



Review Article

AN UNEXPLORED DRUG MAMAJJAKA (*ENICOSTEMMA LITTORALE* BLUME)-A DRUG REVIEW

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ABSTRACT

Traditional medicinal system of India consist variety of natural herbs which are playing significant role in human health. Among them *Enicostemma littorale* Blume is one the herbaceous plant of the Gentianaceae family. The bitter nature plant help in curing fever, act as a laxative, useful in skin disorders, rheumatism, snake bite, abdominal disorders, diabetes, obesity and in many more diseases. The plant used in folklore since long time in many diseases. The plant constituents having antimicrobial, antioxidant, antiulcer, anti-inflammatory, hypolipidemic, hypoglycaemic, hepatoprotective and antitumor activity. This review consists of detail description along with its literature review, ethnobotanical uses, phytochemical, pharmacological properties, and toxicological study of *Enicostemma littorale* Blume. The methodology adopted in this review is using Ayurvedic literature and modern scientific research-based publications including journal and periodicals. This review provide base for future research work in different aspect in the field of drug research.

INTRODUCTION

Ayurveda uses the innate power of herbal medicine to bring out wonderful results on the human body. Ayurvedic herbs are natural and safe for human life. The use of different parts of the herbs in traditional medicinal system viz., *Ayurveda*, *Siddha* and *Unani* etc. treat various disease is in vogue for several centuries. Medicinal plants act as alternative source for treating several ailments since their use increase day by day [1]. According to World Health Organization (WHO) herbal medicine serve the health need of about 80% of world's population, especially for millions of people in the vast rural area of developing countries[2]. The plant *Enicostemma littorale* Blume is one among them and it plays a vital role in human healthcare. *Enicostemma littorale* Blume, commonly known as *Chhota Chirayata* in Hindi or *Mamejua* in Gujarati, and

Nagajihva or *Mamajjaka* in Ayurveda, is a perennial herb of Gentianaceae family with sessile lanceolate leaves. It is found distributed common in coastal areas around Gujarat and surrounding state.

AIM AND OBJECTIVE

To review the phytochemical and pharmacological properties of *Mamajjaka* (*Enicostemma littorale* Blume).

MATERIAL AND METHOD

The methodology adopted in this review is using Ayurvedic literature and modern scientific research-based publications including journal and periodicals.

DISCUSSION

Detail Description of Plant

A perennial glabrous herb 10-50cm high, branched from the base, stem erect or procumbent, sub quadrangular or subterete, glabrous. Leaves are sessile, variable, 3.2-6.3cm by 3-16mm, linear or linear to oblong or elliptic-oblong or lanceolate, obtuse or acute, glabrous, 3-nerved, the midnerve is strong and the marginal nerves often obscure. Flowers are sessile, arrange in axillary clusters all along the stem. Calyx 3mm long, lobes 1.5mm long, ovate-oblong, obtuse,

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with narrow membranous margins. Corolla white in colour, 6-8mm long, tubular, lobes 2.5mm long, lanceolate, acute. Capsule 4mm long, ellipsoid, slightly narrowed at the base, rounded at the apex, apiculate with the remains of the style^[3] (fig 1.).

Taxonomy



Fig. 1. *Enicostemma littorale* Blume

Kingdom: Plantae
 Subdivision: Angiospermae
 Class: Dicotyledonae
 Subclass: Gamopetalae
 Series: Bicarpellatae
 Order: Gentianales
 Family: Gentianaceae
 Genus: *Enicostemma*
 Species: *Littorale*

Natural Habitat

The crop grows well in areas having 700-800mm rainfall with warm climate, temperature ranging 25-35°C during summer months and in winter season, temperature should be in between 2-5°C. States of Gujarat, Maharashtra, Rajasthan, and Madhya Pradesh are suitable for its cultivation. However, it can

also be grown in some other state of country like Andhra Pradesh, Karnataka and Tamil Nadu having similar climatic conditions^[4].

Vernacular names

There are various names of *Mamajjaka* (*Enicostemma littorale*) is mentioned in text as follow: Ayurvedic medical: *Mamejava*, *Mamejav*, *Mamejavo*, *Mamjjak*, *Mamejva*; Hindi/Hindustani: *Kariyatu*, *Chota-kirayat*, *Chota-chiretta*, *Chota-chirayata*; Bombay: *Kada-vinayi*, *Manucha*; Tamil: *Vallari*; Telugu: *Nela-guli*, *Nela-gulimidi*; English name is Indian Whitehead is a common name that applies to *Enicostemma littorale* Blume^[5].

Ethnobotanical uses

Enicostemma littorale Blume plays very crucial role in human healthcare. This drug is traditionally used in India as the plant parts such as leaves and roots were used in traditional practice for treating several diseases like malaria, skin diseases, diabetes, leprosy, stomachic, bitter tonic, laxative, carminative^[6], arthritis, back pain^[7], to reduce fever and as a "tonic" for appetite loss^[8]. The plant is locally used in Tamil Nadu for its medicinal properties, such as Anti-inflammatory, antiulcer activity^[9], hypoglycaemic^[10]. The plant is traditionally used in condition like abdominal ulcers, rheumatism, hernia, itches, insect poisoning and swelling^[11]

Literature review

Mamajjaka (*Enicostemma littorale* Blume) has not been mentioned in the Vedic texts. There is no description in *Brihatrayi* and *Laghutrayi* either. The plant has first been described in *Shodhal Nighantu* in the 12th century. The description of the plant as described in the Ayurvedic literature is presented in below table.

Table 1: Various properties of plants mentioned in classics and modern literature books

Ayurvedic texts / Nighantu	Properties & Action
<i>Shodhal Nighantu</i> ^[12]	<ul style="list-style-type: none"> ➤ Synonyms like <i>Nahi</i>, <i>Nagjihva</i>, <i>Tiktapatra</i> is mentioned. ➤ Used in <i>Ksharkarma</i>
<i>Shaligram Nighantu</i> ^[13]	<ul style="list-style-type: none"> ➤ <i>Katu & Tikta rasa</i>, used in <i>Vataroga</i>, <i>Jwara</i>, <i>Ksharkarma</i>
<i>Bhavprakash Nighantu</i> ^[14]	<ul style="list-style-type: none"> ➤ Antipyretic and anti-helminthic ➤ Substitute of <i>Swertia Chirayata</i>
<i>Nighantu Adarsh</i> ^[15]	<ul style="list-style-type: none"> ➤ Juice of leaves with <i>Piper Nigrum</i> for fever ➤ Powder with buttermilk for malarial fever ➤ Anti-helminthic and antidiarrheal
<i>Priya Nighantu</i> ^[16]	<ul style="list-style-type: none"> ➤ <i>Tikta rasa</i>, <i>Kapha-pitta samak</i> ➤ Used in <i>Madhumeha</i>, <i>Kustha</i>, <i>Vishamjvara</i>

<i>Vanoushadhi Chandrodaya</i> [17]	<ul style="list-style-type: none"> ➤ <i>Katu</i> and <i>Tikta</i> in taste ➤ Antipyretic, anti-helminthic and used in <i>Vata</i> disorders
The Wealth of India [18]	<ul style="list-style-type: none"> ➤ Paste of whole herb mixed with sesame oil is applied externally in skin disorders. ➤ Plant is also used in case of snake bite.
API [19]	<ul style="list-style-type: none"> ➤ <i>Tikta rasa, Laghu & Ruksha guna, Katu vipak, Ushna virya.</i> ➤ Dose – 1-3 gm of powder, Formulation – <i>Vayucchaya Surendra taila.</i>
Quality standard of Indian medicinal plants-ICMR [20]	<ul style="list-style-type: none"> ➤ Macroscopic, microscopic description of plant along with powder microscopy is described. ➤ Quality standard like Ash value, foreign matter, water soluble extractive, ethanol soluble extractive, TLC is mentioned.
Review on Indian medicinal plants -ICMR [21]	<ul style="list-style-type: none"> ➤ Therapeutic uses, properties, Ethnobotanical uses, pharmacognosy of different parts of plant, chemical study, pharmacological studies are mentioned.

Phytoconstituents

This plant comprises of different chemical compounds. Many compounds have been isolated from the drug, *Enicostemma littorale* Blume. The aerial part of the plant gave 34% of dry alcoholic extract and 15.7% of ash [22]. Natarajan and Prasad reported the presence of five alkaloids, two sterols and volatile oil. Betulin, a triterpene saponin was also isolated by earlier workers [23]. Monoterpene alkaloids like enicoflavin, gentiocrucine and seven different flavonoids were found present in the alcoholic extract and the structures were identified as apigenin, genkwanin, isovitexin, swertisin, saponarin, 5-o glucosylswertisin and 5-o glucosylisoswertisin were also isolated by Goshal *et al* [24]. The presence of catechins, saponins, steroids, saponin, triterpenoids, flavonoids and xanthenes and a new flavone C-glucoside named as Verticillside was isolated for the first time in this species [25]. Swertiamarin active compound was isolated from *E. littorale* by using alcoholic extract [26]. Six phenolic acids like vanillic acid, syringic acid, p-hydroxy benzoic acid, protocatechuic acid, p-coumaric acid and ferulic acid were also found [27]. Methanol extract of *E. littorale* was found to be containing different aminoacids like L-glutamic acid, tryptophan, alanine, serine, aspartic acid, L-proline, L-tyrosine, threonine, phenyl alanine, L-histidine monohydrochloride, methionine, iso leucine, Larginine monohydrochloride, DOPA, L-Glycine, 2-amino butyric acid and valine [28]. Swertiamarin is a main active chemical constituent of many crude drugs, which are marketed in Japan and other countries and these crude drugs are normally evaluated by their high swertiamarin content [29].

Pharmacological properties

Table 2: Various pharmacological properties proved in experimental studies

Activity	Material	Methodology	Result
Antimicrobial activity [30]	Chloroform extract	Disc diffusion	Pronounced effect against aspergillus niger and negligible effect against candida albicans at concentration of 100, 200µg/ml.
Antimicrobial activity [31]	Methanolic, ethyl acetate extract	Disc diffusion	Potent antibacterial activity against Staphylococcus aureus, Pseudomonas aeruginosa, Salmonella typhi and Shigella sonnei & antifungal activity against Aeromonas hydrophila and Candida albicans.
Anthelmintic activity [32]	Petroleum ether and ethanolic extract	Adult Indian earthworm, Pheretima posthuma	Five different concentrations of each extract were used in this test, result indicated that ethanolic extract was more potent than the petroleum ether extract.
Antinociceptive activity [33]	Swertiamarin	Hot plate method	Significant increase in the latency period was observed with treatment of swertiamarin at 100

		<i>Tail</i> withdrawal method	and 200 mg/kg body weight after 30 and 45 min. Significant increase in the tail withdrawal reflex was observed with swertiamarin treatment at both the doses with percent protections of 150 and 200, respectively. In both these methods, swertiamarin showed significant activity than standard paracetamol.
Antioxidant activity [34]	Methanolic extract	Gentamycin induced nephrotoxicity in rats	Treatment with <i>Enicostemma littorale</i> Blume shows antioxidant defense mechanism of mitochondrial as well as postmitochondrial fraction, with better improvement seen in mitochondrial fraction. <i>Enicostemma littorale</i> Blume extract was used in antioxidant therapy to counteract mitochondrial and post-mitochondrial oxidative stress generated in kidney due to gentamicin treatment, thus prevented nephrotoxicity.
Antiulcer and anti-inflammatory activity [35]	Methanolic extract	Aspirin, ethanol, pyloric ligation induced ulcer in rats	In the pyloric ligation model of ulcers, the volume of gastric secretion, acidity and pH were estimated, and the ulcer index, tissue GSH levels and lipid peroxidation levels in all the models of ulcers. Prior treatment with the aqueous extract of <i>Enicostemma littorale</i> Blume showed a significant decrease in the ulcer index against aspirin, ethanol challenge and pyloric ligation. The extract also reduces the total acidity, free acidity, volume of gastric secretion and elevated the gastric pH.
Antitumor activity [36]	Methanolic extract	Dalton's ascitic lymphoma in Swiss albino mice	Methanolic extract of <i>Enicostemma littorale</i> Blume increase the peritoneal cell counts. Tumour cell growth was found to be inhibited when animal was to be underwent intraperitoneal inoculation with DAL cells, After 14 days of inoculation, methanolic extract is able to reverse the changes in the haematological parameters, protein and PCV consequent to tumour inoculation.
Hepatoprotective activity [37]	Ethanollic extract	CCL ₄ induced liver injury in albino wistar male rats	After giving <i>Enicostemma littorale</i> Blume extract the hepatic marker such as aspartate transaminase and alanine transaminase, alkaline phosphatase, acid phosphatase, total bilirubin, total protein and albumin in serum were also restored to normal level in comparison to respective controls.
Antihyperlipidemic activity [38]	Aqueous extract	Cholesterol fad rat model	Hypercholesterolaemic diet and aqueous extract of <i>Enicostemma littorale</i> Blume given to rats (1.5g/100g body weight/day) for 6 weeks. The treatment with this extract decreases the activities of erythrocyte CAT, SOD and LPO levels and

			reduced the level of glutathione levels, liver and kidney cholesterol when compared to cholesterol fed untreated rats.
Hypoglycaemic activity ^[39]	Aqueous extract	Alloxan induced diabetic rat model	Treating diabetic rats with oral administration of aqueous <i>Encostemma littorale</i> Blume whole plant extract daily for 45 days significantly decreases the blood glucose, TBARS, SOD, CAT and GPx. The effectiveness of extract was compared with standard drug insulin. It was observed that an administration of insulin (6 units/kg) to alloxan induced diabetic rats for 45 days brought back all the parameters to near normal status. <i>Encostemma littorale</i> Blume extract at the dose of 2 g/kg was more effective.
Diabetic neuropathy activity ^[40]	Plant extract	Alloxan induced diabetic neuropathy	Extract of <i>Encostemma littorale</i> was given to the rats for 45 days. The changes in lipid peroxidation and antioxidant enzymes like SOD, GPx and CAT levels, decrease in Na-K+ ATPase activity was also restored with extract treatment. This study provides experimental evidence for the preventive effect of <i>Encostemma littorale</i> Blume on nerve function and oxidative stress in animal model of diabetic neuropathy.

Toxicity Profile

The toxicity profile of Swertiamarin active component has also been reported by using acute and sub chronic toxicity studies. In the acute toxicity study, different oral doses of Swertiamarin (5–2000mg/kg) was given to the rats. The results showed that Swertiamarin did not produce any significant toxicity, behavioural responses, physiological changes, physical observations (skin, fur, eye mucous membrane, behaviour patterns, tremors, salivation and diarrhoea of the rats) or mortality in the investigated groups when compared to the controls, as observed during acute toxicity experimental study of 15 days. There were no changes in weight seen in the animals. In the sub chronic toxicity test, the rats were free of intoxicating signs and physical changes even when the highest dose of Swertiamarin (500mg/kg) was used throughout the drug dosing period of 50 days. Additionally, no mortality was observed throughout the experimental period of toxicity study^[41].

CONCLUSION

Encostemma littorale Blume is one of the herbaceous medicinal plants. The plant is difficult to propagate because of poor seed-germination though its mass cultivation through conventional as well as tissue culture techniques is in demand. The plant has immense potential to cure various diseases and

disorders present in society. In present time, scientific proof regarding the medicinal benefits of *Encostemma littorale* Blume, should be the objective of further research. This review helps researcher to develop further preclinical, clinical research work on *Encostemma littorale* Blume.

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