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Evaluation of Anticonvulsant Activity of *Tragia plukenetii* R. Smith Leaf Extracts against Chemoshock Induced by Pentylenetetrazole in Mice.

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ABSTRACT

The aim of this study was to evaluate the anticonvulsant activity of *Tragia plukenetii* R. Smith leaf extracts against pentylenetetrazole induced convulsions in swiss albino mice. 20 swiss albino mice were selected and divided into five groups of four mice. The treatment groups were Group 1: Control group (0.9% normal saline, 5ml/ kg, i.p); Group-2: Standard group (Sodium valproate at a dose of 75 mg/kg, i.p); Group 3: Benzene leaf extract (TPBE-100mg/kg i.p); Group 4: Chloroform leaf extract (TPCE-100mg/kg i.p); Group 5: Methanolic leaf extract (TPME - 100mg/kg i.p). After 90 minutes of drug administration (pretreatment with anticonvulsant drug) all the treatment group animals were injected pentylenetetrazole 80mg/kg i.p. The anticonvulsant effect was evaluated using the effect of drugs on five phases of pentylenetetrazole induced convulsions such as a) tonic flexion, b) tonic extensor, c) clonic convulsion, d) stupor, e) recovery or death. The methanolic leaf extracts of *Tragia plukenetii R. Smith* shown significant anticonvulsant effect and therefore it was concluded that it may be useful in the treatment of tonic-clonic seizures.

Keywords: *Tragia plukenetii,* pentylenetetrazole, chemoshock, anticonvulsant, tonic-clonic, bioflavonoid.

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INTRODUCTION

The whole plant of *Tragia plukenetii* R. Smith (Family: Euphorbiaceae) is a erect, sub erect or prostrate herb, sometimes annual, up to 90 cm long, rarely more and liansccent ; indumentum sparse, mostly of painful stinging hairs, distributed throughout India from Punjab and lower Himalayas eastwards to Assam and Meghalaya, ascending up to an altitude of 750meters and southwards to Kerala. *Tragia plukenetii R. Smith* has been reported to possess having anti convulsant, analgesic, anti inflammatory, anti catatonic, learning and memory enhancement effects [1-8].

Epilepsy affects more than 50 million people worldwide. According to WHO reports, approximately 30% of patients suffering from epilepsy do not respond to currently available antiepileptic treatment. Even though the cause of drug resistance is still unknown, numerous neurological disorders such as cortical dysplasia, hippocampal sclerosis, mutations in ion channels and receptors, neuroinflammation and some autoimmune processes are linked to the development of pharmaco resistance in epilepsy. Therefore, there is a constant demand for novel therapeutics and more efficacious treatment options in the field of epilepsy. Epilepsy is a chronic neurological disorder characterized by recurrent unprovoked seizures. The seizures are transient signs and or symptoms abnormal, excessive or synchronous neuronal activity in the brain. Different types of epilepsies, i.e. generalized tonic-clonic seizure, petitmal, absence seizures or myoclonic seizures can be studied in laboratory studies.

There are two procedures used to study convulsions, and to test anti convulsant drugs in laboratory animals. The convulsions in rat or mice can be induced by giving high voltage current near brain (maximal electroshock) or by suitable CNS stimulants (chemoshock). Pentylenetetrazole closes the GABA-linked chloride channels in the brain. Therefore, it produces clonic convulsions. The pentylenetetrazole induced convulsions are divided into five phases such as a) tonic flexion b) tonic extensor c) clonic convulsion d) stupor and e) recovery or death. A substance is known to possess anticonvulsant property if it reduce or abolishes the tonic or clonic phase of convulsions. Onset of various phases of convulsions (sec) and their type, nature and severity (straub's tail, jerky movement of whole body, convulsions, and clonic convulsions) were observed and recorded.

MATERIALS AND METHODS

The pentylenetetrazole induced convulsions in swiss albino mice employed in this study is approved by Institutional Animal Ethics Committee of Chalapathi Institute of Pharmaceutical Sciences, Guntur and carried out as per CPCSEA guidelines. 20 swiss albino mice of either sex (body weight: 20-25g) obtained central animal house facility of Chalapathi Institute of Pharmaceutical Sciences were used in the study. The animals were housed in standard laboratory conditions (12-hr light/dark cycle, 21 ± 1°C, and relative humidity of 55 ± 5%) with free access to food and water prior to the experiments. Each animal was used only once in the experimental procedures. All experiments were carried out between 9 a.m. and 3 p.m. After 7 days of acclimatization to laboratory conditions, the animals were randomly assigned to five experimental groups, each consisting of four mice. The treatment groups were Group 1: Control group (0.9% normal saline, 5ml/ kg, i.p); Group-2: Standard group (Sodium valproate at a dose of 75 mg/kg, i.p); Group 3: Benzene leaf extract (TPBE-100mg/kg i.p); Group 4: Chloroform leaf extract (TPCE-100mg/kg i.p); Group 5: Methanolic leaf extract (TPME - 100mg/kg i.p). After 90 minutes of drug administration (pretreatment with anticonvulsant drug) all the treatment group animals were injected pentylenetetrazole 80mg/kg i.p. The anticonvulsant effect was evaluated using the effect of drugs on onset, nature and severity of five phases of pentylenetetrazole induced convulsions such as a) tonic flexion, b) tonic extensor, c) clonic convulsion, d) stupor, e) recovery or death [9].

Statistical Analysis

All the values are expressed as mean ± SD. Statistical significance was determined using One Way - ANOVA, followed by Dunnet's test. $P<0.05$ was considered to be significant.

RESULTS

Drugs used in the treatment of grandmal epilepsy act by multiple mechanisms a): phenytoin sodium prolongs the activation of Na^+ channels, b): barbiturates open the chloride channels, c): sodium valproate open

the chloride channels also reduce the flow Ca^{++} through T-type Ca^{++} channels. Maximal electroshock seizures produce tonic convulsion (characterized by extension of hind limbs) and clonic convulsion (characterized by continuous cycling motion of limbs). The group treated with normal saline showed tonic extensor phase and clonic phase convulsion and the duration was more than 10 seconds. The groups treated with phenytoin sodium and other *Tragia plukenetii R Smith* leaf extracts did not exhibit the extensor phase of convulsion. *Tragia plukenetii R Smith* leaf extracts already which is reported to possess flavonoids produced significant anticonvulsant activity when compared to the other treatment groups (Table 1and Figure 1). *Tragia plukenetii R Smith* methanolic leaf extracts (TPME-100mg/kg, i.p) showed significant anti-convulsant activity (***p<0.05) when compare to the control group.

Table1: Anti-convulsant activity of phenytoin against MES.

S.No	Treatment	% of Convulsions (Mean± SEM values)			
		Flexion	Extensor	Clonus	Stupor
1	Control	25±1.41	15±1.41	12±1.41	5±1.19
2	Standard (Phenytoin 25mg/kg, i.p)	17±0.94***	11±0.94***	5±0.94***	3±0.94***
3	TPBE - (100mg/kg, i.p)	24±0.47	14±0.47	14±0.47	4±0.47
4	TPCE - (100mg/kg, i.p)	20±0.94	13±0.94	7±0.94	4±0.47
5	TPME - (100mg/kg, i.p)	16±0.47***	9±0.47***	4±0.47***	3±0.47***

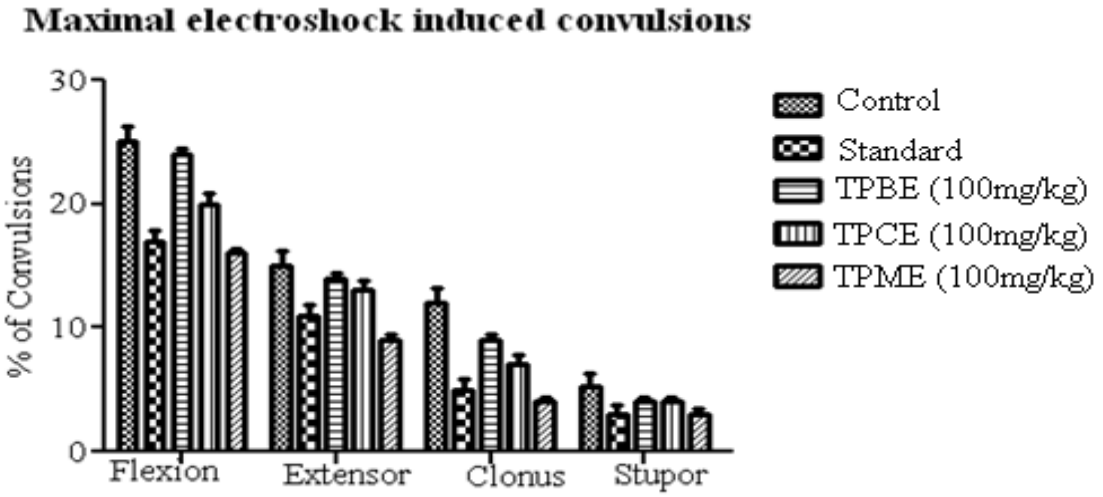

Figure 1: Anticonvulsant activity of *Tragia plukenetii* R. Smith leaf extracts.

CONCLUSION

The methanolic extract of *Tragia plukenetii* R. Smith has shown significant anti convulsant activity when compared to other treatments. The presence of bioflavonoid in the methanolic leaf extract of *Tragia plukenetii* R. Smith would have acted through several mechanisms i.e. prolongation of activation of Na^{+} channels or opening of chloride channels and therefore abolishing the tonic and clonic convulsions. It can be therefore ascertained that phytocompounds from *Tragia plukenetii* R. Smith may be useful to find breakthrough therapeutics for grandmal epilepsy.

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