Phytochemical and pharmacological review on *Enicostemma axillare* linn. (Gentianaceae)

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**ABSTRACT**

The review presents the scientific information on pharmacological, phytochemical and traditional uses of the plant *Enicostemma axillare* linn. (Gentianaceae). This review reports the phytoconstituent isolated from whole plant. A comprehensive assessment of the biological activities of different extracts is included and possible mechanisms and Phytochemicals involved have been correlated. The plant *Enicostemma axillare* is perennial herb found throughout India. It is indigenous medicine in the treatment of fever, as a bitter tonic and forms one of ingredient of many hypoglycemic marketed formulations. Folk medicine uses includes as in typhoid fever, as cooling agent, as stomachic, as laxative, as blood purifier, in dropsy, rheumatism, hernia, swelling and in insect poisoning. Plant extract reported to have antioxidant, antimicrobial, anti-inflammatory, anti-epileptic, hepatoprotective, hypcholesterolimic, antinoiciceptive and antiedematogenic activities. It is reported to contain alkaloids, cardiac glycosides, tannins, flavonoids, saponins sterols, terpenoids etc. Swertiamarin is a secoiridiods isolated from ethyl acetate extract.

**Key words:** *Enicostemma axillare*, folk medicine, Phytochemicals, Pharmacological activities.

**INTRODUCTION**

In India, we have a rich heritage of plant based health care systems like Ayurveda, Unani and Siddha which have high degree of social acceptance, as they provide quality health care a large segment of our population. According to NMPB (National Medicinal plants Board) has highlighted that 6000 plants are used in the folk and documented system of medicine. In India *Enicostemma axillare* linn. is commonly known as *Katvinaye* and in Sanskrit it is known as *Mamajjakah*. It is a perennial herb, 50cm inch in height found throughout the greater part of India. It is very bitter plant and used in indigenous medicines in the treatment of fever and as a bitter tonic [17]. It also used as a substitute for chirata. It is used in folk medicine in typhoid fever, as cooling agent, as a stomachic, as a laxative, as a blood purifier, in dropsy, rheumatism, hernia, swelling and in insect poisoning [11]. In ethanomedicine it is used for snake bite. The availability of complete standardized data of herbal plant for manufacturing herbal formulation is very difficult task but such type of review articles overcome this type of problem to some extent. The present review article provides detail information regarding phytochemical and pharmacological activities of *Enicostemma axillare* and this will definitely in future helpful for formulation of ayurvedic dosage form using plant extract.

**TAXONOMICAL STUDY** [1, 18]

- Kingdom- Plantae
- Division- Magnoliophyta
- Class- Magnoliopsida
- Order- Rubiales
- Genus – *Enicostemma*
- Species- *Axillare*

**PHYTOCHEMICAL INVESTIGATION:**

1. The preliminary phytochemical screening of various extracts of *Enicostemma axillare* linn. Showed the presence of alkaloids in chloroform extract, fats and oils in petroleum ether and chloroform extract, tannins and phenols in methanol and water extract, saponins, flavonoids and carbohydrates in methanol and water extracts. Proteins and amino acids were present in chloroform, methanol and water extracts. [5, 6, 7]

2. Methanolic extract of *Enicostemma axillare* is a rich source of vitamin C and vitamin E. [11]

3. In phytochemical study of different parts of *Enicostemma axillare* of plants showed presence of cardiac glycosides in leaf and root, reducing sugar higher in leaf, steroids comparatively higher in leaf and flower, high levels of terpenoids seen in flower, maximum quantity of alkaloids found in leaves. When we compare the above results, it is quite interesting to note that flavonoids, alkaloids and saponins are comparatively less in whole plant. [8]

4. By using Atomic Absorption Spectroscopy showed that presence of 0.38% of organic matter, Sodium 0.53%, Potassium 0.41%, Iron 0.37% inorganic elements are found in *Enicostemma axillare* linn. [12]

5. Swertiamarin is a secoiridiods glycosides was found to contain a major constituents of the extract isolated from *Enicostemma axillare* linn.[3, 6, 7]

**PHARMACOLOGICAL ACTIVITIES:**

1. **In vitro Antioxidant Activity:**

   Four successive extracts(Pet.ether,Chloroform,ethyl acetate and Methanol) of whole plant of *Enicostemma axillare* showed invitro antioxidant activity, which were examined using nine different methods. In the 2, 2’-azino-bis (3-ethylbenzo-thiazoline-6-sulfonic acid) diammonium salt (ABTS) method, all the four extracts shows potent antioxidant activity with IC$_{50}$ values ranging from 13.26 to 24.36 µg/ml. The chloroform extract in water, Nitric acid and hydroxyl radical using deoxyribose and lipid peroxidation showed potent antioxidant activity with IC$_{50}$ values of 16.99±0.38, 60.66±0.30, 25.06±0.12 and 94.66±2.40 µg/ml respectively. Potent activity was also observed for the Pet. Ether extract with the H$_2$O$_2$, and Nitric oxide method. All the extract showed moderate total antioxidant capacity using phosphomolybdenum method. [19]
2. Antimicrobial and Antioxidant activity:

Invitro antimicrobial activity (well diffusion method) of aqueous, hydroalcoholic, Methanolic, chloroform and ethyl acetate extracts of leaves of *Enicostemma axillare* plant has been evaluated by using six bacterial species and some fungi such as *Staphylococcus aureus, Bacillus subtilis, Proteus vulgaris, Escherichia coli, Pseudomonas aerogenosa, Shigella sonni, Aspergillus niger and Candida albicans* observed that chloroform, ethyl acetate and hydroalcoholic extract showed prominent antimicrobial activity with highest zone of inhibition against all microorganisms.

Invitro antioxidant activity of each extract except ethyl acetate by Nitric oxide and DPPH method shows antioxidant activity following sequence: Methanol > Hydroalcohol > Aqueous > Chloroform.[9]

3. Hypocholesterolemic and Antioxidant activity:

The plant consists of flavonoids and phenolic compounds which exert cardiovascular benefits. The 85% Methanolic extract of plant *Enicostemma axillare* showed hypocholesterolemic effect in fructose induced hyperlipidemic animals. The dose of *Enicostemma axillare* (150mg/kg) decreased the level of cholesterol, Triglycerides, LDL and VLDL and increased HDL level. The extract might be inhibitors of HMG CO reductase by 3 fold. Due to rich source of vitamin C, vitamin E and tannins inhibits the formation of OX-LDL. Hence this extract displays antioxidant activity by increasing activity of enzymatic antioxidant like GP, and catalase and non-enzymatic antioxidant like GSH. Hence *Enicostemma axillare* is rich source of phytoconstituent which are used as potent hypocholesterolemic and antioxidant agent in pharmaceutical industry.[3]

4. Antioxidant and Hepatoprotective Activity:

Swertiamarin isolated from *Enicostemma axillare* of successive ethyl acetate extract showed antioxidant and Hepatoprotective effect against D-galactosamine induced acute liver damage in rats. The dose of Swertiamarin (100-200mg/kg BW) interaperitontially against D-galactosamine which induced liver injury is used. The dose caused significant restoration of all the altered biochemical parameters i.e. elevation of antioxidant enzymes catalase, superoxide dismutase and glutathione and decreased level of MDA in serum liver and kidney to become normal. The potent dose 100 and 200 mg/kg for 8 days showed Hepatoprotective activity due to Invitro antioxidant property.[9]

5. Antiedematogenic and Free Radical Scavenging Activity:

Swertiamarin from ethyl acetate extract shows antiedematogenic activity using Carrageenan-formalin and Histamine–induced Paw edema methods in rats. In this method, edema inhibition obtained after 5hr. Induction were 38.60%, 52.50% and 45.44% for 100mg/kg, 200mg/kg BW Swertiamarin. The 100mg/kg Diclofenac sodium used as standard.

It also shows Invitro antioxidant activity using seven different methods. Out of which good activity observed in ABTS (2.83 µg/ml, IC50), Hydrogen peroxide methods (5.70 µg/ml, IC50) moderate activity in hydroxyl radical by deoxyribose (52.56 µg/ml, IC50) and lipid peroxidation methods (78.33 µg/ml, IC50) respectively.

Hence total antioxidant capacity was found to be 4.51mM of ascorbic acid per gram of Swertiamarin.[9]

6. Invitro anti-inflammatory activity

Methanolic extract (ME) of whole plant *Enicostemma axillare* (EA) was evaluated for anti-inflammatory activity by albumin denaturation assay; proteinase inhibitory activity at different concentrations. Aspirin, Diclofenac and Indomethacin were used as standard drugs. The result shows EA ME at conc. range of 100-500 µg/ml significantly (p<0.01) protects the heat induced protein denaturation.

At the concentration 400 and 500 µg/ml EA ME showed significant (p<0.01) inhibition of 42 and 53% of proteinase inhibitory action. At the concentra-

tion of 100 and 200 µg/ml did not show significant (p>0.05) activity. Heat induced haemolysis of erythrocyte was significantly (p<0.05) inhibited at conc.400 and 500 µg/ml. Hypotonicity induced haemolysis and lipooxygenase activity were significantly (p<0.01) inhibited at concentration range 200,500 µg/ml and 400,500 µg/ml respectively.

It indicated Methanolic extract of *Enicostemma axillare* can be potential source of anti-inflammatory agent.[20]

7. Antinociceptive activity

Swertiamarin is used to relive pain. Three different methods in mice, for in vivo antinociceptive activity were carried. In the hot plate method a significant increase in latency period was observed at 100mg/kg and 200mg/kg BW of Swertiamarin after 30 and 45 min.

The percent protection observed after 45 min. was 109.42 (100mg/kg bw) 147.42(200mg/kg bw) and 157.14 (standard Paracetamol). In second method increases in the tail withdrawal reflex was observed in which Swertiamarin gave percent protection 150(100mg/kg) and 200 (200mg/kg). In third method, acetic acid induced writhing Swertiamarin at 200mg/kg BW showed potent and both peripheral and central antinociceptive activity than that of Paracetamol.[9]

8. Anti epileptic activity

In the present study, initially acute toxicity studies were carried out. The aqueous and chloroform extract of *Enicostemma axillare* were not toxic up to the recommended dose 2000mg/kg body weight orally as per OECD guidelines. The antiepileptic activity by maxima electroshock (MES) and pentyleneetetrazole (PTZ) induced seizures in albino wistar rats shows onset of myoclonic spasm and clonic convulsion were delayed in test group of dose 200 and 400 mg/kg bw of aqueous and chloroform extract. Anticonvulsant activity observed against MES and PTZ animal models. The percent protection of chloroform extract 200mg and 400mg dose in MES 82.43%, 83.04%, respectively in PTZ induced convulsion 200mg and 400mg respectively. It is better than Hydroalcoholic extract in MES induced 200mg(2.75%) and 400mg(70.93%) and PTZ induced 200mg(70.02%) and 400mg(71.58%) respectively.[14]

9. Antibacterial activity

The organic solvent extract of enicostemma axillare by disk diffusion and broth dilution technique shows antibacterial activity against gram positive bacterial strains. Results revealed that methanol extract of enicostemma axillare showed activity against B.subtilis and were not bactericidal at 100mg/ml (MBC). [21]

CONCLUSION:

The extensive literature survey review that *Enicostemma axillare* is an important medicinal plant found throughout India, having diverse pharmacological spectrum. One novel chemical constituent Swertiamarin isolated from it showed Antinociceptive, antiedematogenic and free radical scavenging and Hepatoprotective too. Further evaluation need to be carried on other phytoconstituent isolation from category of alkaloid flavonoids and steroids and their practical clinical evaluation which can be used for the welfare of humenbeing.

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