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## Anti-convulsant activity of methanolic extract of *Butea monosperma* leaves

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### ABSTRACT

The Anticonvulsant activity of methanolic extract of leaves of *Butea monosperma* (100,200,400mg/kg;p.o) was assessed by using Maximal Electroshock seizure(MES), Pentylenetetrazole (80mg/kg;s.c) and Strychnine(4mg/kg;i.m) induced seizures in mice.The extract significantly delayed the onset of convulsions induced by Pentylenetetrazole(PTZ) and Maximal Electroshock seizure(MES) in a dose dependent manner. Anticonvulsant effect of the extract was comparable to clinically used antiepileptic drugs (Diazepam). But, the extract did not protect the Strychnine induced seizure at significant level even in the dose of 400mg/kg;p.o. These results suggest that the extract of *Butea monosperma* leaves possess anticonvulsant activity against Maximal Electroshock and Pentylenetetrazole induced seizure. The extract could have exhibited the activity by interfering with GABA, glutamatergic mechanism.

Keywords: Anticonvulsant, *Butea monosperma*, Maximal Electroshock seizure (MES), Pentylenetetrazole(PTZ), Strychnine.

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## INTRODUCTION

Epilepsy is a neurological disorder that affects a wide range of people throughout the world. It is a disorder of brain characterized by unpredictable and periodic occurrence of a transient alteration of behavior due to the disordered, synchronous and rhythmic firing of populations of brain neurons. Incidence of epilepsy in developed countries is approximately 50 per 100,000 while that of developing countries, it is 100 per 100,000. It has been observed that the presently available antiepileptic drugs are unable to control seizures effectively[1]. The conventional antiepileptic agents like phenytoin, carbamazepine and sodium valproate carry with them several serious side effects notably neurotoxicity. As majority of antiepileptic drugs are consumed life long, concomitant administration of other drugs predisposes to the risk of drug interaction. However, newer antiepileptics like gabapentin, vigabatrin, lamotrigine, etc are used supplemental to the conventional agents[2]. Thus, it is necessary to investigate for an antiepileptic agent that is highly efficacious as well as safe in terms of drug related toxicity. The aim of treating an epileptic patient is not only to abolish the occurrence of seizures but also to lead a self-sustained life[3].

In the Ayurvedic system of medicine, flowers of *Butea monosperma* (Lam) Kuntz (also known as Bastard Teak; Family: Fabaceae) are used as tonic, astringent, aphrodisiac, and diuretic. Flowers are reported to have astringent, diuretic and anti-inflammatory activity[4]. Roots are reported to be useful in the treatment of filariasis, night blindness, helminthiasis, piles, ulcers and tumors. Alcoholic concentrate of petals exhibit antiestrogenic activity and decoction of flowers is useful in diarrhoea and show anti-implantation activity. Flowers contain butin, butein, butrin, isobutrin, palasitrin, coreopsin and isocoreopsin, chalcones, and auronas[5,6].

This study is to evaluate the anti-convulsant activity of the Methanolic extract of *Butea monosperma* leaves (MEBM) using Maximal electroshock induced convulsion (MES) model, Pentylentetrazole (PTZ) and strychnine induced seizure model.

## MATERIALS AND METHODS

**Preparation of Extract:** *Butea monosperma* leaves were collected from Meerut, Uttarpradesh, India in the month of December 2008. The leaf was authenticated by Prof. Dr. P. Jayaraman Ph.D., The Director, Plant Anatomy Research Centre (PARC), Pharmacognosy Institute, West Tambaram, Chennai. The powdered dried leaves were defatted by extraction with petroleum ether (60-80°C). The defatted material was then extracted with ethanol (95%) for 72 hrs by hot percolation method and subjected to vacuum distillation. The final product was then freeze-dried and stored in the refrigerator. Preliminary phytochemical investigations of the extract were conducted as per the procedures described by Kokate[7] which revealed the presence of flavanoids, saponins, carbohydrates, phenolic compounds and alkaloids.

**Drugs:** PTZ and Diazepam were purchased from Sigma Chemical Co (Hyderabad, INDIA). Different concentrations of the drugs were prepared freshly by suspending in gum acacia in water. The solvents used were of analytical grade. Ethanol, Petroleum ether (BDH, Mumbai, India) and Gum acacia in water (M/S Hi-media, Mumbai, India) were used as solvent and vehicle respectively.

**Animals:** Albino mice weighing between 18-22 g were used. The animals were obtained from Animal house, SRM College of Pharmacy, Chennai. They were placed at random and allocated to treatment groups in polypropylene cages with paddy husk as bedding. Animals were housed at room temperature and relative humidity of 30-70%. A 12:12 hour light:dark cycle was followed. All animals were allowed to free access to water and fed with standard commercial pelleted rat/mice chaw. All the experimental procedures and protocols used in this study were reviewed by the Institutional Animal Ethics Committee (IAEC) and were in accordance with the guidelines of the IAEC.

## Anticonvulsant Study

Maximal electroshock-induced seizure model: All the drugs were administered orally 30 min prior to the electroshock. The electroshock was induced in animal by passing a current of 45mA for 0.2 sec duration through electro-convulsimeter (Techno India) using corneal electrodes. The incidence and duration of extensor tonus were noted. In this type of seizure model, the animals were divided into five groups with six animals.

Grouping:

- Group I : Control group- vehicle treated.
- Group II : Standard (Diazepam, 1 mg/kg;p.o)[8]
- Group III : Methanolic extract of Butea monosperma(100mg/kg).
- Group IV : Methanolic extract of Butea monosperma (200mg/kg).
- Group V : Methanolic extract of Butea monosperma(400mg/kg).

Pentylenetetrazole-induced seizure model: All the drugs were administered orally 30 min prior to the administration of Pentylenetetrazole (80 mg/kg) by subcutaneous route. The animals were observed for 1 hour by placing in a separate cage. The onset of clonic convulsion were noted[9].

Strychnine-induced seizure model: All the drugs were administered orally 30 min prior to the administration of strychnine (4mg/kg) by intramuscular injection. Any mouse that did not convulse within 30min was considered protected[10].

Statistical analysis: The values were expressed as mean  $\pm$  SEM. The statistical analysis was carried out by one way analysis of variance (ANOVA) followed by Dunnet's-test.  $P < 0.05$  was considered significant.

## RESULTS

The anticonvulsant activity of Butea monosperma at various dose levels viz, 100,200 and 400mg/kg;p.o was studied by Maximal electroshock, Pentylenetetrazole and Strychnine induced seizure models.

In the MES model, Butea monosperma (100mg/kg, 200mg/kg,400mg/kg) showed significant reduction in duration of convulsion in a dose dependent manner. The effect of the extract(400mg/kg) was comparable to that of the standard drug diazepam.(Table1)

In Pentylenetetrazole induced seizure model, MEPM produced significant ( $p < 0.05$ ) reduction in onset of convulsion and the effect at 400mg/kg dose was comparable to that produced by diazepam. (Table 2)

In Strychnine induced seizure model, the extract did not show significant anti-convulsant activity even at highest dose, 400 mg/kg.

## DISCUSSION

The results of the present study indicate that the methanolic extract of Butea monosperma leaves possesses significant anticonvulsant activity except that in strychnine induced convulsions. GABA is an inhibitory neurotransmitter while glutamic acid is an excitatory neurotransmitter in the brain. Inhibition of GABA and enhancement of glutamate activity have been shown to be underlying factors in epilepsy[11,12]. Diazepam, the standard antiepileptic drug had anticonvulsant effect on both PTZ-induced seizures and maximal electroshock-induced seizures[13].

The maximal electroshock test is the most widely used animal model in antiepileptic drug discovery, because seizure induction is simple and the predictive value for detecting clinically effective antiepileptic is high. This method identifies the drug with activity against generalized tonic-clonic seizures and partial seizures using

clinically established antiepileptic drug. The pharmacology of acute maximal electroshock dose not differs from the pharmacology of generalized tonic-clonic seizures in genetic models with chronic epilepsy[8]. It has often been stated that antiepileptic drugs that block MES-induced tonic extension act by blocking seizure spread. Moreover, MES-induced tonic extension can be prevented either by drugs that inhibit voltage-dependent  $\text{Na}^+$  channels, such as phenytoin, valproate, felbamate and lamotrigine or by drugs that block glutamatergic excitation mediated by the N-methyl-D-aspartate (NMDA) receptor, such as felbamate[14]. Thus the anticonvulsant activity exhibited by the extract shows that it could have blocked the seizure spread by inhibiting  $\text{Na}^+$  channels and glutamatergic excitation through NMDA receptor. The study also suggests that the extract would be effective against generalized tonic-clonic and partial seizures.

PTZ is a most frequently used substance as well an acute experimental model in the preliminary screening to test potential anticonvulsant drugs. The mechanism by which PTZ is believed to exert its action is by acting as an antagonist at the  $\text{GABA}_A$  receptor complex[10,11]. On the other hand, drugs that reduce T-type  $\text{Ca}^{2+}$  currents, such as ethosuximide can prevent seizures induced by PTZ[13]. Drugs protecting against tonic – clonic seizures induced by PTZ are considered to be useful to control myoclonic and absence seizures in humans[9]. The clonic seizure in PTZ model could be due to decreased seizure threshold[15]. Since the Butea monosperma extract delayed the occurrence of PTZ induced convulsion, it is probable that it may be by interfering with GABA aminergic mechanism and  $\text{Ca}^{2+}$  channels.

Strychnine has been demonstrated to have a well defined mechanism of convulsant action reported to be by directly antagonizing the inhibitory spinal cord and brainstem reflexes of glycine and thus increasing spinal reflexes[10]. Failure to inhibit strychnine induced seizures by the extract indicates its lack of effect on the glycine receptors in the spinalcord. The flavanoids present in Buteamonosperma could have exhibited anticonvulsant activity because the flavanoids possess anticonvulsant activity[8]. Further studies are needed for identifying the molecule responsible for the anticonvulsant activity.

Table1: Effect of Butea monosperma extract on Maximal Electroshock induced model

Treatment	Tonic hind limb extension phase in sec(mean±SEM)	Convulsions(%)	Mortality
Control	19 ± 1.23	100	100
MEBM(100mg/kg)	10.63 ± 1.38*	66	20.0
MEBM(200mg/kg)	5.24 ± 1.08*	50	20.8
MEBM(400mg/kg)	1.54 ± 0.62*	25	22.0
Diazepam(2mg/kg)	0	0	0

Values are expressed in mean±SEM. \*P < 0.05 when compared to control, n=6

Table 2: Effect of Butea monosperma extract on Pentylentetrazole induced model

Treatment	Dose (mg/kg)	Onset of clonic convulsions in sec (mean±SEM)	Incidence of convulsions (%)
Vehicle		109.5 ± 9.8	100
MEBM	100	382.5±11.6 *	66.6
	200	815.6 ± 23.3*	33.3
	400	A	0
Diazepam	2	A	0

n = 6, \*P<0.05 when compared to control, A = Absence of convulsions..



## CONCLUSION

Thus, the methanolic extract of *Butea monosperma* leaves possesses anticonvulsant property against MES and PTZ induced seizures which could be by interfering with GABA, glutaminergic mechanism and Na<sup>+</sup>, Ca<sup>2+</sup> channels.

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