ANTI-CONVULSION ACTIVITY OF DOLICHANDRONE FALCATA ON PENTYLENETETRAZOLE (PTZ) INDUCED SEIZURES MODEL

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Article Info
Received 25/02/2014
Revised 15/03/2014
Accepted 25/03/2014

Key words: Anti-convulsion activity, Dolichandronefalcata, Pentylentetrazole (PTZ).

ABSTRACT
Investigation of anti-convulsion activity of aqueous extract of Dolichandronefalcata (AEDF) in Pentylentetrazole (PTZ) induced seizures model in albino wistar rats. Acute toxicity of extract was non toxic up to the recommended dose 2000 mg/kg, p.o. Animals were treated with AEDF at doses of 200 and 400 mg/kg body weight. In Pentylentetrazol induced seizure model, onset of myoclonic spasm and clonic convulsion was delayed in the AEDF treated groups. AEDF showed anti-convulsion activity against PTZ animal model. However, further studies still needed to be carried on exposure of the extract to humans.

INTRODUCTION
Epilepsy is usually controlled, but cannot be cured with medication, although surgery may be considered in difficult cases. However, over 30% of people with epilepsy do not have seizure control even with the best available medications. Not all epilepsy syndromes are lifelong some forms are confined to particular stages of childhood. Epilepsy should not be understood as a single disorder, but rather as syndromic with vastly divergent symptoms but all involving episodic abnormal electrical activity in the brain [1]. The alternative drug therapy for the management of this disease can be by the use of medicinal plants and their active principles.

Dolichandronefalcata Seem.,Bignoniaceae, is a is a small deciduous tree with bluish grey bark, peeling in irregular woody scales and also commonly known as Medshingi.It growing on hedges of cultivated fields and frequently in hill forest, occasionally seen in dry scrub forests.Dolichandronefalcata bark is traditionally used in the treatment of fractured bones and used as a fish poison. In this plant Chrysin (flavone) was identified and reported for different biological activities such as anti-oxidant, anti-allergic, anti-inflammatory, anti-cancer, antiestrogenic and anxiolytic activities by previous authors [2-7]. In Ayurveda, the stem bark of Dolichandronefalcata is used for cure the ulcer, pain and epilepsy. But still no depth scientific study has been performed on Dolichandronefalcata stem-bark pharmacological properties. The aim of present study was to investigate the antiulcer effect of aqueous extract of stem bark of Dolichandronefalcata in different animal models. Since the anti-convulsion effect of Dolichandronefalcata has been experimentally not confirmed. Therefore, the aim of the present investigation was to evaluate the claimed anti-convulsion activity of Dolichandronefalcata in albino wistar rats.
MATERIALS AND METHODS

Plant collection and Preparation of plant extract

The stem-bark of *Dolichandronefalcata* was collected from the forest of agasthyamalai hills, tirunelveli district, Tamilnadu, India. It was identified and authenticated by Dr.V.Chelladurai, Research Officer Botany, C.C.R.A.S., Govt. of India. The collected stem bark of *Dolichandronefalcata* was shadow/air dried in room temperature without sunlight. The dried material was extracted in 1 litre of boiling water for 2-3 h and concentrated to half of the volume by boiling in a water bath. The yielded brownish extract was cooled and filtered using Whatman filter paper. The filtrate extract was concentrated up to 100 ml on rotavapour under reduced pressure. The yield value was found to be 12.5%. The concentrated plant extract was lyophilized into powder used for the further pharmacological study which is suspended to 1% tween 80.

Animals

Albino Wistar strain of rats, weighing about 180-220 g were obtained from Department of Pharmacology, Southern Institute of Medical Sciences, Guntur. Andhra Pradesh, India and used for the screening models. According to guidelines, animals were kept in animal house at an ambient temperature of 25°C and 45–55% relative humidity, with 12 h each of dark and light cycles. Animals were complete fed pellet diet and water *ad libitum*. For screening anti-ulcer efficiency purpose the animals were kept fasting overnight but were allowed free access to water. The experimental protocol was approved by the Institutional animal ethical committee.

Acute toxicity study

The acute oral toxicity study was done for aqueous extract of stem-bark of *Dolichandronefalcata* (AEDF) according to OECD 420 guideline using fixed dose method [8]. Animals were divided into two groups, three animals each, fasted overnight. The started dose AEDF 2000 mg/kg b.wt.was administered to the Group I & 2 respectively. After oral administration of AEDF, the behavioral changes and signs of toxicity such as body temperature, CNS activity, urination, defecation etc were observed for 24 hrs. If AEDF does not showed any toxicity symptoms, lower dose 200 mg/kg b.wt.and higher dose 400 mg/kg b.wt. were selected for further studies [8].

ANTI-CONVULSION ACTIVITY

Effect on Pentylenetetrazole (PTZ) induced seizures

Albino wistar rats of either sex weighing 160 to 220 gm were divided into four groups of six animals each. The first group received vehicle control (1% w/v SCMC, 1ml/100 g) whereas Group-II received standard drug (Diazepam, 4mg/kg) intraperitoneal, Group-III and IV, aqueous extract of *Dolichandronefalcata* (AEDF) (200 and 400 mg/kg/body weight) p.o respectively for 20 days. On the 20th day, Pentylenetetrazole (PTZ) (90mg/kg body weight, s.c.) was administered to all the groups to induce clonic convulsions. Animals were observed for a period of 30mins post – PTZ administration. The parameters noted were mean onset time of convulsions, duration of convulsion and recovery/Death (% recovery or % of survival) due to PTZ [9].

Statistical analysis

The data were expressed as Mean ± S.E.M. and statistically analyzed using one way ANOVA followed by Tukey-Kramer’s Multiple comparison test, p<0.05 was considered significant.

RESULTS

Effect of AEDF on PTZ Induced epilepsy

The AEDF at doses of 200 mg/kg and 400 mg/kg significantly delayed the onset of clonic convulsions (p<0.01) in dose dependent manner. Whereas, the standard drug diazepam (4mg/kg, i.p) delayed the onset of clonic convulsions. Diazepam treated animals have shown 100% protection against PTZ induced seizures whereas AEDF 200 mg/kg and 400 mg/kg have shown 83.33% and 100% protection respectively (Table 1).

Table 1. Effect of aqueous extract of *Dolichandronefalcata*(AEDF ) On PTZ induced seizers in rats.

<table>
<thead>
<tr>
<th>Group</th>
<th>Design of Treatment</th>
<th>Onset of convulsions(sec.)</th>
<th>Duration of convulsion(sec.)</th>
<th>Protection mortality %</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Vehicle control</td>
<td>169.33±1.52</td>
<td>61.29±1.42</td>
<td>50</td>
</tr>
<tr>
<td>II</td>
<td>Diazepam(4mg/kg)</td>
<td>605.14±2.29*</td>
<td>24.14±1.52*</td>
<td>100</td>
</tr>
<tr>
<td>III</td>
<td>AEDF 200</td>
<td>415.47±2.33**</td>
<td>44.42±2.62**</td>
<td>83.33</td>
</tr>
<tr>
<td>IV</td>
<td>AEDF 400</td>
<td>542.17±2.64**</td>
<td>30.16±2.19**</td>
<td>100</td>
</tr>
</tbody>
</table>

Values are expressed as mean ± SEM of six observations. Comparison between Group I Vs Group II, Group II Vs Group III & GroupIV. Statistical significant test for comparison was done by ANOVA, followed by Dunnet’s ‘t’ test. *p<0.05,** p<0.01; ns-non significant.
DISCUSSIONS AND CONCLUSION

In India, studies have reported the prevalence rate of epilepsy varying from 1710 to 9780 cases per million populations. The modern conventional anticonvulsion drugs (AEDs) are effective in approximately 50% of patients, many cases still remain resistant to AED treatment [10]. These drugs are associated with vast array of side effects including chronic toxicity, teratogenesis, adverse effects on cognition and behavior among others [11]. Thus, due to aforementioned reasons and others, it is pertinent to look for affordable and conventional alternative medicine with view to providing a better protection and activities particularly medicinal plants.

We found that treatment with AEDF on PTZ induced rats significantly reduce the duration of convulsion and delayed the onset of clonic convulsion. Although animal models based on pentylentetrazole (e.g. pentylentetrazole threshold, and acute convulsions) have still been widely used for drug screening, the mechanism by which pentylentetrazole elicits its action has not been completely understood. One generally accepted mechanism by which pentylentetrazole exerts its action is by acting as an antagonist at the picrotoxin sensitive site of the GABA$_A$ receptor complex [12-14].

Since PTZ has been shown to interact with the GABA neurotransmission [22] and PTZ induced seizures can be prevented by drugs that enhance gamma amino butyric acid type A (GABA$_A$) receptor-mediated inhibitory neurotransmission such as benzodiazepines and phenobarbital [15,16], the antagonism of PTZ-induced seizures suggests the interaction of the AEDF with the GABA-ergic neurotransmission.

The study concluded AEDF possesses an anticonvulsant effect which results from potentiate the activity of GABA. However, more precise mechanisms of AEDF anticonvulsant activity and the relationship between the seizure and GABA$_A$ receptor subunits and the other neurotransmitter systems which may explain how AEDF produce anticonvulsant effect must be investigated further.

REFERENCES

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