

# CURATIVE FLOWERS AND OBVIOUSLY STIRRING MIXES PER ANTIEPILEPTIC ASSETS

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## ABSTRACT

The anticonvulsant activity of various *Calotropis procera* root extracts was tested in rats using seizures induced by maximal electroshock (MES), pentylenetetrazol (PTZ), lithium-pilocarpine, and electrical kindling. The chloroform extract of *Calotropis procera* roots had the most significant (P0.01) anticonvulsant effect in the MES test, decreasing the duration of hind limb extension (extensor phase), clonus, and the duration of the stupor phase compared to the controls. In the PTZ test, the chloroform extract had a highly significant (P0.001) effect, and the aqueous extract had a significant (P0.01) effect by delaying the onset of convulsions compared to the controls.

**Index terms:** Epilepsy, anticonvulsant, medicinal plants, antiepileptic, seizure

## INTRODUCTION:

Recurrent seizures are the hallmark of one of the most complex subgroups of neurological disorders known as epilepsy, which has a prevalence of 0.5–5% worldwide [1]. In India, the prevalence of epilepsy ranges between 4.15 and 7.03 per 1000 people. India's results were higher, reaching 600 per 100,000 person-years. Seizures are caused by anything that disrupts the normal pattern of neuron activity, from abnormal brain development to trauma to illness [2]. Numerous problems can cause epilepsy. Seizures can be classified as: Generalised seizures that happen when seizure activity is widespread in the left and right hemispheres of the brain and the affected people lose consciousness, albeit briefly (except in myoclonic seizures). A focal seizure may only affect a small area of a lobe or a large portion of one hemisphere [3]. However, seizures have been reported to be triggered by a variety of medications, including antidepressants, antibiotics, levodopa, antipsychotics, and thiazide diuretics [2].

More than 30% of patients had refractory epilepsy, and 30–40% of patients experienced antiepileptic side effects, raising concerns about the limited efficacy of these medications [4,5]. Numerous medicinal plants have antiepileptic properties, according to earlier studies [6]. They altered different neurotransmitter receptor systems, increased GABA activity, engaged benzodiazepine sites with benzodiazepine agonist-type activity, blocked NMDA receptors, blocked sodium channels, and decreased Ca<sup>2+</sup> influx into the cell to have antiepileptic effects. [7-9]. The list of Indian medicinal plants with anticonvulsant or epilepsy-treating properties is discussed. About 50% of patients take modern anticonvulsant medications to effectively control epileptic seizures; another 25% may improve, and the remaining patients do not experience any appreciable benefits. In addition, unfavorable side effects of clinically prescribed medications frequently make treatment challenging, driving a demand for new anticonvulsant types. Finding new antiepileptic drugs involves looking into naturally occurring compounds that may belong to new structural classes [10].

Medicinal plants with antiepileptic activity:

The methanolic extract of *Brassica nigra* seed decreased seizure intensity and duration. Furthermore, the *Brassica nigra* extract increased SOD and NO levels while decreasing MDA levels in brain tissues of pentylenetetrazole (PTZ)-induced kindling in mice [10,11].

The antiepileptic activity of methanolic extract of *Brassica nigra* seeds on maximal electroshock-induced seizures (MES), pentylenetetrazole (PTZ), picrotoxin (PIC), and bicuculline-induced seizures in mice was investigated. In the PTZ, PIC, and bicuculline-induced seizure models, the extract (200 and 400 mg/kg, orally) significantly delayed the onset of tonic seizures and reduced the duration of incidence of seizures, whereas, in the MES model, the extract shows a significant effect in abolishing tonic hind limb extensions by inhibiting voltage-dependent Na<sup>+</sup> channels or by blocking glutamergic excitation mediated by the N-methyl-D-aspartate (NMDA) receptor [12]

### **Eupatorium birmanicum:**

*Eupatorium* (Asteraceae) species are used medicinally for a variety of ailments in Europe, America, and Asia as an emetic, purgative, diaphoretic, laxative, and emmenagogue [13]. In Manipur, a variety of ailments such as leucorrhoea, stomach ulcers, and localized burning sensations on the skin are treated with the leaves of *E. birmanicum* [14]. Extract of *Eupatorium birmanicum* shortens the time of MES's tonic hind limb extension and clonic convulsion brought on by Pentylenetetrazole-induced seizure [15].

### **Glychrizza glabra**

In Maximal Electroshock-induced seizures the ethanolic extract of *Glychrizza glabra* roots and rhizomes did not reduce hind limb tonic extension. However, it significantly and dose-dependently delayed the onset of clonic seizures caused by Pentylenetetrazole and protected all rats from picrotoxin-induced seizures. The extract and fractions were also tested for acute toxicity. Thin layer chromatography and various chemical reagents were used to conduct phytochemical screening of the extract and fractions for active constituents. In the PTZ test, the extract and fractions had an anticonvulsant effect [16].

### **Calotropis procera**

The anticonvulsant activity of various *Calotropis procera* root extracts was tested in rats using seizures induced by maximal electroshock (MES), pentylenetetrazol (PTZ), lithium-pilocarpine, and electrical kindling. The chloroform extract of *Calotropis procera* roots had the most significant (P0.01) anticonvulsant effect in the MES test, decreasing the duration of hind limb extension (extensor phase), clonus, and the duration of the stupor phase compared to the controls. In the PTZ test, the chloroform extract had a highly significant (P0.001) effect, and the aqueous extract had a significant (P0.01) effect by delaying the onset of convulsions compared to the controls.

### **Centella asiatica**

*Centella asiatica* (Mackinlayaceae) aqueous extract (100 and 300 mg/kg) was tested for anticonvulsant activity against pentylenetetrazole (30 mg/kg i.p.). The extract at a dose of 300 mg/kg orally decreased the PTZ-induced seizures and improved the learning deficit, whereas a lower dose (100 mg/kg) failed to improve the seizure but improved the learning deficit [24].

### **Bacopa monnieri**

It had neuroprotective effects in glutamate-mediated excitotoxicity during seizures as well as cognitive damage associated with pilocarpine-induced epilepsy. The anticonvulsant activity of an ethanolic extract of *Bacopa monnieri* was tested using various convulsive models (pentylenetetrazol, maximal electroshock, and strychnine-induced convulsion in rats, hypoxic stress-induced convulsion in mice, and lithium-pilocarpine-induced status epilepticus) [25]. The ethanolic extract of *Bacopa monnieri* was given orally to rats and mice at doses of 50 and 55 mg/kg, respectively, 2 and 4 hours before the convulsive stimuli. The ethanolic extract of leaves shows anticonvulsant activity in all models tested, with a mechanism of action similar to that of benzodiazepines (GABA agonists) [26].

### **Carissa carandas**

Carissa carandas is from the Apocynaceae family and its ethanolic root extract of (200 and 400 mg/kg) significantly reduced the duration of seizures induced by maximal electroshock (MES) in mice, and protect animals from pentylenetetrazole-induced tonic seizures and delays the onset of picrotoxin and N-methyl-Daspartic acid-induced tonic seizures. There was no effect of the extract on bicuculline-induced seizures [27]

### **Withania somnifera**

The Pentylenetetrazole seizure threshold for the onset of the tonic extension phase was raised by Withania somnifera root extract. Co-administration of a subeffective dose of exogenous GABA, a GABA receptor agonist, or diazepam, a GABA receptor modulator, raises the seizure threshold. The anticonvulsant activity of Withania somnifera root extract includes GABAergic modulation against the Pentylenetetrazole seizure threshold paradigm [28]. roots and rhizomes against PTZ and PTX-induced convulsions was mediated in part by the GABA Benzodiazepine receptor complex [29,30] .

### **Cyperus rotundus**

The roots and rhizomes of cyperus rotundus were tested in seizures induced by pentylenetetrazol (PTZ) and picrotoxin (PTX) and showed anticonvulsant activity in mice. Following PTZ and PTX administration, pretreatment with a hydroalcoholic extract of Cyperus rotundus roots and rhizomes (50-200mg/kg) resulted in a dose-dependent decrease in the incidence of both clonic and generalised tonic-clonic seizures (p0.05). The latency to seizure was increased when a sub-effective dose of CR (50 mg/kg, p.o) was combined with a sub-protective dose of diazepam (0.5 mg/kg, i.p).

### **Ficus platyphylla**

The saponins-rich fraction (SFG) obtained from Ficus platyphylla stem bark was studied in mice with Pentylenetetrazole, Strychnine, and MES-induced seizures. Saponin-rich fraction protects mice from seizure caused by pentylenetetrazole and strychnine and significantly delayed the onset of myoclonic jerks and tonic seizures. SFG did not protect mice from maximal electroshock seizures. In a neonatal rat brain slice model of tonic-clonic epilepsy, SFG did not abolish spontaneous discharges induced by 4- aminopyridine, nor did it modulate chloride currents through the GABAA receptor channel complex in cultured cortical cells. In these cultured cells, however, it was able to non-selectively suppress excitatory and inhibitory synaptic traffic, as well as block sustained repetitive firing and spontaneous action potential firing. It most likely works by blocking voltage-gated sodium channels [17,18] .

### **Nigella sativa**

Thymoquinone is a major constituent of Nigella sativa seeds, the anticonvulsant effect of thymoquinone was studied in mice using pentylenetetrazole (PTZ) and maximal electroshock (MES) seizure models [19] . Thymoquinone at 40 and 80 mg/kg, i.p, delayed the onset of seizures and reduced the duration of myoclonic seizures in PTZ-induced seizures. Thymoquinone had a protective effect against mortality of 71.4% and 100%, respectively. In the MES model, however, thymoquinone did not reduce seizure duration but did provide complete protection against mortality [20,21] .

### **Antiepileptic studies of naturally occurring compounds:**

Undesirable side effects of clinically used drugs frequently make treatment difficult, creating a demand for new types of anticonvulsants. The investigation of naturally occurring compounds, which may belong to new structural classes, is one approach to the search for new antiepileptic drugs.



Sr.no	Compound	Plant	Action	Reference
1.	Rhynchophylline	Uncaria	Noncompetitive NMDA receptor antagonists	[42]
2.	Wogonin	Scutellaria baicalensis	Enhancement of GABA activity	[43]
3.	Aconitine	Aconitum variegatum.	GABAA-mediated inhibition and NMDA	[44]

### Conclusion:

Epilepsy is a serious brain disorder; the drug used to treat epilepsy should have the greatest effect on controlling seizures while having the fewest side effects. All AEDs on the market have some negative side effects that cause neuronal cell loss. As previously stated, neurodegeneration may affect the protective activity of some antiepileptic drugs. Medicinal plants can exert antiepileptic activity through a variety of mechanisms, such as modulation of neurotransmitter receptor systems, enhancement of GABA activity, interaction at benzodiazepine sites with benzodiazepine agonist-type activity, blocking NMDA receptors, blocking sodium channels, and decreasing Ca<sup>2+</sup> influx into the cell. The curative value of plant medicines with few side effects has accelerated research into natural drug sources. The current review highlighted medicinal plants with antiepileptic properties to encourage further research in this area.

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### CONFLICT OF INTEREST

No conflict of interest associated with this work.

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