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Morphological characteristics and Phyto-pharmacological detailing of Hatishur (*Heliotropium indicum* Linn.): A concise review

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Abstract

Ethnomedicinal practices used in better health treatment system from ancient time. Phytomedicines are now an essential area of better treatment and high prospects in many nations. It is less expensive as well as has better cultural and societal recognition, has better feasibility with the human physiological system and has decidedly fewer side effects.

Heliotropium indicum Linn. (Family- Boraginaceae) an annual herbaceous medicinal weed and it is commonly known as Indian heliotrope. It is not only a common weed but also it is an important medicinal herb, too. These medicinal herbs are found in tropical and temperate parts of the world along with India, Bangladesh, and some other African countries. Extensive literature studies suggested that the various parts of the plant are reported to possess anti-microbial, anti-tumor, anti-tuberculosis, antiplasmodial, anti-cataract, anti-fertility, wound healing, anti-inflammatory, antinociceptive, analgesic and histo-gastro protective properties.

Many pyrrolizidine categories of alkaloids have been separated from this particular medicinal plant. Maximum alkaloids which are isolated from *Heliotropium indicum* are toxic effects and for that reason use of *Heliotropium indicum* in internal therapy is not recommended. External methods to cure wound healing and skin infections are less risky, still much more research study is needed.

The present review study deals with natural habitat, pharma phytochemical screening, botanical, taxonomical and other critical biological aspects of *Heliotropium indicum*. The main phytochemicals found in this plant are tannins and alkaloids. The present review may be helpful for identification and preparation of a clear monograph of *Heliotropium indicum*.

Keywords: *Heliotropium indicum*, phytochemicals, ethno medicine, alkaloids, medicinal weed

Introduction

The inflorescence of *Heliotropium indicum* turned their rows of flowers towards the sun. 'Helios' meaning in Greek languages is 'sun,' and the 'tropium' word comes from another Greek word 'tropein.' The meaning of this word is 'to turn' [1].

Heliotropium indicum Linn. (Fig. A) is comes under the family Boraginaceae. Maximum plants under in the family Boraginaceae are herbs. Many of the plants of this family Boraginaceae are used as garden plants, and few others are treated as weeds. The Bengali name of this plant species is Hatishur. The genus *Heliotropium* comprised approximately 250 plant species and distributed in tropical and temperate zones of different parts of the world [2].

Heliotropium indicum is termed as 'Indian heliotrope' is highly endemic in India and Bangladesh. It is also found in different parts of the world, especially in many African countries.

The plant is an annual, erect; ascending hirsute branched about 20 to 60 cm tall and coarse foetid herb. The leaves are opposite or sub-opposite, alternate or straight forward or sub-alternate, ovate to obovate, hairy, and acute, 5 to 10 cm long. Leaf margins undulate, nerves on either side, serrulate or cordate, or veins conspicuous beneath the leaves. The petiole is about 4 to 10 cm long. The flowers are green and approximately 5 mm in diameter. Flowers develop apically within the cymose, at maturity nutlets are present at the base of the inflorescence (cyme). Flowers are white or whitish violet, regular, sessile, axillary. Sepals-5, 3 mm long, diffused with hairs in outside, deep green, linear to lanceolate and uneven or unequal. Distributed branched, hirsute with hairs in the stem and the root is tap root and branch. The fruits are dry 2 to 4 lobed, with or without united nutlets, 3 to 6 mm long. It is an endemic weed in disturbed areas, garden or lawns, roadside, anthropogenic habitats or waste places and settled areas. It is found in sunny locations with around 800 m altitude. Throughout the year flowers are observed in this plant species.

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All the plant parts of these medicinal weed possess different pharmacological activities. The plant leaves highly used in an ethnomedicinal systems such as eye diseases, conjunctivitis, cataract, and pharyngodynia. The roots of *Heliotropium indicum* are used as astringent, expectorant, infusion and febrifuge. The water extract of leaves was showed activity against Schwart's leukemia [3, 4, 5, 6].

Taxonomic classification

Domain: Eukaryota
Kingdom: Plantae
Phylum: Spermatophyta
Subphylum: Angiospermae
Class: Dicotyledonae
Order: Boraginales
Family: Boraginaceae
Genus: *Heliotropium*
Species: *Heliotropium indicum*

Identification



Fig 1: Plant of *Heliotropium indicum*

Botanical name: *Heliotropium indicum* Linn.
Common name: Indian Heliotrope, Hatishur (Bengali) (Fig. 1)
Synonym: *Argusia indicum*, *Heliotropium parviflorum*, *Tiaridium indicum*

Botanical morphology



Fig 2: Natural Habitat of *Heliotropium indicum*

Habitat: It is an endemic hirsute medicinal weed in disturbed areas, garden or lawns, roadsides, anthropogenic habitats and waste places (Fig. 2). It is found in approximately 1000 m altitude.



Fig 3: Stem, Leaves, and Inflorescences

Growth: An annual coarse foetid herbaceous plant with erect, branched growth form upto 60 cm long. Slightly woody at the base of the plant (Fig. 3).



Fig 4: Leaves

Foliage: Leaves (Fig. 4) are 4-10 cm long and 2-5 cm wide, opposite or sub-opposite, alternate or sub-alternate, ovate to obovate, and acute, with a wavy or undulate, serrulate or cordate leaf margin, nerves on either side or veins conspicuous beneath the leaves. The leaf surface is covered in short hairs which may be quite stiff. The leaf blade extends down the length of the petiole. Distinctly petiolate, petioles 5 cm tall with a sub-truncate base or ovate.



Fig 5: Inflorescence & Flowers

Flowers: Flowers (4-5 mm wide) are regular, sessile, axillary, slightly purple or white or whitish violet (lilac) with a small yellow center and having a narrow tube with lobes formed a plate shape. The thin cyme inflorescence (Fig. 5) is similar as a string or twisted of beads with a prominent curl at the apex. The flowers (Fig. 5) are green and approximately 5 mm in diameter. Flowers develop apically within the cymose inflorescence, tip coiled; at maturity of the flower, nutlets are

there at the base of the inflorescence. Flowers arranged at one side of cyme inflorescences. Sepals number is five, 3 mm long, diffused with hairs in outside, deep green, linear to lanceolate and uneven or unequal. Calyx lobes ciliate, 3 mm long; Stamens are five and borne in a corolla tube, terminal, corolla-tube 4-6 mm long; petals rounded. The ovary is 4-lobed.



Fig 6: Seeds

Fruits: The fruits (Fig. 6) are known as nutlets. Fruits are dry, indehiscent 2 to 4 lobed, 3 to 6 mm long, with or without united nutlets, ovate, ribbed separated into two nutlets, each nutlet is two-celled and beaked.



Fig 7: Stem & Root

Stem and Roots

Wide distributed, branched or unbranched, hirsute with hairs in the stem and the root (Fig. 7) system is long tap root, and it is highly branched [3, 4, 5, 6, 7].

Genetics

Chromosome number of *Heliotropium indicum* Linn. is $2n=22, 24$.

Traditional Uses

Heliotropium indicum is used in ethnomedicine for giving protection to human from many diseases from ancient time. The different ethno pharmacological report suggested the uses of *Heliotropium indicum* in a different mode of studies. In Kancheepuram district of Tamil Nadu, India tribal communities use *Heliotropium indicum* to heal skin infections, poisonous animal bites, stomach problems and nervous diseases⁸. Malasar tribal communities of Tamil Nadu,

using leaves sap in hot water with coconut oil to protect dandruff⁹. At Cachhar district of Assam in India use root sap to treat eye disease, and fresh leaf paste is applied externally to cure wounds¹⁰. Leaf extract is used externally to prevent rheumatoid arthritis in southern parts of India¹¹.

Many countries in Africa use *Heliotropium indicum* to cure several serious diseases. It is used to treat inflammation and tumors. It is also used to treat malaria, abdominal and skin diseases. 22% of *Heliotropium indicum* extracts were used for the treatment of malaria and it was reported¹². In Jamaica, infusion of the whole plant parts is used for fever, vein disease, stomach infections and to cure a cold and cough. The plant is used externally in the vaginal cavity to induce abortion in pregnant women. Women take a decoction of the flowers for the treatment of menorrhagia¹³. In Philippines and Senegal, the plant parts are used as a diuretic and to protect kidney stone^[14, 15].

In Rodrigues, the infusion of the whole plant is used for curing herpes, and the paste of plant parts is used for cleansing and dressing of wounds and ulcers. This infusion is applied externally to the body parts. The juice of the bark is used orally by women for curing dysmenorrhea^[16]. The warm aqueous decoction of the flower and buds is taken orally by the women as an emmenagogue in a small dose and abortive in an extensive treatment in West Indies^[17]. In Thailand, the dried inflorescence is chosen to do permanent sterilization when taken orally in case of women. The dehydrated and powdered inflorescence mixed with milk or water and is used taken orally at the time of menses to get the desired result^[18].

Extract of the leaves is used to treat the fever, poisonous animal bites (taken with sugarcane juice), diarrhea, dyspepsia, skin infections, menstrual dysfunction and ulcers^[19, 20]. In Gabon, the powdered leaves are applied to cure gum infections. In Tanzania, root extract is administered orally treat some several diseases. In Madagascar and Mauritius, plant decoction is used as a diuretic and is in kidney diseases. In the Gambia, the whole plant parts are applied by women to make false hair. The infusion of leaves and roots together is also used for curing whooping cough in children in Nicaragua and leaf extract is applied to cure skin diseases^[21, 22]. In Amazon, the sup of leaf and root is used externally in animal stings and bites^[23]. The paste is advised to treat sores and warts in Taiwan and allied countries^[24].

In Malaysia, Myanmar, Philippines, and Indonesia, the plant parts extract are used to protect putrefaction, to cure pyoderma, to treat gonorrhoea, mouth diseases and ringworm infection. The infusion of the dried and powdered roots parts is taken orally in the Philippines to promote menses and seeds are applied to cure cholera, malaria, and for healing injuries^[25].

Phytochemical Constituents

The whole plant of *Heliotropium indicum* Linn. contains various phytochemicals. Among them, pyrrolizidine alkaloids are most important. Pyrrolizidine alkaloids are a common constituent of a diverse genus of *Boraginaceae* family. They exhibit high toxicity on liver and lungs. Cytotoxicity and other mutagenic and carcinogenic properties have also been reported in different studies. The plant grown under greenhouse conditions showed the highest content of alkaloids at the beginning of the flowering period. The young leaves, seedlings, and inflorescences showed high alkaloid levels, and with aging, the concentration of alkaloids decreased 20% in the leaves. The highest alkaloid content was found in the roots and inflorescence, and these also had the

highest relative amounts of N-oxide, ranging from 60–90% of the total alkaloid content. No significant age-dependent differences in N-oxides were found. The active principle was found to be Indicine-N-oxide which has been synthesized efficiently. Indicine N-oxide has reached Phase I clinical trials in advanced cancer patients.

Additionally, pyrrolizidine alkaloids are excreted in milk, and the use by lactating mothers is a toxicity hazard to babies. Different researchers in many research investigations have characterized various pyrrolizidine alkaloids, and most of them showed hepatotoxic activity. The identified alkaloids are included heliotrine, lasiocarpine, indicine, 12-acetyl indicine, indicating, indicine-N-oxide, retronecine, tracheal-thamide, quinidine, echinate, heleurine, lasiocarpine-N-oxide, quinidine, putrescine, spermine, spermidine and lindelofidine [26, 27, 28, 29, 30, 31, 32].

NMR and HREIMS studied the structures of the essential alkaloids. Helindicine and lycopsamine alkaloids were observed with moderate antioxidant property [33].

Hydro distillation extracts produced the essential oil of *Heliotropium indicum* and analyzed by gas chromatography (GC) and gas chromatography-mass spectrometry (GC-MS). Aldehydes (52.8%) happened in the highest amount, and it was phenyl acetaldehyde (22.2%), (E)-2-nonenal (8.3%) and (E, Z)-2-nonadienal (6.1%), with a significant quantity of hexahydro farnesyl acetone (8.4%). In another experiment, the volatile oil was isolated by hydro distillation and analyzed by a combination of GC-FID and GC-MS. The nitrogen-containing lipid fraction contained C₁₆, and C₁₈ acids esterify with 1-cyano-2-hydroxymethylprop-1-en-3-ol [34].

Ghosh *et al.* (2018) investigated the plant pigments of *Heliotropium indicum* along with other medicinal herbs. Research investigation showed that highest amount of chlorophyll-a and total chlorophyll concentration and second highest amount of total carotenoids was found in this herbs among the other experimental herbaceous plants [35]. Though another study showed that plant pigments (chlorophyll-a, chlorophyll-b, total chlorophyll and total carotenoids) might fluctuate with the various environmental factors like air pollution [36]. In another research study, it was concluded that this plant pigments concentration varies with different season also [37].

Different Parts of the Plant contains various phytoconstituents. These are as follows:

Aerial Parts

Aerial parts of the plants contain pyrrolizidine alkaloids, indicine, echinitine, supinine, heleurine, heliotrine, lasiocarpine, acetyl indicine, indicine, and indicine-n-oxide. The plant also possesses rapone and lupeol and an ester of retronecine [22-28].

Root

Roots contain a high amount of estradiol. Joao Sammy N. Souza *et al.*, 2005, isolated a new pyrrolizidine alkaloid with unusual structural features helindicine, together with the known lycopsamine, from the roots [33, 38].

Seeds

Presence of cynoglossine, europine-N-oxide, heleurine-N-Oxide, heliotridine-N-Oxide, heleotrine-N-Oxide and heliotrine have been identified from the seeds. Seeds contain heliotrine as major chemical constituents. The seeds contain 12% oil and 1.8% nitrogen [39, 40].

Leaves

Aqueous leaf extracts of *Heliotropium indicum* from seedlings contains phenolic compounds. The alkaloids trachelanthamidine and retronecine and the pyrrolizidine precursor amines (in leaves and inflorescence) putrescine, spermidine and spermine were isolated and identified in the leaves [41].

Total Plant

Apart from alkaloids, several triterpenes and steroids including β -amyrin, lupeol, chalinasterol, β -sitosterol, stigmasterol and campesterol, hexacosane-1-ol, an ester of retronecine have been reported from the whole plant. Other compounds reported from the entire plant parts include rapanone and hexacosane-1-ol [27, 42, 43, 44]. The major constituents of the essential or volatile oil were phytol (49.1%), 1-dodecanol (6.4%) and β -linalool (3.0%) [45]. The main bioactive compounds found in the different extracts of *Heliotropium indicum* are tannins and alkaloids [46].

Pharmacological property

Various solvent extracts of *Heliotropium indicum* have been investigated, and it showed different bioactivities in animal models and reported to possess anti-oxidant, wound healing, anti-tussive, anti-bacterial, anti-fertility, anti-tumor, anti-hyperglycemic, anti-tuberculosis, anti-inflammatory, histogastro protective, anti-ulcer, anti-cataract, analgesic and anti-pyretic properties. These properties are described as follows.

Anti-oxidant Property

From research investigation, it is found that ethanolic extract of *Heliotropium indicum* exhibits significant reducing power and free radical scavenging activity. It showed anti-oxidant activity by inhibiting DPPH and hydrogen peroxide radicals. This activity is higher in DPPH and lowers in hydrogen peroxide [47].

Wound Healing Property

Alcoholic extract of *Heliotropium indicum* showed wound healing activities in an animal model. Research investigation concluded that alcoholic extract possesses wound healing activity in the *n*-butanol crude extract and from this extract, two alkaloids Pestalamide B and Glycinamide, N-(1-oxooctadecyl) glycyl-Lalanyl-glycyl-L-histidyl were isolated and identified. These two bioactive compounds are responsible for wound healing. In research study petroleum ether, chloroform, methanol, and aqueous extracts were used to evaluate for their wound healing activity in an animal model. The results showed that a significant increase in wound healing with both methanolic and water extracts in comparison with other extracts in this study. Promising increase in the granulation tissue weight, hydroxyl proline content, and increased activity of SOD and catalase percentage in the methanolic extract in dead space wound model. The study validates its ethnomedicinal uses [48, 49, 50, 51].

Anti-cataract Property

Ethanol extract of leaves of the plant was showed the anti-cataract property. The galactose-induced rats were used for the study. The research investigation showed that *Heliotropium indicum* and vitamin E treated rats were responded to positively in the experiment. A significant increase in the lens glutathione, soluble protein, and water content was found in the study [52].

Anti-inflammatory Property

The anti-inflammatory and antinociceptive activities of the plant were showed significantly high in carrageenan-induced hind paw edema and cotton pellet granuloma inflammation models in chloroform leaf extract in an animal model. In another study, various extracts of *Heliotropium indicum* has been reported significant anti-inflammatory activity in acute and sub-acute models of inflammation [53, 54, 55].

Analgesic Property

In a research investigation, the significant analgesic property was found in ethanolic and water extracts. A 14-day orally administered of 1-2g/kg of the ethanolic extract in Sprague-Dawley animals produced pathological effects on the different organs such as the heart, kidney, liver, and lungs. Though ethanolic and water extracts have shown analgesic property, still it could have cumulative toxicity in the prolonged period, continuous and abrupt use is not recommended [56].

Diuretic Property

In an experiment methanolic extract of the dried roots of the plant showed significant diuretic activity in animals. The extract has resulted in substantial writhing inhibition in acetic acid-induced writhing in experimental mice. The diuretic effects were revealed by the electrolyte loss ratio (Na^+/K^+ excretion ratio was 1.38 and 1.45 at the doses of 200 and 400 mg/kg respectively) as that of the standard diuretic furosemide (1.37) which was applied in the said experiment [57, 58].

Anti-bacterial and Anti-fungal Property

Heliotropium indicum was showed significant anti-microbial properties in a dose-dependent way against different such as *Staphylococcus aureus*, *Bacillus subtilis*, *Bacillus pumilus*, *Pseudomonas aeruginosa*, *Micrococcus glutamicus*, *Serratia marcescens*, *Escherichia coli* and *Proteus vulgaris* alcoholic extracts. In the experiment fungi used were *Rhizopus oryzae*, *Aspergillus niger* and *Aspergillus wentii*. And yeast like *Saccharomyces cerevisiae* and *Candida albicans* were selected in this research study to do test the anti-microbial effects by agar cup-plate diffusion method. In another research study the anti-fungal property of the water crude extract of leaves was tested against *Fusarium oxysporum*, and anti-bacterial effects of methanolic extract were tested against, *Klebsiella* spp., *Pseudomonas mirabilis*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Bacillus subtilis* and *Escherichia coli*. The aerial parts of the plant have shown activity against *Staphylococcus aureus*, *Staphylococcus pyogenes*, *Staphylococcus pneumoniae*, *Klebsiella pneumoniae*, *Escherichia coli* and *Shigella dysenteriae* strains on methanolic extracts [3, 59, 60, 61, 62].

Anti-plasmodial Property

Heliotropium indicum is ethnomedicinally used for curing malaria. In an experimental study, the plant extract has not shown any effects on malaria diseases directly. Though the plant is used for hyperthermia or colics, which are two significant symptoms of malaria, this could explain its remedial use measure for malaria. So the research study showed indirect anti-plasmodial activity [63].

Anti-tuberculosis Property

From the aerial parts of the plant volatile oil was isolated by hydro distillation method and characterized by a combination of GC and GC-MS. The principal constituent of the volatile oil was phytol, 1-dodecanol, and beta-linalool and which

showed prominent anti-tuberculosis activity against *Mycobacterium tuberculosis* H37Ra in the Alamar blue assay system. The study showed noticeable anti-tuberculosis effects with a MIC of 20.8 $\mu\text{g/ml}$ [45].

Anti-tumor Property

The methanolic extract of aerial parts of the plant contains a significant level of the anti-cancer property. Various extracts of *Heliotropium indicum* resulted in substantial effects in many tumor systems in the laboratory. Most of the alkaloids which were identified from the plant are hepatotoxic, and therefore internal use is not recommended to date. Ethanol extract showed anti-proliferative property against human breast adenocarcinoma cell line using MTT assay in the research study [32, 44, 63, 64, 65, 66, 67, 68, 69, 70].

Anti-fertility Property

Heliotropium indicum ethnomedicinally used for anti-fertility properties. The petroleum ether extract of the different plant parts showed evident anti-fertility effects in the animal model. In another research investigation, n-hexane and benzene fractions of the ethanolic extract of the plant parts showed anti-fertility effects when used in anti-implantation and abortifacient models in animals. In-vitro sperm motility investigations were also done in various concentrations of the extracts. The research study showed that the plant parts have significant abortifacient property and moderate activity on implantation and sperm motility [44, 71, 72].

Anti-ulcer Property

Ethanolic extract of *Heliotropium indicum* leaves and root were investigated for its anti-ulcer effects against pylorus ligation induced gastric ulcer in animals. The research study showed that a prominent decrease in gastric volume, free acidity, total acidity, and ulcer index. The said experiment concluded that the plant extract has anti-ulcer effects in an animal against the drug-induced gastric ulcer [73].

The anti-ulcer properties of the water extracts of the powdered leaves of the plant parts in indomethacin-induced gastric ulcerated mucosa have been observed. The study concluded that a common morphological feature of the various portions of the mucosa layer pointed out the water extract has gastro-protective property. The water and ethanolic extracts of the roots has significant uterine stimulant effect in animal models. The plant is traditionally used in Nigeria to cure ulcer and fever. The anti-ulcer impacts of the water extracts of the powdered leaves were investigated in animals. The study showed that water extract of the powdered leaves of has dose-dependent prominent gastro-protective property. The gastro-protective activity of the water extract of the powdered leaves demonstrated against indomethacin-induced ulceration in animals might be due to plants essential phytochemicals such as tannins, alkaloids and saponin [74, 75, 76, 77].

Relaxant / Receptor Property

95% Ethanolic extract of the roots of *Heliotropium indicum* showed weak, smooth muscle relaxant effects on guinea pig ileum and rabbit duodenum. A research investigation was done to observe the receptors that possibly mediate the effects on smooth muscles. The activity of different concentrations of agonist drugs and a water extract from the plant were investigated on isolated guinea-pig ileum, rabbit jejunum, and rat uterus and anococcygeus [77].

The extract showed dose-dependent effects to the acetylcholine, methylcholine, carbamylcholine, nicotine,

histamine, and oxytocin used on the smooth muscle preparations in the said experiment. The extract was prominently stable to plasma cholinesterase. The receptor activity of the plant parts suggests its ethnomedicinal uses like abdominal pain relief, hypertension, impotence and sexual obstructions [78].

Anti-anaphylactic Property

In a research study, Ashoka MS and Shashidhar CS, 2011 showed anti-anaphylactic activity on leaves extract of *Heliotropium indicum*.

Anti-tussive Property

Heliotropium indicum is used for anti-tussive property in a traditional system of medicine. In a research study, the anti-tussive activity was observed in ethanolic extract of leaves of the plant. The anti-tussive properties of the ethanolic extract were investigated in animals in the citric acid saturated chamber. The study showed that 100% of ethanolic extract syrup recorded the lowest number of cough of 2.0 which statistically comparable with dextromethorphan. However, animals treated with 50% extract syrup had a mean cough number of 4.67. This observation concludes that *Heliotropium indicum* has significant anti-tussive properties [79].

Toxicity Studies

Research investigation showed that the methanolic extract of the dried and powdered roots of *Heliotropium indicum* has cytotoxic effects in the animal model. The methanolic extract has shown significant writhing inhibition in acetic acid-induced writhing in experimental animals. The crude methanolic root extract resulted in the most prominent cytotoxic activity against brine shrimp *Artemia salina* (LC50 = 47.86 µg/ml and LC90 = 75.85 µg/ml) [57].

The Acute Toxicity studies performed as per the accepted protocol of OECD guidelines in animals. The study was aimed at proving the therapeutic index, *i.e.*, the ratio between the pharmacologically effective dose (ED) and the lethal dose (LD). The plant parts contain various alkaloids. These are hepatotoxic, and for that reason, internal uses are not permitted. But these compounds are used for cancer treatment and clinical trials. Toxicity studies are not done entirely for this plant [44, 80].

Conclusion

Heliotropium indicum Linn. has the vast potential for botanical, phytochemical, pharmacological and nutritional properties. From the above review study and explanation, it is observable that *Heliotropium indicum* Linn. has been used as an crucial phytomedicinal source for many diseases in various parts of the world, as it is briefly discussed in the review article. The review showed the different ethnomedicinal uses, biological, taxonomical and other important biological or biochemical aspects of *Heliotropium indicum* Linn. As the toxicity studies not appropriately done yet, detailed pharmacological research is needed for this plant as its ethnomedicinal utility is enormous throughout the world [44, 80]. The review found the loop holes or lacunae for future work also.

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Conflict of Interest

The author declares no conflict of interest.

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