IAMJ

INTERNATIONAL AYURVEDIC MEDICAL JOURNAL

Review Article ISSN: 2320-5091 Impact Factor: 6.719

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

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https://doi.org/10.46607/iamj12p9032025

(Published Online: March 2025)

Article Received: 11/02/2024 - **Peer Reviewed:** 28/02/2025 - **Accepted for Publication:** 13/03/2025.

ABSTRACT

Mamajjaka(Enicostemma littorale Blume), a perennial herb, holds a significant place in Ayurveda, known for its "*Pramehaghna*" (Antidiabetic) properties and its ability to balance *pitta* and *kapha doshas*. This traditionally used for various ailments, including rheumatism, skin diseases, abdominal disorders, and fever. Studies have shown that *Enicostemma littorale* can reduce blood glucose and serum insulin levels in diabetic patients. The plant has been reported to enhance glucose-induced insulin release from pancreatic islets, potentially through a K(+)-ATP channel-dependent pathway. Beyond its antidiabetic effects, Enicostemma littorale exhibits antioxidants, anti-inflammatory, and antihyperlipidemic properties. Studies have identified various phytochemicals, including swertiamarin, apigenin, and isovitexin, which may contribute to its antidiabetic activity. Enicostemma littorale is generally considered low toxicity, with studies indicating that it does not produce significant toxicity in rats. Studies have shown that heavy metals in Enicostemma littorale are below the WHO/FDA permissible limits. Clinical trials have shown the safety and antidiabetic activity of Enicostemma littorale in diabetic and prediabetic patients. The plant has been used in folklore for a long time in many diseases. In this review, the study methodology adopted used Ayurvedic literature and modern scientific research-based publications, including online databases, journals and periodicals. This review provides a basis for future research work in different aspects of the field of drug research in Ayurveda.

Keywords: Antidiabetic, *Mamajjaka*, Enicostemma littorale Blume

INTRODUCTION

Aushadha (Drug) is considered the second most crucial part of *Pāda Chatushtaya* after *Bhishag* (Physician)[1]. Āyurvedic literature contains an infinite number of herbs. The action of these drugs has been explained based on the theory of *Rasa*, *Guna*, *Veerya*, *Vipaka* and *Prabhava*. The drug should be suitable for the patient and against the disease and *Doṣha* involved. The right choice of drug for a particular disease plays a vital role in the treatment. The review of the drug *Mamajjaka*(Enicostemma littorale Blume) as an antidiabetic was done with the help of various texts and research studies. The ingredient poses hypoglycemic activities. This drug is easily available, economically affordable and has a high degree of clinical effects mentioned there in against diabetic people. *Mamajjaka* is the drug which contains all the properties of an ideal drug described by *Charakacharya*. Drugs that will be used in *Chikitsa* must have properties opposite to the vitiated *Dosha* taking part in the disease process, which applies to Madhumeha Chikitsa.

AIM AND OBJECTIVE

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

MATERIAL AND METHOD

This review study adopted a methodology based on Ayurvedic literature as well as modern scientific research-based publications, including online databases, journals, and periodicals.

DISCUSSION

MĀMAJJAKA[2]

- **Latin name** - *Enicostemma littorale Blume.*
- **Family** - Gentianaceae
- **English name** - White head
- **Sanskrit name** - *Mamajjaka*, *Nahi*, *Nāgajihva*, Tiktapatra, *Kṛmihṛta*, *Kṣārakarma*, *Kṣitaukṣapa* etc.
- **Synonyms- Hindi:** *Kaḍavi Nāyi*, *Chota Kirāyta*

Gujrathi: *Māmejvo*
Tamil: *Vallari*, *Vellārugu*
Malyalam: *Vellāruka*, *Vallari*.
Telugu: *Cevvu-kurti*
Kannada: *Karibandita*, *Sogade*

Distribution and Propagation:

It is common in coastal areas and is found throughout India at elevations up to 450 meters. Seeds naturally propagate it in waste places.

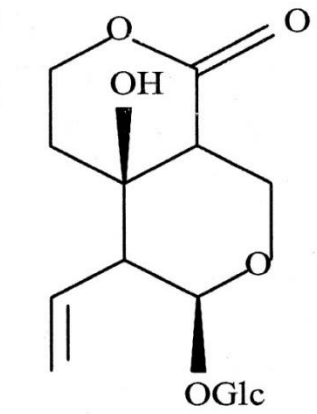
Description:

A procumbent annual herb up to 50 cm in height from a thick root stack, stems and branches are quadrangular; leaves simple, opposite, sessile, linear, linear-oblong or elliptic- lanceolate, glabrous, 3-nerved, marginal nerves often obscure; flowers white, tubular, in whorled axillary clusters; Fruits ellipsoid, capsules narrowed at the base and rounded at the apex with the remains of the style. Flowering – fruiting August to December.

Chemical composition:

The whole plant contains:

I. A bitter glycoside,
II. Ophelic acid,
III. Swertiamarine(bitter principle),
IV. Charatin
V. Tannins
VI. Two alkaloids: one gentianine and others not confirmed.



Structure of Swertimarin

Properties action:

- *Rasa*: Tikta
- *Guna*: *Laghu,* Ruksha
- *Virya*: *Ushna*
- *Vipaka*: *Katu*
- *Karma*: *Kapha-Pitta Shamaka*

Properties:

The Plant is bitter, Stimulant, Thermogenic, Digestive, Carminative, Stomachic, Laxative, antihelmintic, Anti-inflammatory, Liver tonic, urinary astringent, depurative, revulsive and anti-periodic.

Therapeutic use[3]:

Indicated in *Vishama jwara, Atisara, Krimi, Madhumeha*. *Deepana, Amapachaka, Krimighna, Kushtaghna, Raktaprasadana*.

It is the best medicine for the *Prameha,* especially in *Sthula Madhumeha*(Obese Diabetic), due to its *Tikta Rasa* and *Laghu, Ruksha Guna*.

It is also used in *Kushta*(Skin disease) Patients, as the *Kushta* is *Santarpaṇottha Vyadhi*. Due to the Amapachana effect, it can be used in *Jwara* (Fever) cases.

Dose: 1-5 gm

Useful part: *Panchanga*

Mode of Action (*Āyurvedic* view):

In *Āyurveda*, the pathogenesis of *Prameha* is closely related to *Sleshma* and *Kleda*.[4] In *Samprapti* (pathogenesis) of *Prameha*, there is *Jatharagni mandya* and *Dhatwagnimandya*. Due to this *Agnimandya*, there is a provocation of *Kleda* and *Dhatu Shaithilya* observed. The action of *Tikta Rasa* (Swertiamarine) is *Kaphamāṁsameda-Lekhana, Mukha Shodhana - Rochana, Kushta- Kandughna, Trishna -Daha-Shamana, Mutra-Kleda-Śoṣanam*.[5] *Mamajjaka* with its *Tikta Rasa, Ushna Virya, Katu Vipaka,* and *Laghu, Ruksha Guna* reduce the *Kapha. Kleda, Mutra, etc., in patients of Prameha,* and thus it reduces symptoms like polyuria (*Probhoota Mutrata*). The *Ruksha, Ushna Guna* and *Tikta Rasa* of *Mamajjaka* cause *Ama Pachana, Agnidepana and Kleda Shoshana* and thus help in *Samprapti Vighatana (*breakdown of Pathogenesis*) of Prameha,* especially *Sthula Madhumeha (*Type-2 DM)

Pharmacology (Modern view):

The chemical composition of *Mamajjaka* shows the presence of bitter principle-*swertiamarine,* along with alkaloids like gentianine. This acting principle may be potentiating the glucose-dependent insulin release from pancreas β-cells, which possibly reflects one of the factors responsible for the decreased blood sugar level.[6]

IN VITRO- STUDY OF THE DRUG:

1) Oral administration of the *E.Littorale* extract for 45 days increased hexokinase activity. It decreased the activity of the Glucose 6-phosphate and fructose 1,6-bisphosphatase significantly in the serum, liver and kidney of diabetic rats. The extract lowered the concentration of thiobarbituric acid reactive substances and lipid hydroperoxidase significantly in the brain and increased it significantly in the heart in diabetic rats. *E. Littorale* administration increased the concentration of reduced glutathione and glutathione peroxidase activity in diabetic rats. The activities of

superoxide dismutase and catalase were increased significantly by *E.littorale* treatment in diabetic rats.[7]

2) The aqueous extract of Enicostemma littorale was tested for its hypoglycemic activity on normoglycemic, hyperglycemic and alloxan-induced diabetic rats. In the short experiment, blood sugar lowering activity was not observed in normoglycemic and glucose-loaded hyperglycemic rats. But in the case of diabetic rats, the fall of blood sugar after 30 days of treatment with the aqueous extract was found to be significant ($p<0.001$). The decrease in plasma glucose level was accompanied by GHb and glucose-6, phosphate activity in the liver.[8]

3) The antidiabetic activity of Enicostemma littorale (*Mamajjaka*) leaf extracts was investigated in Streptozotocin-induced diabetic albino rats. A comparison was made between the action of different extracts of Enicostemma littorale (*Mamajjaka*) and the known antidiabetic drug glibenclamide (600 µg/kg b. wt.) E. littorale aqueous extract (ELAE) and ethanolic extract (ELEE) showed significant antidiabetic activity. In Streptozotocin -induced model, blood glucose levels of these extracts on 7th day of the study were 132.00±4.955 mg/dl (ELAE) and 163.3±28.69 mg/dl (ELEE) in comparison of chloroform extract (210.8±14.91 mg/dl). These extracts also prevented body weight loss in diabetic rats. ELAE and ELEE showed potent antidiabetic effects in Streptozotocin-induced diabetic rats. The drug has the potential to act as an antidiabetic drug.[9]

OTHER STUDIES[10]:

1. Antimicrobial activity of *E. littorale*[11]:

Tanna *et al.* . reported the antifungal activity of E. littorale blume. The chloroform extract shows pronounced activity against *Aspergillus niger* (*A. niger*) and negligible activity against *Candida albicans*(*C. albicans*) at the concentration of 100, 200 µg/mL. The ethyl acetate extract shows slight activity against *A. niger* and moderate activity against C. *albicans*. The ethanol extract shows pronounced activity against *A. niger* and *C. albicans.*

2. **Antihelminthic activity of *E. littorale*[12]:**

Mishra and Shukla reported that *E. littorale* exhibits antihelminthic effects. Petroleum ether and ethanolic extracts of aerial parts of *E. littorale Blume* were prepared and evaluated separately for finding an antihelminthic effect on adult Indian earthworm, *Pheretima posthuma*

3. Antihyperlipidemic activity of *E. littorale*[13]:

A new study demonstrates a new property of swertiamarin as a potent lipid-lowering agent when compared to arraying, and it may also contribute cardioprotective and antiatherosclerotic effects. The swertiamarin and atorvastatin, when orally fed, also lowered the total serum cholesterol and triglycerides.

4. Antinociceptive effect of *E. littorale*[14]:

Swertiamarin is being used to relieve pain. Iridoids present in a wide variety of medicinal plants possess a large number of medicinal properties. In the study by Jaishree V., the in vivo antinociceptive activity of swertiamarin isolated from E. axillary was carried out using three different methods in mice. The results proved that swertiamarin from E. axillary possesses both peripheral and central antinociceptive activity.

5. Antioxidant activity of *E. littorale*[15]:

Clinically, the usage of aminoglycosidic antibiotics was limited since they induce nephrotoxicity. Oxidative stress is the main reason for this complication. Mukundray *et al.* investigated the role of *E. littorale* Blume as a promising antioxidant therapy in gentamicin-induced nephrotoxicity in rats.

6. Antiulcer and anti-inflammatory activity of *E. littorale*[16]:

The aerial parts of *E. littorale* against aspirin, ethanol and pyloric ligation-induced ulcers in rats and bovine serum albumin (BSA) denaturation were examined for antiulcer and anti-inflammatory effects by Roy *et al.* It was reported that the methanolic extract of E. littorale possesses antiulcer activity. Its anti-inflammatory activity may be attributed to its antioxidant potential.

7. Antitumour activity of *E. littorale*[17]:

The antitumour activity of methanolic extract of *E. littorale* has been evaluated against Dalton's ascitic lymphoma (DAL) in Swiss albino mice by Kavima-

ni *et al.* A significant enhancement of mean survival time of methanolic extract of *E. littorale* treated tumour bearing mice was found with respect to control group.

8. Hepatoprotective activity of *E. littorale*[18]:

The study by Gite *et al.* revealed that the extract reduced all the elevated biochemical parameters since it has hepatotoxin detoxication properties. *E. littorale* possesses a chemical compound called swertiamarin, which has antioxidant and hepatoprotective properties against D-GalN-induced hepatotoxicity given at 100 and 200 mg/kg body weight orally for 8 days, which might be due to its *in vitro* antioxidant activity.

9. Hepatomodulatory activity of *E. littorale*[19]:

The hepatomodulatory response of ethanol extract of *E. littorale Blume* was examined for oxidative stress-induced liver injury by carbon tetrachloride (CCl_4) in albino wistar male rats. Gupta *et al.* suggested that hepatomodulation by *E. littorale Blume* against oxidative stress is mediated through interference with free radical generation and reduction in fat metabolism

10. Antihyperinsulinemic activity of *E. littorale*[20]:

Insulin resistance is responsible for the development of hyperglycemia in NIIDM patients. Aqueous extracts of *Aegle marmelos* and *E. littorale* reduce hyperglycaemic conditions in diabetic animals. Administration of aqueous extracts of *A. marmelos* and *E. littorale* for 15 days prevented hyperglycemia and hyperinsulinemia induced by a diet high in fructose.

11. Diabetic neuropathy activity of *E. littorale*[21]:

Poor glycemic control and oxidative stress are among the main reasons for the development of diabetic neuropathy. The protective effects of *E. littorale Blume* were investigated for hypoglycemic and antioxidant effects in alloxan-induced diabetic neuropathy in male Charles foster rats by Bhatt *et. al.*

This study provides experimental evidence for the preventive effect of E. littorale on nerve function and oxidative stress in an animal model of diabetic neuropathy. Hence, *E. littorale* may be clinically tried to treat diabetic neuropathy.

12. *E. littorale* as a new target for islet neogenesis[22]:

Gupta *et al.* . highlighted an islet neogenic property of one herbal plant, *E. littorale* Blume. An active herbal compound SGL-1 was isolated and purified from the extract of E. littorale and used to differentiate two model stem cell lines PANC-1 and NIH3T3, which showed tremendous islet neogenic potential and significant islet yield compared to the control serum-free medium.

This preliminary data does offer the exciting possibility of an alternative source for increasing islet mass that can be used to treat diabetic patients.

13. Nutritional information of *E. littorale:*

A daily intake of 2 g of *E. littorale* fresh leaves is recommended for diabetic patients since it is highly nutritious.[23]

The nutritional analysis report of the Indian Council of Medical Research suggests that 100 g of fresh *E. littorale* contains 140 kcal energy, 7 g of protein, 0.7 g of fat, 26.5 g of carbohydrate, 4.2 g of fibre, 8.4 g of minerals, 49.9 mg of iron, 1.641 mg of calcium, and 81 mg of phosphorous[24]

CONCLUSION

*Mamajjaka(*Enicostemma littorale Blume) is a relatively uncommon plant described in Ayurveda. *Mamajjaka*(Enicostemma littorale Blume), used by Ayurvedic physicians for a long time as an ingredient of medicinal preparations for the treatment of diabetes, obesity, liver disorders, acid peptic disorders, skin disorders and fever, showed its immense therapeutic value. *Mamajjaka* (Enicostemma littorale Blume) contains a number of active phytoconstituent but out of them Swertiamarin is major one. Previous pharmacological studies showed *that Mamajjaka* (Enicostemma littorale Blume) exhibit a potent hypoglycemic, antihyperinsulinemic, islet neurogenerative, antidiabetic, antihyperlipidemic, antioxidant, antiulcer, anti-inflammatory, antitumor, hepatoprotective, hepatomodulatory, antifungal, antibacterial, antihelminthic and antinociceptive effect in different experimental animal models. Apart from Swertiamarin, most of the other bioactive ingredients are unex-

plored, and there is only limited knowledge of the mechanisms of action of bioactive compounds present in *Mamajjaka*(Enicostemma littorale Blume). Scientific proof regarding the medicinal benefits of *Mamajjaka*(Enicostemma littorale Blume) should be the objective of further research. This review helps the researcher to develop further preclinical and clinical research work on *Mamajjaka*(Enicostemma littorale Blume).

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Source of Support: Nil
Conflict of Interest: None Declared

How to cite this URL: Amit Nampalliwar: As an Antidiabetic Drug Mamajjaka (Enicostemma Littorale Blume) - A Drug Review. International Ayurvedic Medical Journal {online} 2025 {cited March 2025}