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Evaluation of anti-convulsant activity of *Mucuna pruriens* seed extracts

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ABSTRACT

The anticonvulsant activity of butanol seed extract of *Mucuna pruriens* was investigated by studying the effects on seizures induced by pentylentetrazole and maximal electroshock convulsive methods in mice. *Mucuna pruriens* (100 and 200 mg/kg) significantly reduced the duration of convulsion in tonic seizure induced by pentylentetrazole (80mg/kg, intraperitoneally). *Mucuna pruriens* (100 and 200 mg/kg orally) significantly reduced the tonic extensor convulsion in both the experimental models and the effects were compared with diphenylhydantoin in maximal electroshock method and Sodium valproate in pentylentetrazole induced seizures method as standard control respectively. The data obtained suggest that *Mucuna pruriens* have mild to moderate anticonvulsant property and may be due to involvement of Gamma amino butyric acid.

Keywords: anticonvulsant activity, butanol extract, *Mucuna pruriens*, pentylentetrazole.

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INTRODUCTION:

Epilepsy is a common chronic neurological disorder, characterized by recurrent unprovoked seizures¹. Incidence of epilepsy in developed countries is approximately 50 per 100,000 while that of developing country is 100 per 100,000². It has been observed that the presently available antiepileptic drugs are unable to control seizures effectively in as many as 25% of the patients³. The conventional antiepileptic agents like phenytoin, carbamazepine and sodium valproate carry with them several serious side effects notably neurotoxicity⁴. 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 agents⁵. Thus, it is necessary to investigate for an antiepileptic agent that is highly efficacious as well as safe in terms of drug related toxicity.

Mucuna pruriens Linn. Is belongs to the family fabaceae, commonly known as cowhage plant or kapikacho or kevach in Hindi, is the most popular drug in Ayurvedic system of medicine⁶. *Mucuna pruriens* is a twinning herb found all over tropical parts of India. It, an Indian indigenous leguminous plant, is well known for producing itch. This property is attributed to the trichomes (hair) present on the pods. It has been established that this unique property is accounted by the presence of 5-hydroxy tryptamine (5-HT) in the hair⁷. It is also likely that histamine and kinin like substances may also be responsible. Some reports show that anti-histaminics afford protection against the itch⁸. It has been reported to be anti-diabetic⁹. *Mucuna pruriens* seeds are herbaceous forage and food legumes that have for a long time found widespread usage as rotation crops for management of various pests and pathogens, as well as in soil improvement and weed control^{10, 11}. *Mucuna pruriens* plant possess valuable medicinal properties and it has been studied for various activities like itching¹², antioxidant¹³ anti diabetic¹⁴, anti neoplastic, anti epileptic, antimicrobial¹⁵ aphrodisiac¹⁶ and anthelmintic activity¹⁷. *Mucuna pruriens* has also been shown to be neuro-protective and as a fertility agent (in men). It also has analgesic and anti-inflammatory activities¹⁸. The aim of this present study is to evaluate the anti-convulsant activity of butanol extracts of *Mucuna pruriens* seed by studying the effects on seizures induced by pentylentetrazole and maximal electroshock convulsive methods in mice.

MATERIALS AND METHODS

Plant material

The seeds of *Mucuna pruriens* were purchased from local market of Dehradun, Uttarakhand. The seeds were washed with water, shade-dried and were pulverized with a mechanical grinder.

Extraction

The coarse powdered seeds of *Mucuna pruriens* were loaded into soxhlet extractor and were subjected to extraction for about 25–30 h with butanol. After extraction the solvent was distilled off and the extract was concentrated under reduced pressure on a water bath at a temperature below 50°C to a syrupy consistency. Then it was dried in the dessicator. The yield was about 8%.

Animals

Male mice 25 ± 2 g, with three months of age, were used throughout this study. The animals were randomly housed in appropriated cages at 25 ± 2 °C on a 12 h light/dark cycle (lights on 06:00-18:00) with free access to food and water. The protocol of study was approved by animal ethics committee of the department and the experiments were carried out as per the guidelines of CPCSEA.

Drugs

Sodium Valproate (50 mg/kg, intraperitoneally) used as a standard drug for potentiation study in PTZ induced seizures method.

Diphenylhydantoin (Parke Davis India, 20 mg/kg) used as standard drug to see the potentiation effect of test drug in MES method.

Pentylenetetrazole (Bochemzer-knoll, Ltd. used as convulsion inducer.

Test drug butanolic seed extract of *Mucuna pruriens* was used for the present study in volume 10ml/kg body weight, orally. The doses were selected by preliminary trials.

Acute oral Toxicity study

The acute oral toxicity study was carried out as per the guidelines set by Organization for Economic Co-operation and Development (OECD), registered under (CPCSEA), ministry of Social Justice and Empowerment, Government of India. Different doses of extract (80, 100, 120, 240, 480, 960 and 1200 mg/kg) were administered orally to groups of male mice ($n = 6$) and the groups were observed for 48 hr and at the end of this period mortality was recorded for each group.

Induction of seizures

Pentylenetetrazole (PTZ)-induced convulsion

In the present study (PTZ), five groups were employed and each group comprised six animals. PTZ (80 mg/kg i.p.) was used to induce clonic convulsions. Animals were divided into five groups ($n = 6$), control group received vehicle (10 ml/kg) and standard group was treated with Sodium Valproate (50 mg/kg, i.p.) 30 min prior to the injection of PTZ (80 mg/kg, i.p.). The

remaining groups were treated with 100 and 200 mg/kg of butanol extract orally. After 30 min of drug administration, the mice were treated with PTZ at a dose of 80 mg/kg (i.p.). Immediately after the injection of the convulsant, mice were individually placed in plastic boxes and observed for the time onset of clonic seizures, percent clonic seizures and deaths. The incidence of deaths was noted until 48 h after the injection of PTZ.

Group-I (pentylenetetrazole - treated control group), mice were administered with pentylenetetrazole (80 mg/kg) via intraperitoneal route.

Group-II (vehicle + PTZ-treated control group), Mice were administered with vehicle 10 ml/kg, intraperitoneal 30 min prior to the injection of Pentylenetetrazole (80 mg/kg, intraperitoneal).

Group-III (sodium valproate + PTZ-treated standard control group), mice were administered with sodium valproate 50 mg/kg, intraperitoneal 30 min prior to the injection of pentylenetetrazole.

Group-IV (low-dose extract + pentylenetetrazole treated group), mice were administered with extract 100 mg/kg, oral 60 min prior to the injection of pentylenetetrazole.

Group-V (high-dose extract + pentylenetetrazole treated group), mice were administered with extract 200 mg/kg, oral 60 min prior to the injection of pentylenetetrazole.

Maximal electroshock (MES) test

Maximal electroshock test (MES) that induces reproducible tonic convulsion characterized by tonic hind limb extension (THE) was performed. In this experiment, electroconvulsive shock (150 V, 0.2 s) was delivered through electrodes (ECT UNIT 7801- Ugo Basile) to induce tonic hind limb extension (THE). In the present study one group was employed and group comprised six animals. The group is underwent to shock and then treated with the vehicle further treatment with the extract and last with the Diphenylhydantoin.

Statistical analysis:

The data obtained in experimental models were evaluated by one way analysis of variance (ANOVA) followed by Dunnett's test. Differences between means were considered to be statistically significant when $p < 0.05$. Data obtained from the study were statistically analyzed using one-way ANOVA. A value of $P < 0.05$ was considered to be statistically significant.

RESULTS AND DISCUSSION

The butanolic extract of *Mucuna pruriens* inhibited in a significant manner, pentylenetetrazole-induced seizures as assessed in terms of time of appearance of Straub's tail and onset of jerky movements of whole body and convulsions. The activity of the plant may be due to the activity of present alkaloid as GABA Potentiating effect. In conclusion, agents that have the ability of

attenuating the appearance of seizures might also have anticonvulsant ability. The results of the anticonvulsant activity of butanolic extract of *Mucuna pruriens* seeds on PTZ induced convulsions are shown in Table 1. The butanolic extract (100 and 200mg/kg) of *Mucuna pruriens* seeds exhibited a significant anticonvulsant effect by increasing the latency, onset of clonic convulsion and decreases onset of tonic seizures. The butanolic extract also exhibited a dose dependent significant reduction in various phases of epileptic seizures on comparison with the reference standard Diphenylhydantoin 20mg/kg i.p. There was also a significant reduction in the time required for the righting reflex (recovery) in the extract treated groups (Table 2).

Table 1: Effect of butanolic extract of *Mucuna pruriens* seeds on MES induced seizures in mice.

Treatment	Time duration (sec)			
	Tonic flexion (mean ±SEM)	Tonic extension (mean ±SEM)	Clonic stupor (mean ±SEM)	Mortality
Control	45±1.48	67±6.24	200±4.23	100
Diazepam 20mg/kg	53±6.34*	95±9.40*	378±23.4*	00
Extract 100mg/kg	41.6±5.21*	60±6.05**	219±37.6*	22.03
Extract 200mg/kg	60.8±7.02*	A	357±45.1*	20.13

*P < 0.05, **P < 0.001 compared with control, n = 6.

Table 2: Effect of butanolic extract of *Mucuna pruriens* seeds on pentylenetetrazol induced seizures in mice.

Treatment	Dose mg/kg	Onset of clonic convulsions in sec (mean ±SEM)	Incidence of convulsions (%)
Control	Vehicle	147±24.67	100
Sodium Valproate	50	A	0
Butanol Extract	100	654.7±54.2*	65.3
Butanol Extract	200	A	15.07

n = 6 in each group, *P < 0.05 when compared to the vehicle treated group. A = Absence of convulsions.

CONCLUSION

It can be concluded from the study that the anticonvulsant effects of butanolic seed extract of *Mucuna pruriens* may be via nonspecific mechanisms. However, extensive studies are needed to evaluate the precise mechanism, active principles, and remedy for convulsive disorders.

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