activity against human pathogens namely *Staphylococcus aureus*, *Bacillus subtilis*, *Streptococcus pyogenes*, *Pseudomonas auroginosa*, *Klebsiella pneumoniae*, *Aspergillus niger*, *Trichoderma viride* and *Candida albicans* using the well diffusion method. The results revealed that the leaf extract showed the highest inhibitory activity against both bacteria (*Staphylococcus aureus* in 22 mm) and fungi (*Candida albicans* in 24 mm). Among the leaf extracts *H. indicum* possess the highest inhibitory activity then the root extracts. Phytochemical analysis of all the extracts showed that the antimicrobial activity of the plant material is due to the presence of antimicrobial compounds. The ethanolic extract of the medicinal plant *H. indicum* have been investigated by GC-MS to identify compounds responsible for its therapeutic activity. Two kinds of extracts of plant were investigated. The tincture was prepared by mixing all parts of the plant (roots and leaves) with a 50% alcoholic solution for 30 days. In parallel, another study was performed to identify the distribution and the concentration of the active compounds in the roots and leaves of this plant. For this purpose, alcoholic extracts were prepared from each part of the plant and studied separately.

Naveen Goyal *et al.*^[63] carried out review on Bioactive phytoconstituents and plant extracts from genus *Heliotropium*. The alkaloids mainly pyrrolizidine alkaloids are the main constituents of *Heliotropium* species, which are responsible for several activities such as anti-tumoural, anti-microbial, and anti-viral effects. Phenolic compounds, terpenoids, and quinones have also been found in this genus.

Kabita Mahato *et al.*^[64] carried out anthelmintic activity against *Pheretima posthuma* using mebendazol as a reference standard. Forty five worms were collected and divided into nine groups, washed in normal saline solution before releasing into 10ml of respective drug solutions using distilled water as vehicle. Different concentrations of (25mg/ml, 50 mg/ml and 100mg/ml, test MEH and AEH and standard solution were prepared before the commencement of the experiment. Time for paralysis and time for death were recorded. Crude methanolic extract with different concentrations of 25 mg/ml, 50 mg/ml, 100 mg/ml produced dose-dependent paralysis. Time of paralysis and death increased with concentration of 25 mg/mL, 50 mg/mL as compared with that of standard drug mebendazole. Methanolic extract of *Heliotropium indicum* Linn. (*H. indicum*) decreased paralysis and death time at 100 mg/mL as compared to aqueous extract of *H. indicum* Linn. Results are expressed as mean \pm SEM (P<0.05) of 5 worms in each group. This shows that the methanolic extract of *H. indicum* (Boraginaceae) possess better activity than aqueous extract of the same to treat intestinal worm infections.

Clement Afari *et al.*^[65] checked anti-cataract activity of an aqueous whole plant extract of *Heliotropium indicum*. The effect of 30, 100 and 300 mg kg⁻¹ extract on the development of 30 µmol kg⁻¹ sodium selenite-induced cataract in 10-day-old rat pups was investigated for 21 days. Soluble lens proteins alpha A and alpha B crystallins, total lens protein, total lens glutathione, and aquaporin 0 in enucleated lens homogenates were determined spectrophotometrically. Histopathological studies on the lenses were also performed. The 2,2-diphenyl-1-picrylhydrazyl scavenging effect and linoleic acid autoxidation (antioxidant properties) of the extract (0.1–3.0 mg ml⁻¹), compared to *n*-propyl gallate, were assessed using standard procedures. Cataract scores showed that the extract, at all dose levels, significantly alleviated selenite-induced cataracts ($P \leq 0.001$). Markers of lens transparency (aquaporin 0, alpha A and B crystallins), as well as total lens proteins and lens glutathione levels, were significantly preserved ($P \leq 0.01$ – 0.001). The extract exhibited potential activity against scavenging free radicals and inhibition of lipid peroxidation. Epithelial and lens fiber integrity in the histopathological assessment were maintained with HIE treatment. The aqueous whole plant extract of *H. indicum* significantly inhibited the development of cataracts in rats through multiple mechanisms.

Gordon A *et al.*^[66] assessed anthelmintic activity of extracts of *Heliotropium indicum* against free-living and parasitic stage of *Trichuris* spp. Various crude extracts from *Heliotropium indicum* at 10 mg/mL, 50 mg/mL, 100 mg/mL and 150 mg/mL were used to evaluate the anthelmintic activity on *Trichuris* spp. Phytochemical analysis on the crude extract showed the presence of compounds such as Alkaloids, saponins, tannins, Reducing sugar, flavonoids and Anthraquinones. All extracts had effect on the motility of *Trichuris* spp. Basic crude extracts had the lowest motility score at all concentration levels followed by Albendazole, Acid crude extract and basic crude extract within the 150 minutes of test. ANOVA performed at 0.05 significant level reveals that, there was significant reliable difference in motility above 30 minutes at all test levels both within and between groups at all the levels of concentration. The basic crude extract exhibited the lowest paralysis and death time at all concentrations levels with (158.4±0.59) min and (190.4±0.32) min respectively for paralysis and death at the 150 mg/mL. The acidic crude basic at the highest concentration caused paralysis and death at (406.7±0.56) min and (430.2 ±0.34) min respectively. The Neutral crude extract exhibited the highest paralysis and death time at all concentrations levels with (412.6±0.43) min and (425.3 ± 0.43) min respectively at 150mg/mL. The extracts exhibited anthelmintic activity and thus could be an inexpensive and readily available source of *Trichuris* spp treatment.

Jyoti Sharma *et al.*^[67] studied the effect of different concentrations of alcoholic extract of *Heliotropium*

indicum on inhibition of aluminium corrosion. Inhibition efficiency of the extract is found to vary with concentration. Using weight loss data, corrosion rate and thermodynamic parameters such as energy of activation for corrosion of aluminium (Ea), heat of adsorption of the inhibitors on the metal surface (Q) were calculated. The entire study concludes that the seed extract of the *Heliotropium indicum* is more effective corrosion inhibitor for aluminium in acid medium.

Karim Samira *et al.*^[68] carried out biological investigations of medicinal plants *Heliotropium indicum* indigenous to Bangladesh. As a part of this, clot lysis, antimicrobial and membrane stabilizing potentials of ethanolic extracts of the leaves of *Heliotropium indicum* (*H. indicum*) was investigated. Crude ethanolic extracts of *H. indicum* leaves were extracted successively using solvents of different polarity range and determined qualitatively and quantitatively for the presence of different bioactive constituents/fractions which were assessed for their possible clot lysis, antimicrobial and membrane stabilizing activities as compared with the standard drugs. For the thrombolytic activity, the petroleum ether soluble fraction showed the highest percent of clot lysis (35.4%) among all fractions, while streptokinase and water resulted in 65.15% and 3.77% clot lysis, respectively. With respect to the membrane stabilizing activity, carbon tetrachloride fraction of *H. indicum* prohibited the hemolysis of erythrocytes brought about by osmotic induction (39.24%) or by heat (40.20%). The other fractions exhibited less membrane stabilizing effect. By contrast, acetyl salicylic acid resulted in 72.25% ± 0.30% inhibition of osmotically induced hemolysis and showed a lesser protection of heat induced hemolysis (42.56%). Crude ethanolic extracts were moderately sensitive against known pathogenic microbes. Flavonoid and tannin substances were detected and quantified.

Marian H. Villa *et al.*^[69] investigated antitussive and antibacterial activities of ethanol extract of *H. indicum* leaves and to elucidate the phytochemical components. The antitussive effect of the extract was evaluated in the citric acid saturated chamber in mice while antibacterial activity was evaluated using disc diffusion assay. Results showed 100% of extract syrup of *H. indicum* significantly recorded the lowest number of cough of 2.0 which statistically comparable with dextromethorphan. However, mice treated with 50% extract syrup had a mean cough number of 4.67. *H. indicum* ethanol extract also showed antibacterial activity against *K. pneumoniae* and *S. pyogenes* having zone of inhibitions of 9.55 mm and 9.81 mm, respectively. Air-dried leaves of this plant contain alkaloids, saponins, cardiac glycosides and terpenoids.

Ashwini Kumar *et al.*^[70] observed biosystematics of three species of Boraginaceae viz., of *Heliotropium indicum*, *Trichodesma indicum* and *Trichodesma zeylanicum*. All the three species showed a marked

difference in leaf and inflorescence morphology, stomatal behaviour, epidermal trichome, pollen grain characteristics and stem anatomy, hypodromous and brochidodromous venation of their leaves. The shape of leaves was landeolate to ovate. The inflorescence was pale blue to white. Length of inflorescence was found to be 4.0 to 6.5. The stomatal Index in these three species varied greatly. *T. indicum* and *T. zeylanicum* showed presence of anomocytic stomata with 16mm in length and 12mm width and Stomatal Index was 34.88 and 44.68 respectively. *Heliotropium indicum* exhibited anisocytic stomata which were 12mm long and 10mm wide. The Stomatal Index was 32.65. All the three species showed unicellular glandular hairs which differed in forms. All the three species showed tricolpate pollen grains, but varied in their form and size. All the three species showed more or less similar stem anatomical features with differences only in their hypodermal layers. Numerical analysis with reference to morphological, stomatal, pollen grains, trichomes, stem anatomy and stomatal index was carried out for 31 characters. It was found that *Heliotropium indicum* showed similarity with *Trichodesma indicum* in only eight characters and with *Trichodesma zeylanica* in only nine characters. *Trichodesma indicum* and *T.zeylanicum* showed resemblances in twenty two characters. On the basis of matching coefficient it was seen that *Heliotropium indicum* showed only 25.80% resemblance with *T. indicum*, and 29.03% with *T. zeylanicum*. *Trichodesma maindicum* and *T. zeylanicum* showed 70.96% resemblances, and therefore might be considered as same species of the genus *Trichodesma*.

Muhammad Khurm GHORI *et al.*^[71] carried out Phytochemical screening on genus *Heliotropium* and it revealed the presence of many bioactive components especially pyrrolizidine alkaloids, terpenoids and flavonoids. A large number of extracts and bioactive constituents of different species of genus *Heliotropium* showed significant biological activities such as antimicrobial, antitumor, antiviral, anti-inflammatory, wound healing, cytotoxicity and phytotoxicity. Different plants of genus *Heliotropium* were examined for pharmacognostic characters. This review throws light on various medicinal effects of the plants, isolation of a large number of secondary metabolites and important pharmacognostic characteristics of genus *Heliotropium*.

Aswini. R *et al.*^[72] carried out preliminary phytochemical screening and antibacterial activity of methanolic extracts of (leaf and stem) *Heliotropium Indicum* L. (Family: Boraginaceae). Preliminary phytochemical studies reveal presence of various phytochemicals like Alkaloids, Flavonoids, Phenols, Terpenoids, Steroids, Saponin and carbohydrates. Antibacterial activity against *Bacillus subtilis*, *Streptococcus mutants*, *Escherichia coli* and *Bacillus cereus*. and antimicrobial activity against *Escherichia coli* have been proved. Maximum clear zone of inhibition was found in *Escherichia coli* bacteria. This

plant leaf is essential for prevent the Human Breast cancer.

Md Nahid Akter *et al.*^[73] collected and documented data about the medicinal plants and formulations of a folk medicinal practitioner practicing in Ichapur village of Jessore district, Bangladesh. The practitioner used a total of 33 plants distributed into 26 families for treatment of a number of ailments, which includes menstrual problems, various types of pain, abscess, pus in ears, rickets, bleeding from external cuts and wounds, scrotum tumour, gastric and liver disorders, insomnia, sexual disorders, gastrointestinal tract disorders, jaundice, respiratory tract infections, skin disorders, urinary tract infections, helminthiasis, burning sensations in chest and hair loss.

CONCLUSION

This review throws light on complete study of *Heliotropium Indicum* along with research done on it. It shows the importance of *Heliotropium* species in various ailments although it is found as weed in some areas. Further research is necessary to get clear picture of active constituents responsible for the therapeutic activity of the drug.

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