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INVESTIGATION OF EFFECT OF CELASTRUS ON THE BRAIN AMINES WITH INDUCTION OF SEIZURES

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ABSTRACT

Epilepsy is the CNS disorder in which brain activity becomes abnormal causing seizures, and period of unusual behavior,loss of awareness and sensation. The world population are affected by 0.5 to 1% . The mechanism of epileptic seizures are excessive and abnormal neuronal activity in the brain of the cortex. The most common type of seizures are convulsive, generalized seizures and partial seizures. The present study was reported to identify the effect of Celastrus paniculata in rats brain of biogenic amine levels after induced seizures of MES & PTZ models. In *Celastrus paniculata* extract treated rats, monoamines such as NA, DA, 5-HT and GABA levels significantly restored on forebrain. Thus EECP increases the seizure threshold and decreased the susceptibility to MES and PTZ induced seizure in rats. Hence we suggest that ethanol extract of leaves of *Celastrus paniculata L.* possess antiepileptic properties that may be due to restored the biogenic amines in rat brain.

Keywords: Brain amines, Extract, Herbal, *Celastrus paniculata*.

INTRODUCTION

Epilepsy is the CNS disorder in which brain activity becomes abnormal causing seizures, and period of unusual behavior,loss of awareness and sensation. The world population are affected by 0.5 to 1% . The mechanism of epileptic seizures are excessive and abnormal neuronal activity in the brain of the cortex. The most common type of seizures are convulsive, generalized seizures and partial seizures. The generalized seizures may affect both hemispheres of the brain. Focal seizures affects one hemisphere of the brain and then progressed as generalized seizures. Remaining 40% seizures are non convulsive, that is absence seizures which shows reduced level of consciousness and lasts about 10seconds. The occurance of seizures because of imbalance between inhibitory and excitatory signals which consists of serotonin, GABA, dopamine, nor adrenaline. Dopamine mad serotonin are implicated in pathophysiology of seizures but are controversial. Synthetic molecules are present involved in epileptic drugs. The medicinal plants are used for the treatment of epilepsy which causes anti convulsant activity and anticonvulsant screening by animal model which shows invaluable source to produce new anti epileptic compounds [1-3].

Other species of plants having stinging hairs occurs from melanesia to other tropical asia & australia. Children who are affected with fits, expulsion of afterbirth and sickness after birth are cured by using the liquid which was extracted from leaves. Venereal diseases are treated by using the tea which was made of leaves and stinging needles. The leaves of fiji are used for the treatment of convulsion & theses leaves are used for the treatment of joints/bone pain, intestinal filariasis and postnatal depression. The present study was reported to identify the effect of Celastrus paniculata in rats brain of biogenic amine levels after induced seizures of MES & PTZ models [4-6].

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MATERIALS AND METHODS

Preparation of extracts

Leaves of the whole plants were dried in shade, separated and made to dry powder. It was then passed through the 40 mesh sieve. A weighed quantity (60gm) of the powder was subjected to continuous hot extraction in Soxhlet Apparatus. The extract was evaporated under reduced pressure using rotary evaporator until all the solvent has been removed to give an extract sample. Percentage yield of ethanolic (95%) extract of *Celastrus paniculata* was found to be 17.5 % w/w.

Animals used

Albino wistar rats (150-230g) of either sex were obtained from the animal house. The animals were 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)

Experimental design

Albino wistar rats were divided into four groups of six animals each. Group I received vehicle control (1% w/v SCMC, 1ml/100 g) whereas Group-II received standard drug (Phenytoin, 25mg/kg) *i.p*, Group-III and IV, received 95% ethanolic extract of the leaves of *Celastrus paniculata* (L.) (200 and 400 mg/kg b.w) *p.o* respectively for 14 days. On the 14th day, Seizures are induced to all the groups by using an Electro convulsiometer. The duration of various phases of epilepsy were observed.

Pentylenetetrazole (90mg/kg b.w, *s.c*) was administered to other groups to induce clonic convulsions after above respective treatment. Animals were observed for a period of 30mins post– PTZ administration.

Determination of brain mono amines

On the 14th day after observed the convulsion all groups rats were sacrificed, whole brain was dissected out and separated the forebrain. Weighed quantity of tissue and was homogenized in 0.1 mL hydrochloric acid - butanol, (0.85 ml of 37% hydrochloric acid in one liter *n*- butanol for spectroscopy) for 1 min in a cool environment. The sample was then centrifuged for 10 min at 2,000 rpm. 0.08 mL of supernatant phase was removed and added to an Eppendorf reagent tube containing 0.2 mL of heptane (for spectroscopy) and 0.025 mL 0.1 M hydrochloric acid. After 10 min of vigorous shaking, the tube was centrifuged under same conditions to separate two phases. Upper organic phase was discarded and the aqueous phase (0.02 mL) was used for estimation of Serotonin, Nor Adrenaline and Dopamine assay [7-9].

Estimation of brain GABA content

The brain amino butyric acid (GABA content was estimated according to the method of Lowe et al., (1958) [10] Animals were sacrificed by decapitation and brains were rapidly removed, and separated forebrain region. It was blotted, weighed and placed in 5ml of ice-cold trichloroaceticacid (10% w/v), then homogenized and centrifuged at 10,000rpm for 10min at 0°C. A sample (0.1ml) of tissue extract was placed in 0.2ml of 0.14 M ninhydrin solution in 0.5M corbonate-bicorbonate 1 buffer (pH9.95), kept in a water bath at 60°C for 30min, then cooled and treated with 5ml of copper tartarate reagent (0.16% disodium carbonate, 0.03% copper sulphate and 0.0329% tartaric acid). After 10min fluorescence at 377/455nm in a spectofluorimeter was recorded.

Statistical Analysis

The data were expressed as mean ± standard error mean (S.E.M).The Significance of differences among the group was assessed using one way and multiple way analyses of variance (ANOVA). The test followed by Dunnet's test p values less than 0.05 were considered as significance.

RESULTS

Noradrenaline of Table 1 &2 shows the noradrenaline levels are reduced significantly($P<0.001$) in forebrain of controlled epileptic aanimals of MES & PTZ models. In animals, The dose EECP 200&400 mg/kg of standard drugs diazepam and phenytoin are highly significant ($p<0.05$ & $p<0.01$) at forebrain of dopamine levels of rats. In table 1&2 of MES & PTZ models, the forebrain of epileptic controlled animals shows reduced dopamine levels significantly ($p<0.01$). The EECP doses 200 & 400 mg/kg shows the standard diazepam & penytoin drugs which treats animals having highly significant ($p<0.05$& $p<0.01$). dopamine levels in rats forebrain. The forebrain of epileptic controlled animals of MES & PTZ models shows reduced serotonin levels significantly ($p<0.01$). EECP dose 200 & 400 mg/kg of standard phenytoin & diazepam drugs are used to treat animals which shows highly significant serotonin levels in forebrain of Rats.

GABA

In this MES and PTZ model, observes reduced GABA levels $p<0.01$) in forebrain of epileptic controlled drugs. The dose EECP 200&400 mg/kg of pen yt and diazepam standard drugs are used to treat animals which shows highly significant GABA levels in rats forebrain.

DISCUSSION

In present study, the established antiepileptic drugs such as Phenytoin and diazepam restored the monoamine levels on brain. Similarly EECP significantly ($p<0.05$ & $p<0.01$) increased monoamines levels in forebrain of rats. Many drugs that increase the brain contents of GABA have exhibited anticonvulsant activity against seizures induced by MES and PTZ [18]. MES is probably the best validated method for assessment of anti-epileptic drugs in generalized tonic-clonic seizures**.**

Table 1: Effect of EECP on brain chemicals in PTZ induced epilepsy

Group	Design of Treatment	Noradrenaline	Dopamine	Serotonin	GABA
I	Vehicle Control(SCMC 1ml/100gm)	766±6.73	652.67±4.24	192±3.02	286±2.56
II	MES (SCMC 1ml/100gm)	434.72±3.45$^{a\,**}$	482.81±5.52 $^{a\,**}$	74±2.93 $^{a\,**}$	233.29±3.36 $^{a\,**}$
III	Phenytoin 25mg/kg,*i.p*	590±5.22 $^{b\,**}$	699.74±4.63$^{b\,**}$	100.25±4.80$^{b\,**}$	290.93±2.47 $^{b\,**}$
IV	EECP 400 mg/kg,*p.o*	574.19±6.13^{b**}	657±2.89^{b**}	90.42±1.04^{b**}	279.6±3.18^{b**}
V	EECP 200 mg/kg,*p.o*	750.45±5.39^{b*}	83.90±5.6^{b*}	85±0.93^{b*}	273.78±4.9^{b**}

Values are expressed as mean ± SEM of six observations. Comparison between: **a**- Group I Vs Group II, **b**- Group III Vs Group IV and Group V. Statistical significant test for comparison was done by ANOVA, followed by Dunnet's 't' test *p<0.05;** p<0.01; Units = pg/mg of wet tissue.

Table 2: Effect of EECP on brain chemicals in PTZ induced epilepsy

Group	Design of Treatment	Noradrenaline	Dopamine	Serotonin	GABA
I	Vehicle Control(SCMC 1ml/100gm)	766±6.67	852.61±4.23	192±3.41	292.94±2.5
II	MES (SCMC 1ml/100gm)	529.22±3.45a **	577.94±5.72 a **	96.7±4.03a **	206.25±1.82a**
III	Diazepam (4mg/kg), p.o	610±4.6b **	900.24±6.59b **	133.94±3.25 b **	293.46±2.43b**
IV	EECP 400 mg/kg,p.o	750.63±5.19b*	896.71±3.67b**	128.68±2.09b*	282±3.54b**
V	EECP 200 mg/kg,p.o	768.21±6.34bns	772.67±5.01b**	117.43±1.92 b	277.72±2.03b**

Values are expressed as mean ± SEM of six observations. Comparison between: **a** - Group I Vs Group II, **b**- Group III Vs Group IV and Group V. Statistical significant test for comparison was done by ANOVA, followed by Dunnet's 't' test *p<0.05;** p<0.01; Units = pg/mg of wet tissue.

CONCLUSION

Our findings support the hypothesis that decreased the monoamines levels in rat brain after induction of seizure. In *Celastrus paniculata* extract treated rats, monoamines such as NA, DA, 5-HT and GABA levels significantly restored on forebrain. Thus EECP increases the seizure threshold and decreased the susceptibility to MES and PTZ induced seizure in rats. Hence we suggest that ethanol extract of leaves of *Celastrus paniculata L.* possess antiepileptic properties that may be due to restored the biogenic amines in rat brain.

CONFLICT OF INTEREST

Authors declare no conflict of interest

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