

Phytochemical and pharmacological potential of *Heliotropium Indicum*: A Review

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Abstract: *Heliotropium indicum* Linn., commonly known as 'Indian heliotrope' is very common in India with a long antiquity of traditional medicinal uses in many countries in the world. It is herb with pale violet flowers belonging to the family Boraginaceae. . It is distributed in the tropical and temperate regions of the world and found throughout India .In folk medicine history, the plants of genus *Heliotropium* include treatments of inflammations, gout, rheumatism, skin diseases, menstrual disorder, and poisonous bites. Now the plant is reported to possess antibacterial, antitumor, uterine stimulant effect, antifertility, wound healing, anti-inflammatory, antinociceptive and diuretic activities. . A large number of extracts and bioactive constituents of different species of genus *Heliotropium* revealed significant biological activities .A few number of chemical investigations have been performed on this plant, as for example, pyrrolizidine alkaloids and other chemical compounds like Indicine-N-Oxide, Tannins, Saponins and Heliotrine were also isolated from this plant

Keywords: *Heliotropium indicum* Linn., Boraginaceae, antifertility, antinociceptive, pyrrolizidine alkaloids

1. Introduction

Natural products play a substantial role in the discovery of new therapeutic agents because of their immense availability in nature, lead to the identification of bioactive molecules which allow the growth of new pharmaceutical agents. In the recent years, because of increasing interest in the use of pharmaceuticals, natural substances are the major source of complementary or alternative medicines, which are used in the treatment of many diseases (1). In the recent years, because of increasing interest in the use of pharmaceuticals, natural substances are the major source of complementary or alternative medicines, which are used in the treatment of many diseases (1). From ancient times, plants are available to humans as a source of therapy. In the 19th century, due to the advancements in the field of pharmaceutical chemistry especially the medicinal chemistry more than 25% of drugs used in well developed countries are of plant origin and about 120 plant derived substances are used in modern system of medicines worldwide (2).

The name "*heliotrope*" originates from the old 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). The plant is an annual, erect, branched hirsute plant about 15 to 50 cm high.

The leaves are simple, alternate or sub-opposite, 4.5 to 10 cm/2.5 to 5 cm, ovate or ovate oblong, margin undulate, sparsely strigose along nerves on either side, serulate or undulate with cordate, minutely pilose beneath nerves and veins conspicuous on the lower side

along the petiole and about 3 to 8 cm long. *H. indicum* may flower throughout the year; the flowering season is very long and new flowers develop apically within the cyme while mature nutlets are already present at the base of the inflorescence. The flowers are white or violet coloured, regular, sessile, two ranked pentamerous, extra axillary. Sepals-5, 2.5 mm long, bristly with a few long hairs outside, free, 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 4-6.. The fruits are dry 2 to 4 lobed of 2 or 4 nearly free, more or less united nutlets, 4 to 5 mm long [7]. It is a common weed in waste places and settled areas, flowering the whole year round [7].

The whole plant is claimed to possess medicinal properties. Theleaves are used for the treatment of ophthalmic disorders, erysipelas and pharyngodynia [8,9].The roots are used as astringent, expectorant and febrifuge. The aqueous extract of leaves wasproved to be active against Schwart's leukaemia [10].Another species of this family, *Heliotropium zeylanicum* was reported to possess antidiabetic,antioxidant and antihyperlipidemic activities in STZ induced diabetic rats [11]. Other species of*Heliotropium* include *Heliotropium bacciferum*, *Heliotropium ovalifolium*, *Heliotropium pterocarpum* [12].The genus *Heliotropium* comprises about 250 species and is distributed in tropical, subtropicaland warm temperate zones of all continents, but only a few species have been systematically investigated [13].

Ethanopharmacology

The knowledge of traditional system of health care is widely threatened in the whole world due to revolutions in traditional philosophy (14). The native people of the area in which the plants occur, used 90% of natural products (15). Traditional and native knowledge of medicinal plants, still remain exist world widely (16). Due to the broad range importance of ethno-pharmacological flora, this review was arranged to collect ethno-medicinal knowledge about the different plants of genus *Heliotropium H. indicum* has been used in different traditional and folklore systems of medicine for curing various diseases.

Heliotropium indicum has been used in different traditional and folklore systems of medicine for curing various diseases.The traditional healers in Kancheepuram district of Tamil Nadu, India use *Heliotropium indicum* to cure skin diseases, poison bites,

stomachache and nervous disorders [17]. Whereas Malasar tribes of Coimbatore district of Tamil Nadu, use Leaf juice boiled with coconut oil to kill dandruff [18]. Different tribes of Cachar district, Assam, India use Root juice of *Heliotropium indicum* to cure ophthalmia and fresh leaf extract is applied externally in fresh cuts and wounds [19]. The leaf paste is applied externally to cure rheumatism in Rayal Seema in Andhra Pradesh, India and skin infection in Nicaragua. The decoction of both leaf and root together is also used for treating whooping cough in children in Eastern Nicaragua [17].

In some African countries, another ethnopharmacological survey reports that *H. indicum* is believed to be useful in treating malaria, abdominal pain and dermatitis. The highest number of usages (22%) was reported for the treatment of malaria (20). 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 females and administered rectally to treat local sores in the rectum (21) while in Phillipines and Senegal, used orally as diuretic and for the treatment of kidney stone (22,23).

In Thailand, the dried inflorescence is believed to produce permanent sterilization when taken orally in females. One gram of the dried and powdered inflorescence mixed with milk or water is used for three days beginning with the fourth day of menses to achieve the desired result. Other folk remedies include use of decoction of the leaves for treatment of fever, insect bites, stings, diarrhea, skin rashes, menstrual disorder and urticaria. The decoction of the leaves is also credited to be useful in curing insect stings (macerated with sugar cane juice), scorpion stings and as abortive in large dose and emmenagogue in small dose [13].

The decoction of both leaf and root together is also used for treating whooping cough in children in Eastern Nicaragua (24). In Amazon, the paste of both leaf and root together is applied externally in scorpion stings, bug bites (25) while the paste is recommended for treating sores and warts in Taiwan (26). In Malaysia, a paste made from the plant is applied to counteract putrefaction, to treat pyoderma 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 sprue. A decoction of the dried roots is drunk in the Philippines to promote menses, while the seeds are used to treat cholera, malaria, and for wound-healing (27).

Chemical constituents

Aerial parts contain pyrrolizidine alkaloids, indicine (Principal), echinitine, supinine, heleurine, heliotrine, lasiocarpine, its N-oxide, acetyl indicine, indicinine and antitumor alkaloid, indicine-N-oxide. The plant also contains rapone and lupeol and an ester of retronecine. Roots contain high amount of estradiol [28]. Helindicine, a new pyrrolizidine alkaloid together with the known lycopsamine were isolated from the roots of *Heliotropium indicum* [29]. Presence of cynoglossine, europine-N-oxide, heleurine-N-Oxide, heliotridine-N-Oxide, helectrine-N-Oxide (30) and heliotrine (31) have been identified from the seeds. The essential oil of *H. indicum*, extracted by hydrodistillation was analyzed by Gas chromatography (GC) and gas chromatography–mass spectrometry (GC-MS). Aldehydes (52.8%) occurred in the highest amount represented by phenylacetaldehyde (22.2%), (E)-2-nonenal (8.3%) and (E, Z)-2-nonadienal (6.1%), with a significant quantity of hexahydrofarnesylacetone (8.4%) [32]. In another experiment, the volatile oil isolated by hydrodistillation was analysed by a combination of GC–FID and GC–MS. The major constituents of the volatile oil were phytol (49.1%), 1-dodecanol (6.4%) and β -linalool (3.0%) [33].

Pharmacological potential

Different extracts of *Heliotropium indicum* have been studied for possible biological activities in various animal models and reported to possess significant antimicrobial, antifertility, antitumor, antituberculosis, anti-inflammatory, histogastroprotective, anti-cataract, analgesic and wound healing activities. These are described in detail in the following section.

The antitumor activity

The antitumor activity of different extracts showed significant activity in several experimental tumor systems. The active principle was isolated and found to be N-oxide of the alkaloid, indicine (34). Indicine-N-oxide has reached Phase 1 clinical trials in advanced cancer patients. In early clinical studies the possibility of using Indicine N-oxide for the treatment of leukemia and tumors was discussed (35). But severe toxic side-effects showed that a therapy with indicine-N-oxide was not justified (36,37). Most of the alkaloids are hepatotoxic and therefore internal use of *Heliotropium* species is not recommended (38).

Anti-inflammatory activity

The crude extract of the whole plant of *H. strigosum* and its subsequent solvent fractions showed anti-inflammatory activity in carrageenan-induced edema and xylene-induced ear edema. In carrageenan-induced edema, the ethyl acetate fraction was most dominant with 73.33% inhibition followed by hexane fraction (70.66%). When the extracts were tested against xylene-induced ear edema, ethyl acetate and hexane fractions were found active with 38.21% and 35.77% inhibition, respectively (39). The chloroform extract of dried leaves of *H. indicum* demonstrates significant anti-inflammatory activity in carrageenan-induced edema and cotton pellet granuloma models of inflammation. The extract of *H. indicum* with a concentration of 150mg/kg body weight showed maximum 80.0% inhibition on carrageenan-induced raw paw edema compared with the positive control drug, diclofenac sodium (40).

Antifertility activity

The petroleum ether extract of the entire plant is reported to possess significant antifertility activity when studied in rats [13]. In another experiment, the n-hexane and benzene fractions of the ethanol extract of *Heliotropium indicum* were studied for antifertility activity in rats using anti-implantation and abortifacient models. In-vitro sperm motility study was also performed using different concentrations of the extract. The study revealed that *Heliotropium indicum* possesses promising abortifacient activity and moderate effects on implantation and sperm motility [13].

The wound healing activity

The wound healing activity of different extracts of *H. indicum* has been reported. Results revealed significant promotion of wound healing of the alcoholic extracts (41,42). In another experiment, six TLC fractions *Sephadex LH-20*, eluent : Methanol-water (6:4) from n-butanol extract of *H. indicum* were evaluated for their *in vitro* wound healing activity on H292 human lung cells using incision wound models in cell culture. Results of the study revealed better wound healing activity (43).

Antituberculosis activity

The volatile oil from the aerial parts of *Heliotropium indicum* was isolated by hydrodistillation and analysed by a combination of gas chromatography (GC-FID) and gas chromatography-mass spectrometry (GC-MS). The major constituent of the volatile oil were phytol, 1-dodecanol and β - linalool and shows significant antituberculosis activity against *Mycobacterium tuberculosis* H37Ra in the Alamar blue assay system with an MIC of 20.8 μ g/ml [44].

Anti-plasmodial properties

Twelve plant species including *Heliotropium indicum* traditionally used in Benin for the treatment of malaria was evaluated in order to validate their use. The results showed that

extracts of *Heliotropium indicum* did not reveal any antiplasmodial activity in this study. As this plant is used for hyperthermias or colics, which are two symptoms of malaria, this could explain its use as adjuvant in mixture remedies [45].

Anticataract activity

The ethanolic leaf extract of *Heliotropium indicum* was found to be having anti cataract activity. The galactose induced rats were divided in to four groups of six animals each. Group I served as vehicle control received distilled water, group II received 30% Galactose diet served as cataract control and Group III and IV received 200 mg/kg of ethanolic leaf extract of *Heliotropium indicum* and Vitamin E 50 mg/kg respectively along with galactose diet. The results showed that, in the groups of *Heliotropium indicum* and vitamin E treated animals

there was significant increase in the lens glutathione, soluble protein and water content as compared to galactose control [46].

Conclusion

The medicinal importance of *H. indicum* is recognized worldwide and described in Indian, Brazilian, Thailand ,Malaysia, Amazon and African folk medicine. For medicinal uses, *H. indicum* is exclusively collected from the wild. The plants are generally collected when fully grown. The plant contains a large number of pyrrolizidine alkaloids. *Heliotropium* can be used for the treatment of various bacterial and fungal infections in modern medicine as it is proved from folk medicinal studies. In addition with anti-inflammatory, antiviral, antitumor, antidiabetic and antihyperlipidemic as well as gastroprotective activities also enhance the medicinal value of *Heliotropium* in future. The toxicity of this plant has not been well studied. *Heliotropium* alkaloids have been considered as potential agents in chemotherapy and clinical trials have been executed. However, the applications in cancer therapy are limited by the toxic effects, in particular the hepatotoxic effect of the pyrrolizidine alkaloids content. therefore internal use of *Heliotropium* species is not recommended. External application to promote wound healing as an anti-infective requires more research. Hence, it provides a wide area for research into the detail pharmacological actions of this drug which has not been explored much compared to its utility.

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