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ANTI-EPILEPTIC ACTIVITY OF *MACARANGA PELTATA ROXB.* ON PENTYLENETETRAZOLE (PTZ) INDUCED SEIZURE IN ALBINO WISTAR RATS

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ABSTRACT

The present study is an investigation of anti-epileptic activity of *Macaranga peltata Roxb.* is a well-known plant which is being used in Northern Thailand, Sri Lanka and India for treating epilepsy. The ethanol extract of *Macaranga peltata Roxb.* (EMP) was subjected to acute toxicity and then screened for anticonvulsant activity on Pentylenetetrazole (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 EMP at doses of 250 and 500 mg/kg body weight. In Pentylenetetrazole induced seizure model, onset of myoclonic spasm and clonic convulsion was delayed in the EMP treated groups. EMP showed anti-epileptic activity against PTZ animal model. However, further studies still needed to be carried on exposure of the extract to humans.

Keywords: Anti-epileptic activity, *Macaranga peltata Roxb.*, Pentylenetetrazole (PTZ).

INTRODUCTION

Epilepsy is more likely to occur in young children or people over the age of 65 years, however, it can occur at any time. As a consequence of brain surgery, epileptic seizures may occur in recovering patients. 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].

Traditional medicinal practices have remained as a component of health care system of many societies in spite of the availability of well-established alternatives [2]. Epilepsy is a condition, which causes seizures to occur. It is one of the most common chronic diseases affecting human beings. According to several publications this can amount to 70% of the people with epilepsies, with a high prevalence of about 0.8% in children below the age of seven years [3]. These observations have led to a shift in focus to the use of herbal remedies in the management of epileptic seizures, probably because these measures fit into the cultures of people and are not usually as expensive as the more refined orthodox drugs. Besides, these orthodox drugs possess many side effects, contraindications and possible interactions with drugs used simultaneously.

The alternative drug therapy for the management of this disease can be by the use of medicinal plants and their active principles. In the present study plants from India with a traditional claim of anti-epileptic activity and neuro protective properties were selected and a poly herbal extract was prepared in ethanol medium.

Macaranga peltata Roxb. is a plant found in northern Thailand, Sri Lanka and India. It is one of the most widely occurring early successional woody species in Sri Lanka, especially in low country wet zone. Some of the many common names include kenda or kanda in Sri Lanka and chandada in India. It is a resinous tree, up to 10 metres (33 ft) tall. Young parts are velvet hairy. Leaves measure

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20 to 50 centimetres (7.9 to 20 in) by 12 to 21 centimetres (4.7 to 8.3 in), are alternately arranged, circular or broadly ovate, entire or minutely dentate, and palmately 9-nerved. The leaf stalk is attached on the lower surface of the leaf, not on the base. Yellow-green flowers occur in long panicles in leaf axils in the months of January to February. Male flowers are minute, numerous, and clustered in the axils of large bracts. One round, black seed is in a spherical capsule 4 to 5 mm across. Kenda leaves are commonly used for flavoring in Sri Lanka. Halapa dough is often flattened on a kenda leaf to soak in the flavor. Kenda leaves are used to wrap jaggery and to treat ulcers and epilepsy [4].

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 antiepileptic activity of this plant. Since the antiepileptic effect of *Macaranga peltata Roxb.* has been experimentally not confirmed. Therefore, the aim of the present investigation was to evaluate the claimed antiepileptic activity of *Macaranga peltata Roxb.* in albino wistar rats.

MATERIALS AND METHODS

Plant collection

The Plant material of *Macaranga peltata Roxb.* leaves was collected from Tirunelveli District, in the Month of January 2013. The plant was authenticated by Dr.V.Chelladurai, Research Officer Botany. C.C.R.A.S., Govt. of India. The voucher specimen of the plant was deposited at the college for further reference.

Preparation of plant extract

The leaves of the *Macaranga peltata Roxb.* are properly washed in tap water and then rinsed in distilled water. The rinsed leaves are dried in an oven at 35^{o}C for 4 days. The dried leaves of *Macaranga peltata Roxb.* was crushed to obtain powder. These powdered samples are then stored in airtight polythene bags protected from sunlight until use. The ethanol extract of each sample was prepared by soaking 10g of powdered sample in 200ml distilled water for 12h. The extracts are then filtered using Whatmann filter paper. Percentage yield of ethanol extract of *Macaranga peltata Roxb.* was found to be 8.5 % w/w.

Preliminary phytochemical screening

The phytochemical examination of ethanol extract of *Macaranga peltata Roxb.* leaves was performed by the standard methods [5]**.**

Animals used

Male albino rats (150-220g) were obtained from the animal house and maintained in a well-ventilated room with 12:12 hour light/dark cycle in polypropylene cages. The animals were fed with standard pellet feed (Hindustan Lever Limited., Bangalore) and water was given *ad libitum*. Ethical committee clearance was obtained from IAEC (Institutional Animal Ethics Committee) of CPCSEA.

Acute Toxicity Study

The acute toxicity of ethanol extract of *Macaranga peltata Roxb.* was determined as per the OECD guideline no. 423 (Acute Toxic Class Method). It was observed that the test extract was not mortal even at 2000mg/kg dose. Hence, 1/10th (200mg/kg) and 1/5th (400mg/kg) of this dose were selected for further study [6].

ANTI-EPILEPTIC 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 *Macaranga peltata Roxb.* (EMP) (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 [7].

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.

Table 1. Effect of ethanolic extract of *Macaranga peltata Roxb.* (EMP) On PTZ induced seizers in rats

Group	Design of Treatment	Onset of convulsions (sec.)	Duration of convulsion (sec.)	Protection mortality %
I	Vehicle control	154.29±1.52	60.16±1.42	50
II	Diazepam(4mg/kg)	542.32±1.19**	23.62±1.33**	100
III	EMP 250mg/kg, p.o	392.64±1.33**	43.65±1.41*	83.33
IV	EMP 500mg/kg, p.o	496.28±1.12**	30.12±1.24**	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.

Figure 1. Effect of ethanolic extract of *Macaranga peltata Roxb.* (EMP) On PTZ induced seizers in rats

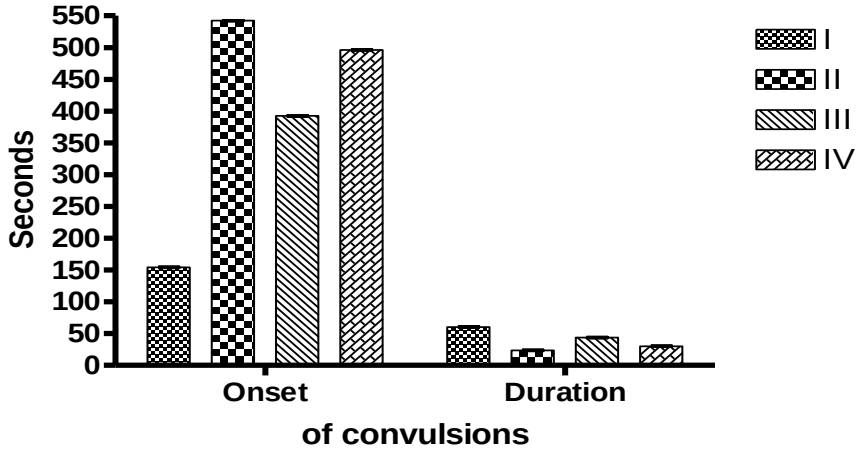
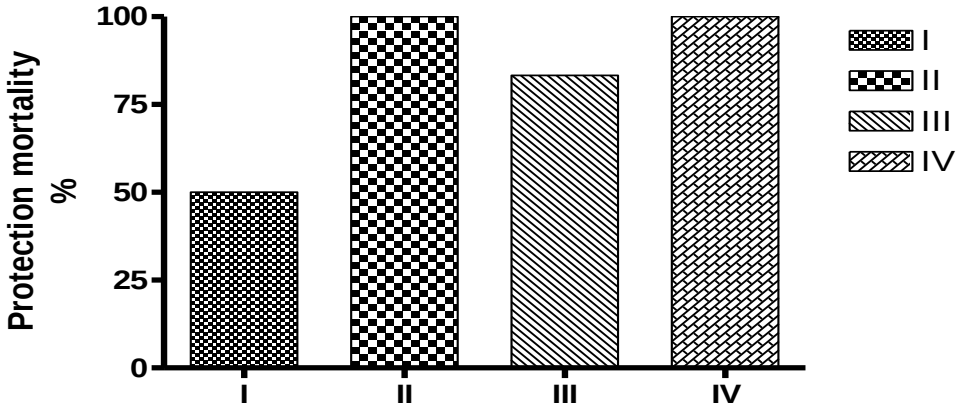


Figure 2. Protection mortality of ethanolic extract of *Macaranga peltata Roxb.* (EMP) On PTZ induced seizers in rats



RESULTS

Phytochemical analysis

The ethanol extract of *Macaranga peltata Roxb.* revealed the presence of steroids, Alkaloids, Reducing sugars, tannins, gums, flavonoids.

Effect of EMP on PTZ Induced epilepsy

The EMP at doses of 250 mg/kg and 500 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 EMP 250 mg/kg and 500 mg/kg have shown 44.90% and 60.74% protection respectively (Table 1).

DISCUSSIONS AND CONCLUSION

In India, studies have reported the prevalence rate of epilepsy varying from 1710 from 9780 cases per million populations. The modern conventional antiepileptic drugs (AEDs) are effective in approximately 50% of patients, many cases still remain resistant to AED treatment [8]. These drugs are associated with vast array of side effects including chronic toxicity, teratogenecity, adverse effects on cognition and behavior among others [9]. 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 EMP 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 GABAA receptor complex [10].

Since PTZ has been shown to interact with the GABA neurotransmission [11] 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 [12-17]**,** the antagonism of PTZ- induced seizures suggests the interaction of the EMP with the GABA-ergic neurotransmission.

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

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