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**Evaluation of anticonvulsant activity of *Mesua ferrea* Linn. ethanolic flower extract**

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**Abstract**

To study the anticonvulsant activity of ethanolic extract of *Mesua ferrea* in albino mice. Anticonvulsant activity for *Mesua ferrea* was evaluated in albino mice of either sex at 3 different dose levels (200, 400 and 600 mg/kg p.o.) by MES assessed using albino mice against Maximum Electroshock Seizure (MES) test. The ethanolic extract of *Mesua ferrea* reduced the duration of hind limb tonic extension (HLTE) in a dose dependent manner against MES model. The ethanolic extract of *Mesua ferrea* inhibits MES-induced convulsions. The extract showed significant ( $p < 0.001$ ) against both MES (maximal electroshock).

Key-Words: Anticonvulsant, *Mesua ferrea* Linn, MES model

**Introduction**

*Mesua* or Iron wood tree, commonly known as Nagapushpam is an important medicinal plant which finds varied uses in Ayurveda, Siddha and Unani. Leaves are used in the form of poultice which is applied to head in severe colds. Bark and roots in decoction or infusion or tincture is a better tonic and are useful in gastritis and bronchitis. Fixed oil expressed from seeds is used as an application for cutaneous affections, sores, scabies, wounds, etc. and as an embrocation in rheumatism. Dried flowers powdered and mixed with ghee, or a paste made of flowers with addition of butter and sugar, are given in bleeding piles as well as dysentery with mucus. They are also useful in thirst, irritability of the stomach, excessive perspiration, cough with much expectoration, dyspepsia, etc. Leaves and flowers are used in scorpion stings. Syrup of the flower buds is given for the cure of dysentery. In Ayurveda, it is an ingredient of "Nagakeshara-adi-Churna", used for bacillary dysentery and in "Naga Keshara Yoga", for piles. In Unani system, the drug is an ingredient of large number of recipes like, "Jawarish Shehryaran" a stomach and liver tonic, "Hab Pachaluna", an appetiser, "Halwa-i-supari pack" a general tonic, etc. Attempts to find out a common neurochemical basis for human or experimental epilepsy have been disappointing. An imbalance between the excitatory and inhibitory neurotransmitters is responsible for seizures.

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At neuronal level, seizure activity often occurs when glutamatergic excitatory neurotransmitters overrides gamma-aminobutyric acid (GABA) mediated inhibition. Several animal models of convulsions have been developed to evaluate anti-seizure activity. Many drugs that increase the brain contents of GABA have exhibited anticonvulsant activity against seizures induced by maximum electroshock (MES).

**Material and methods****Plant material**

The fresh flowers were collected during the month of August 2008, from the Market in Jhansi U.P., The plant materials were identified and authenticated by Dr. Gaurav Nigam, Department of Botany, Bundelkhand University, Jhansi ref. no. BU/BOT/370/ 17-01-09.

**Extraction of plant material**

The shade dried and powdered flower of *M. ferrea* was subjected to successive extraction using ethanol in a Soxhlet apparatus. The extract was concentrated under reduced pressure using rotatory evaporator at temperature not exceeding 40°C and then dried in vacuum oven. The extract was stored in desiccators at cool place.

**Animals**

Mice (20-30gm) of either sex (Bred in Central Drug Research Institute, Lucknow) were used. The animals were obtained from animal house of the Institute of Pharmacy, Bundelkhand University, Jhansi, India. The animals were housed in standard cages with free access of food (standard laboratory rodent's chow) and water. The animal's house temperature was maintained at  $23 \pm 3.0$  °C with a 12-h light / dark cycle (light on from

6.00A.M. to 6.00P.M.). All the experimental procedures and protocols used in this study were reviewed by the Institutional Animal Ethics Committee (IAEC) of the institute (approved by CPCSEA Regd No. 716/02/a/CPCSEA) and BU/Pharm/IAEC/008/027)

#### Acute Toxicity Study

An acute toxicity study relating to the determination of the LD<sub>50</sub> value was performed with different doses of SAP M into different group of mice, each containing ten animals, as per the method discussed by Litchfield and Wilcoxon<sup>5</sup>. The median lethal dose of the extract having anticonvulsant activity was determined by administering 300, 2000, 5000mg/kg i.p. dose and percent mortality was observed 24 h later.<sup>8</sup>

#### Maximal Electroshock-induced Seizure Model

The animals were divided into 5 groups of 5 numbers each swish albino mice and were administered as follows: Group I received vehicle, Group II received Phenytoin (25mg/kg, body weight, p.o., Group III, Group IV and Group V, received 200, 400 and 600mg/kg, body weight, p.o. respectively. Corneal electrodes were used for bilateral delivery of electrical stimulus. Electro convulsive shock (50 mA for 0.2 Sec.) was delivered through corneal electrode to induce Hind Limb Tonic Extensor (HLTE) phase in mice. The electrical stimulus was applied using a stimulator apparatus for five groups of five mice each. The current was applied after 30 min. of administration of ethanolic extract, control and standard. The incidence and duration of HLTE was noted.

#### Statistical analysis

The results of the duration of seizures in electrically-induced seizures were analyzed using the paired Student's t-test, while the proportion of animals that exhibited tonic seizures in electrically induced seizures was analyzed using Chi-squared test. A *p* value of <0.05 was considered as statistically significant.

### Results and Discussion

#### Toxicity assessment

In mice, oral administration of the ethanolic extract at a dose of 500 to 2000 mg/kg did not produce any overt changes in behavior or symptoms of toxicity. The animals showed sign of depression characterized by a decrease in spontaneous activity. The extract was found to be safe up to a dose 2g/kg in mice.

#### MES-induced seizures

Male albino mice pretreated with the ethanolic extract have been significantly protected from convulsions induced by electroshock 30 min. Post dosing. The percentage inhibition achieved at the doses 200, 400, and 600mg/kg were 100% (*p*<0.01), 60% (*p*<0.01) and 100% (*p*<0.001) respectively. Extract at above the

doses, dose dependently prolonged the onset of convulsions in the treated group compared to vehicle treated control group (Table 1). Data from this study show that *M. ferrea* significantly increases the onset time and decreases the duration of seizures by electroconvulsive shock.

The ethanolic extract of flowers of *M. ferrea*, when administered p.o. showed a significant and dose dependent anticonvulsant activity against MES test. MES may be exerting their convulsant effects by inhibiting the activity of gamma amino butyric acid (GABA) at GABA receptors. Gamma amino butyric acid is the major inhibitory neurotransmitter which is implicated in epilepsy. The enhancement and inhibition of the neurotransmission of GABA will attenuate and enhance convulsion, respectively.<sup>9</sup>

Phenytoin standard antiepileptic drugs have been shown to exert their antiepileptic effects by enhancing GABA-mediated inhibition in the brain.<sup>10</sup> It is possible that both standard drugs antagonize MES convulsions in this study by enhancing GABA neurotransmission. Since the ethanolic extract of *M. ferrea* delayed the occurrence of MES convulsions, it is probable that it may be interfering with gabaergic mechanism(s) to exert their anticonvulsant effect. The study showed that ethanolic extract from roots of *M. ferrea* can inhibit voltage dependent Na<sup>+</sup> channels as phenytoin in MES induced tonic seizures.

The ethanolic extract of *M. ferrea* inhibits MES-induced convulsions. However, extensive studies are needed to evaluate the precise mechanism(s), active principles, and the safety profile of the plant as a medicinal remedy for convulsive disorders. The present study demonstrates the potential effectiveness of saponin isolated from the flower of *M. ferrea*, which supports the claim by traditional medicine practitioners as an analgesic and anticonvulsant remedy.

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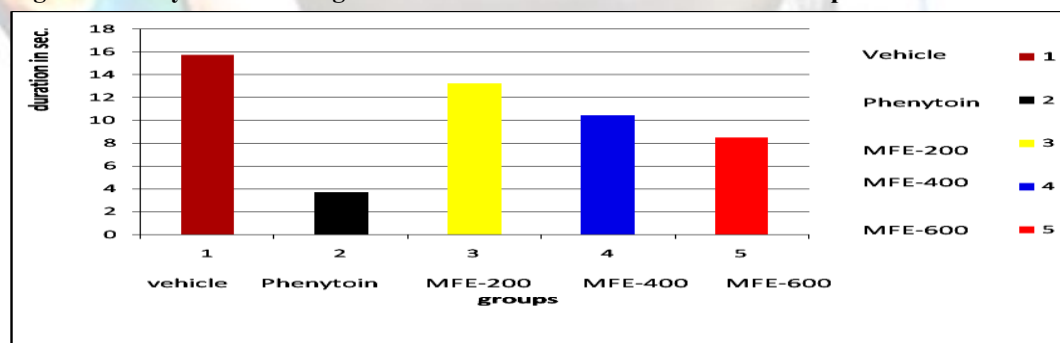
**Table: 1 Effect of *Mesua ferrea* extract on MES induced seizures in mice.**

S/No.	Treatment	Duration of hltte	Mortality (%)	Recovery (%)
1.	Vehicle	15.73±0.35	80	--
2.	Phenytoin	3.71±0.09	0	100***
3.	MFE-200	13.22±0.71	0	71.93**
4.	MFE-400	10.44±0.20	40	64.44***
5.	MFE-600	8.50±0.52	0	56.35 <sup>ns</sup>

Values are mean ±SEM mice were pretreated with Vehicle and *Mesua ferrea* extracts oral 60 min. before the electro convulsive shock. \*\*= $P < 0.01$ , \*\*\*= $P < 0.001$ , <sup>ns</sup>= 0.05 (n= 5)



**Fig. 1: Delivery of MES using electro convulsometer to mice with the help of corneal electrode**



**Fig. 2: Anticonvulsant activity of *Mesua ferrea* on maximal electroshock (MES) induced seizure in mice. Values were expressed as mean ± SEM (n=5); \*\*= $P < 0.01$ , \*\*\*= $P < 0.001$  vs. solvent control.**