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## Pharmacological Activities of Indian Heliotrope (*Heliotropium Indicum* L.): A Review

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### Abstract

*Heliotropium indicum* Linn., commonly known as 'Indian heliotrope', is a herb with pale violet flowers belonging to the family Boraginaceae and is very common in India with a long history of traditional medicinal uses in many countries in the world. It is distributed in the tropical and temperate regions of the world and found throughout India. The plant is reported to possess antibacterial, antitumor, uterine stimulant effect, antifertility, wound healing, anti-inflammatory, antinociceptive and diuretic 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. This review gives an update mainly on the pharmacological activities of *Heliotropium indicum* Linn.

**Keywords:** *Heliotropium indicum* Linn, anti-cataract activity, anti-plasmodial activity, Pyrrolizidine alkaloids, Indicine.

### 1. Introduction

*Heliotropium indicum* Linn. (Family: Boraginaceae) (Fig.1) is derived from the Greek helios, for sun and trope, for turning, suggesting that the leaves and flowers turn towards the sun<sup>[1]</sup>, however, this is not the habit of this species.

The plant is an annual, erect, branched hirsute plant about 15 to 50 cm high. The leaves are always opposite or alternate, ovate to oblong-ovate, somewhat hairy, acute or acuminate, base decurren along the petiole and about 3 to 8 cm long. The flowers are calyx green and about 3.5 mm in diameter. The fruits are dry 2 to 4 lobed of 2 or 4 nearly free, more or less united nutlets, 4 to 5 mm long<sup>[2]</sup>. It is a common weed in waste places and settled areas, flowering the whole year round<sup>[2]</sup>. The whole plant is claimed to possess medicinal properties. The leaves are used for the treatment of ophthalmic disorders, erysipelas and pharyngodynia<sup>[3, 4]</sup>. The roots are used as astringent, expectorant and febrifuge. The aqueous extract of leaves was proved to be active against Schwartz's leukaemia<sup>[5]</sup>.

Another species of this family, *Heliotropium zeylanicum* was reported to possess antidiabetic, antioxidant and antihyperlipidemic activities in STZ induced diabetic rats<sup>[6]</sup>. Other species of *Heliotropium* include *Heliotropium bacciferum*, *Heliotropium ovalifolium*, *Heliotropium pterocarpum*<sup>[1]</sup>.

The genus *Heliotropium* comprises about 250 species and is distributed in tropical, subtropical and warm temperate zones of all continents, but only a few species have been systematically investigated<sup>[7]</sup>.



**Fig 1:** *Heliotropium Indicum* Linn

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## 2. Traditional and folk value

*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 [7]. Whereas Malasar tribes of Coimbatore district of Tamil Nadu, use Leaf juice boiled with coconut oil to kill dandruff [8]. 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 [9]. 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 [7]. In some African countries, Ethnopharmacological survey reports that *Heliotropium 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 [7]. The infusion of the flower is taken orally by females for the treatment of menorrhagia in Jamaica [7]. 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 [7].

### 2.1 Parts used

- Whole plant
- leaves
- flowers
- seeds and
- Roots

Plants are astringent, emollient, vulnerary and diuretic. Leaves are used for ringworm; juice is used in eye disease; decoction is used in fevers and urticaria. Roots are aphrodisiac; used for the cure of night blindness. Decoction of the roots is used in coughs and fevers. Seeds are stomachic. The flowers are considered emmenagogue in small doses and abortifacient in large doses. Aqueous and alcoholic extract of roots are oxytocic [10].

### 3. Chemical constituents

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 rapone and lupeol and an ester of retronecine. Roots contain high amount of estradiol [10]. Helindicine, a new pyrrolizidine alkaloid together with the known lycopsamine were isolated from the roots of *Heliotropium indicum* [11].

Presence of cynoglossine, europine-N-oxide, heleurine-N-Oxide, heliotridine-N-Oxide, heliotrine-N-Oxide and heliotrine have been identified from the seeds [7]. Other

alkaloids such as putrescine, spermidine, homo spermidine and spermine have been identified in the leaves. Apart from alkaloids, several triterpenes and steroids including  $\beta$ -amyrin, lupeol, chalinasterol,  $\beta$ -sitosterol, stigmasterol and campesterol have been reported from the entire plant. Other compounds reported from the entire plant include rapanone and hexacosan-1-ol [7]. It also yields an essential oil which consists mainly phytol (49.1%), 1-dodecanol (6.4%) and  $\beta$ -linalool (3.0%) [12].

## 4. Pharmacological actions

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.

### 4.1 Antimicrobial activity

The alcoholic extract of *Heliotropium indicum* was found to be having antimicrobial activity in a dose dependent manner (100  $\mu$ g/ml, 1 mg/ml, 50 mg/ml and 100 mg/ml) against all the test organisms. The test organisms *Bacillus subtilis*, *Bacillus pumilus*, *Staphylococcus aureus*, *Micrococcus glutamicus*, *Pseudomonas aeruginosa*, *Proteus vulgaris*, *Serratia marcescens* and *Escherichia coli* were used among the Gram positive and Gram negative bacteria. The fungi used were *Aspergillus niger*, *Aspergillus wentii* and *Rhizopus oryzae* while *Saccharomyces cerevisiae* and *Candida albicans* were among the yeast selected for testing the antimicrobial activity by agar cup plate diffusion method [13].

### 4.2 Antifertility activity

The petroleum ether extract of the entire plant is reported to possess significant antifertility activity when studied in rats [7]. 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 [7].

### 4.3 Anti-inflammatory activity

The anti-inflammatory effect of *Heliotropium indicum* leaf was found to possess significant in carrageenan-induced hind paw oedema and cotton pellet granuloma models of inflammation [14]. Chloroform extract of *Heliotropium indicum* was investigated for anti-inflammatory and antinociceptive activities in experimental animal's models. The extract (150mg/kg body weight) showed maximum inhibition (80.0%) and (82.79%) antinociception on carrageenan-induced raw paw oedema and hot plate model in male Swiss albino mice, respectively [15].

### 4.4 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  $\beta$ -linalool and shows significant antituberculosis activity against *Mycobacterium tuberculosis* H37Ra in the Alamar blue assay system with an MIC of 20.8  $\mu\text{g/ml}$  [12].

#### 4.5 Antitumor activity

The methanolic extracts of stem and leaf of *Heliotropium indicum* possessed a good amount of anticancer activity and IC<sub>50</sub> for both the extracts found to be 200 $\mu\text{g/ml}$ . whereas stem extracts exhibited excellent activity up to 64.5% at 200 $\mu\text{g/ml}$  and followed by leaf extract up to 49.67% at 200 $\mu\text{g/ml}$  [16]. The antitumor activity of different extracts of *Heliotropium indicum* showed significant activity in several experimental tumor systems. The active principle was isolated and found to be N-oxide of the alkaloid, indicine [7]. Indicine-N-oxide has reached Phase 1 clinical trials in advanced cancer patients [17]. But severe toxic side-effects showed that a therapy with indicine-N-oxide was not justified. Most of the alkaloids are hepatotoxic and therefore internal use of *Heliotropium* species is not recommended [7].

Ethanol extract of *Heliotropium indicum* showed significant anti-proliferative activity against SKBR3 human breast adenocarcinoma cell line using MIT assay [18].

#### 4.6 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 anti-plasmodial 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 [18].

#### 4.7 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 [19].

#### 4.8 Wound healing effect

Alcoholic extract of *Heliotropium indicum* was studied for wound healing properties in a rat model. Topical application of 10% w/v *Heliotropium indicum* increased the percentage of wound concentration and completed wound healing by the 14<sup>th</sup> day with increased tensile strength indicating rapid collagenization and. This study suggest that the extract of *Heliotropium indicum* possesses wound healing activity [20].

The *n*-butanol crude extract from *Heliotropium indicum* led to the isolation and identification of two alkaloids: Pestalamide B and Glycinamide, N-(1-oxooctadecyl) glyceryl-L-alanyl-glyceryl-L-histidyl. These compounds were isolated for

the first time from *H. indicum* and presented an excellent wound healing activity [21].

#### 4.9 Histo - Gastroprotective activity

*Heliotropium Indicum* is used locally in Nigeria to treat ailments such as ulcer and fever. The histo – gastroprotective activity of the aqueous extracts of the dried leaves of *Heliotropium indicum* was evaluated in Wistar rats, where ulceration of the gastric mucosa was induced via the oral administration of 80mg/kg/bodyweight of Indomethacin. Thus, the aqueous extracts of the dried leaves of *Heliotropium indicum* have dose dependent histo-gastroprotective effects. The histo-gastroprotective potential of the aqueous extract of the dried leaves of *Heliotropium indicum* against indomethacin-induced ulceration in rats might in part be due to its tannins, alkaloids and saponin constituents [22].

#### 4.10 Analgesic activity

The aqueous and ethanolic extracts of *Heliotropium indicum* (30-300mg/kg) dose-dependently inhibited both the first and second phases of the formalin-induced nociception. Oral doses of the aqueous extract (1-5g/kg) in imprint control region mice were well tolerated in acute toxicity studies; however, a 14-day oral administration of 1-2g/kg of the extracts in Sprague-Dawley rats produced pathologic effects on the heart, kidney, liver and lungs. Therefore, although the aqueous and ethanol extracts have analgesic activity, it could have a cumulative toxic effects hence prolonged and continuous use is not advised [23].

#### 5. Conclusion

It can be concluded that *Heliotropium indicum* is a potential source of many chemical constituents and widely used for many health problems. Several pyrrolizidine alkaloids have been isolated from this species. But most of the alkaloids are hepatotoxic and therefore internal use of *Heliotropium* species is not recommended. 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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