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EVALUATION OF ANTI-SEIZURE ACTIVITY OF *BARRINGTONIA ACUTANGULA* EXTRACT ON PTZ INDUCED SEIZURE MODEL IN ALBINO WISTAR RATS

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ABSTRACT

The present study is an investigation of anti-seizure activity of *Barringtonia acutangula* (L.) Gaertn. (Family: Lecythidaceae) an evergreen tree which is being used in Indian traditional medicines for treating epilepsy, diarrhoea, dysentery, cholera and ulcers. The ethanol extract of *Barringtonia acutangula* (EEBA) was subjected to acute toxicity and then screened for anticonvulsant activity on Pentylenetetrazole (PTZ) induced seizures models 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 EEBA at doses of 250 and 500 mg/kg body weight. Study results showed, onset of myoclonic spasm and clonic convulsion was delayed in the EEBA treated groups. EEBA showed anti-seizure activity against PTZ animal models.

KEY WORDS: Anti-seizure activity, *Barringtonia acutangula*, Pentylenetetrazole (PTZ).

INTRODUCTION

Barringtonia acutangula (L.) Gaertn. (Family: Lecythidaceae) an evergreen tree of moderate size is called as Hijja or Hijjala in Sanskrit. The fruit is spoken of as samudra-phala and various part of this plant used as a folklore medicine for curing various ailments like hemiplegia, pain in joints, eye diseases, stomach disorders, anthelmintic, diarrhoea, cough, dyspnoea, leprosy, intermittent fever, and spleenic disorders. An aqueous extract of the bark is found hypoglycemic and is reported to be used in pneumonia, diarrhea, asthma and leaf juice is given for diarrhea. Fruit is bitter, acrid, anthelmintic, emetic, expectorant and vulnerary. It is prescribed in gingivitis, as an astringent and tonic. Whole plant was reported to possess flavonols, phenolic acids, triterpenoids, tannins and steroidal compounds such as barringtogenic acid, tangulic acid and acutangulic acids. The fruit possessed saponins based on barringtogenol B, C and D. The therapeutic potential of this plant were reported to be antitumor, antibiotic, inhibit growth of Helicobacter pylori and antifungal activities [1-7].

Objective of the present study is set to investigate the antiseizure activity of *Barringtonia acutangula* leaves extract. On the basis of the traditional use of the plant for treating convulsion, but no previous pharmacological (or) clinical study was carried out to test the antiseizure activity of this plant. Since the antiseizure effect of *Barringtonia acutangula* has been experimentally not confirmed. Therefore, the aim of the present investigation was to evaluate the claimed anti-seizure activity of *Barringtonia acutangula* in albino wistar rats.

MATERIALS AND METHODS

Plant material

The leaves of *Barringtonia acutangula* was collected from Tirumala hills, Tirupati, Andhra Pradesh. India. The plant was identified and authenticated by Dr.K. Madhava Chetty, Department of botany, S.V.University

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Tirupathi. The voucher specimen of the plant was deposited at the college for further reference. The leaves were dried under shade, powdered and stored in an air tight container.

Preparation of extract

The collected leaves were dried at room temperature, pulverized by a mechanical grinder, sieved through 40mesh. About 120g of powdered materials were extracted with ethanol (90%) using soxhlet apparatus. The extraction was carried out until the extractive becomes colourless. The extracts is then concentrated and dried under reduced pressure. The solvent free semisolid mass thus obtained is dissolved in normal saline and used for the experiment. The percentage yield of prepared extract was around 10.5%w/w.

Phytochemical analysis

The ethanol extract of *Barringtonia acutangula* was subjected to qualitative analysis for the various phyto-constituents. Standard methods were used for preliminary qualitative phytochemical analysis of extract [8].

Experimental Animals

Wister albino rats weighing between 150-200gm each maintained in a 12 h light/dark cycle at a constant temperature 25 ºC with free access to feed (Sai durga feeds and foods, Bangalore) and water. All animals were fasted prior to all assays and were allocated to different experimental groups each of 6 rats. Moreover the animals were kept in specially constructed cages to prevent coprophagia during the experiment. All experiments were carried out according to the guidelines for care and use of experimental animals and approved by Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA).

Acute toxicity study

Acute toxicity study of ethanol extract of *Barringtonia acutangula* was determined by acute toxic class method of OECD guidelines. In acute oral toxicity study mortality was not observed up to 2000mg/kg body weight [9].

Anti-seizure 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) intraperitoneally, Group-III and IV, ethanol extract of *Barringtonia acutangula* (EEBA) (250 and 500 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 [10,11].

Statistical analysis

The data were expressed as Mean ± S.E.M. and statistically analyzed using one way ANOVA followed by Dunnett's test, $p<0.05$ was considered significant.

RESULTS

Phytochemical analysis

The ethanol extract of *Barringtonia acutangula* revealed the presence of alkaloids, triterpenoids, Reducing sugars, tannins, gums, flavonoids.

Effect of EEBA on PTZ Induced Seizure

In rats treated with vehicle, clonic convulsion appeared for 152.09±3.28 seconds after PTZ and all rats died after seizures. The EEBA at doses of 250 mg/kg and 500 mg/kg significantly delayed the onset of clonic convulsions for 390.27±3.16 ($p<0.01$) and 564.64±3.52 ($p<0.01$) seconds respectively in dose dependent manner. Whereas, the standard drug diazepam (4mg/kg, *i.p*) delayed the onset of clonic convulsions for 758.19±3.45 seconds. Diazepam treated animals have shown 86.40% protection against PTZ induced seizures whereas EEBA 250 mg/kg and 500 mg/kg have shown 54.53% and 69.21% protection respectively (Table 2).

Table 1. Effect of ethanolic extract of *Barringtonia acutangula* (EEBA) On PTZ induced Seizures in rats

Group	Design of Treatment	Onset of convulsions (sec.)	Duration of convulsion (sec)	Protection convulsion%	Protection mortality %
I	Vehicle control	152.09±3.28	75.14±1.56	0	50
II	Diazepam(4mg/kg)	758.19±3.45**	10.22±0.42**	86.40	100
III	EEBA 250	390.27±3.16**	34.17±0.33*	54.53	83.33
IV	EEBA 500	564.64±3.52**	23.14±0.22**	69.21	100

Values are expressed as mean ± SEM of six observations. Comparison between Group I *Vs* Group II, Group II *Vs* Group III &Group IV. Statistical significant test for comparison was done by ANOVA, followed by Dunnett's test. *p<0.05;** p<0.01; ns-non significant.

DISCUSSION AND CONCLUSION

In India, studies have reported the prevalence rate of epilepsy varying from 1710 from 9780 cases per million populations. The modern conventional anti-seizure drugs (AEDs) are effective in approximately 50% of patients; many cases still remain resistant to AED treatment [12]. These drugs are associated with vast array of side effects including chronic toxicity, teratogenecity, adverse effects on cognition and behavior among others [13]. 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 EEBA on PTZ induced rats significantly reduce the duration of convulsion and delayed the onset of clonic convulsion. Although animal models based on pentylenetetrazole (e.g. pentylenetetrazole threshold, and acute convulsions) have still been widely used for drug screening, the mechanism by which pentylenetetrazole elicits its action has not been completely understood. One generally accepted mechanism by which pentylenetetrazole exerts its action is by acting as an antagonist at the picrotoxin sensitive site of the $GABA_A$ receptor complex [14].

Since PTZ has been shown to interact with the GABA neurotransmission [15,16] 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 [16] the antagonism of PTZ- induced seizures suggests the interaction of the EEBA with the GABA-ergic neurotransmission.

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

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