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ANTICONVULSANT STUDIES ON LEAF EXTRACT OF *ERYTHRINA INDICA* LAM.

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ABSTRACT

To determine the anticonvulsant activity of the leaf extract of *Erythrina Indica* in mice and rats, and in order to verify the traditional use of the plant in the treatment of epilepsy. The pentyleneterazole (PTZ) and the maximal electroshock seizure (MES) models were used for assessing the anticonvulsant effects of the chloroform leaf extract in mice and rats. The chloroform extract (500 mg/kg p.o) of that produced significant protection (71.4%) against PTZ-induced convulsion and onset of seizures compared with the control group in mice. At 500 mg/kg p.o., the extract also produced significant protection (71.4%) against MES-induced convulsions in mice. The results obtained from this study indicate that the chloroform leaf extract of *Erythrina Indica* may be beneficial in both absence and tonic clonic seizures.

INTRODUCTION: Current available anticonvulsant drugs are able to efficiently control epileptic seizures in about 50% of the patients; another 25% may show improvement whereas the remainder does not benefit significantly [1]. Furthermore, undesirable side effects of the drugs used clinically often render treatment difficult so that a demand for new types of anticonvulsants exists. One of the approaches to search for new antiepileptic drugs is the investigation of naturally-occurring compounds, which may belong to new structural classes.

The plant *Erythrina indica* Lam. is a middle sized tree widely distributed throughout India. Traditionally its leaves are used as laxative, diuretic, emmenagogue, galactagogue and also used in the treatment of anti-helmentic and joints pain [2-4]. In siddha system, it is being considered useful for anticonvulsant activity [3]. Since, no scientific proof about anticonvulsant activity in leaf extract of *Erythrina indica* Lam, an attempt has been made to explore such activity for *Erythrina indica* Lam. In the present work, vacuum dried chloroform extracts were evaluated for anticonvulsant activity.

MATERIAL AND METHOD: The fresh leaves of Erythrina indica Lam were collected from in and around Chennai and identified by Dr. Sasikala, Department of Pharmacognosy, Captain Srinivasamoorty Drug Research Institute of Ayurveda, Chennai.

Preparation of the extract: The coarsely powdered leaves were extracted separately with chloroform by using Soxhlet apparatus. The solvents were removed under vacuum and a crude solid mass was dried and stored in desiccators for further studies. The preliminary phytochemical analysis [4] was under taken to detect the presence of major phytoconstituents in the extracts.

Animals: Albino mice (20-25 g) and albino rats (60-80 g) of either sex were obtained from the animal house

of the Department of Pharmacology, Saastra College of pharmaceutical education and research, Nellore.

Drugs: The drugs used were supplied from the stock of Department of Pharmacology laboratory, Saastra college of pharmaceutical education and research, Nellore and include; Pentylenetetrazole (Sigma) and Phenobarbitone (Merck).

PTZ-induced convulsion in rats: Three groups, each containing seven rats were used to test for the effect of chloroform extract on PTZ-induced seizures. They were treated as follow;

Group I (control): distilled water (0.5 ml p.o.).

Group II: Phenobarbitone (30 mg/kg i.p.).

Groups III-: Chloroform extract (500 mg/kg p.o.) was administered.

After a pretreatment time of 60 minutes, PTZ (85 mg/kg i.p.) was administered to the three groups of animals. The onset of convulsion, number of animals that convulsed and number of animals that were protected were recorded**[5].**

PTZ- induced convulsion in mice: A total of twenty-one mice were divided into three groups of seven animals each. They were treated as follow;

Group I (control): distilled water (0.5 ml p.o.).

Group II: Phenobarbitone (30 mg/kg i.p.).

Groups III: Chloroform extract (500 mg/kg p.o.) was administered.

After a pretreatment time of 60 minutes, PTZ (85 mg/kg i.p.) was administered to the six groups of animals. The onset of convulsion, number of animals that convulsed and number of animal that were protected were recorded [5]**.**

Electrically- induced Seizure in mice: Twenty-one male mice were allotted into three groups of seven animals each and treated.

Group I (control): distilled water (0.5 ml p.o.).

Group II: Phenobarbitone (30 mg/kg i.p.).

Groups III-: Chloroform extract (500 mg/kg p.o.) was administered.

After a pretreatment time of 60 minutes, a CFP stimulator (model 8048) was used to deliver a stimulus of 50 Hertz at 20 volts via ear electrodes to the different groups. The animals were observed for 2 minutes. The onset of tonic hind limb extension and number of animals protected was recorded [6].

Statistical analysis: The data are expressed as mean ± S.E.M. The data were statistically analyzed using One-Way Analysis of Variance (ANOVA), followed by Duncan's multiple range post test and Chi square test. Values of $p < 0.05$ were considered significant.

RESULTS:

The effect of chloroform extract on PTZ-induced convulsion in rats: Intraperitoneal administration of PTZ induced tonic-clonic convulsions with 100% mortality in the control group. The chloroform extract (500 mg/kg p.o.) significantly ($p < 0.05$) increased the onset of convulsion in rats compared with the control group. Extract (500 mg/kg p.o.) offered 42.9% protection against PTZ- induced convulsion in rats (**Table 1**).

TABLE 1: EFFECT OF CHLOROFORM EXTRACT OF *ERYTHRINA INDICA* ON PENTYLENETETRAZOLE-INDUCED SEIZURES IN RATS

Treatment	Onset of convulsion (seconds)	Number convulsed/number used	Mortality (%)	Protection (%)
Distilled water	44.3 ± 1.69	7/7	100	0
Phenobarbitone *(30 mg/kg)*	-	-	0	100
Erythrina indica 500 mg/kg	129.5 ± 6.90*	4/7	57.1	42.9

Results are expressed as mean ± S.E.M. and as % mortality and protection (n=7). *p < 0.05 compared with control; One-way ANOVA followed by Duncan post test and Chi square test

The effect of chloroform extract on PTZ-induced convulsion in mice: The extract (500 mg/kg p.o.) significantly ($p < 0.05$) increased the threshold of PTZ-induced convulsion in mice compared with the control group. At 500 mg/kg p.o., the extract produced significant protection (71.4%) against PTZ-induced convulsion in mice (**Table 2**).

The effect of chloroform extract on MES-induced convulsion in mice: The extract (500 mg/kg p.o.) significantly *(p* < 0.05) increased the threshold of MES-induced convulsions in mice compared with the control group. At 500 mg/kg p.o., the extract produced (71.4%) protection in mice (**Table 3**).

TABLE 2: EFFECT OF CHLOROFORM EXTRACT OF *ERYTHRINA INDICA* ON PENTYLENETETRAZOLE-INDUCED SEIZURES IN MICE

Treatment	Onset of convulsion (seconds)	Number convulsed/ number used	Mortality (%)	Protection (%)
Distilled water	42.0 ± 0.85	7/7	100	0
Phenobarbitone *(30 mg/kg)*	-	0/7	0	100
Erythrina indica 500 mg/kg	120.5 ± 0.50	2/7	28.6	71.4*

Results are expressed as mean ± S.E.M. and as % mortality and protection (n=7). *p < 0.05 compared with control; One-way ANOVA followed by Duncan post test and Chi square test

TABLE 3: EFFECT OF CHLOROFORM EXTRACT OF *ERYTHRINA INDICA* ON MAXIMAL ELECTROSHOCK-INDUCED SEIZURES IN MICE

Treatment	Onset of convulsion (seconds)	Number convulsed/ number used	Mortality (%)	Protection (%)
Distilled water	9.86±0.67	7/7	100	0
Phenobarbitone *(30 mg/kg)*	-	0/7	-	100
Erythrina indica 500 mg/kg	27.0±1.00*	2/7	28.6	71.4*

Results are expressed as mean ± S.E.M. and as % mortality and protection (n=7). *p < 0.05 compared with control; One-way ANOVA followed by Duncan post test and Chi square test

DISCUSSION: The chloroform extract *of Erythrina indica* increased the threshold of PTZ-induced convulsion in rats and offered protection against PTZ-induced convulsion. The protection offered against PTZ-induced convulsion in mice (71.4%) was significant compared to that produced in rats (42.9%). Clonic seizures induced by PTZ are blocked by drugs that reduce T-type calcium currents (Ethosuximide) and drugs that enhance inhibitory Neuro-transmission by GABAA receptors (benzodiazepine, Phenobarbital and Valproate) [7].

Convulsants whose actions previously were unexplained (including penicillin and PTZ) may act as relatively selective antagonist of the action of GABA [8-9]. The fact that the extract protected animal against PTZ-induced seizures may suggest that the plant extract contains compound(s) that facilitate GABAergic transmission. The extract also increased the threshold of seizures and offered protection in the MES test.

It has been found empirically that drugs which inhibit PTZ-induced convulsions and raise the threshold for production of electrically-induced seizures are generally effective against absence seizures, whereas those that reduce the duration and spread of electrically-induced convulsions are effective in tonic-clonic seizures [10].

The results of this study shows that the chloroform extracts *of Erythrina indica* possess anticonvulsant properties which are possibly mediated partly via facilitation of GABA transmission. These results suggest that the leaves of *Erythrina indica* will be beneficial in the management of absence and tonic-clonic seizures. The present study is a preliminary attempt in evaluating the anti-convulsants activity of *Erythrina indica* leaf extract. Further pharmacological investigations are warranted in this direction for establishing its detailed mechanism of action and for substantiating its traditional and folk claims.

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