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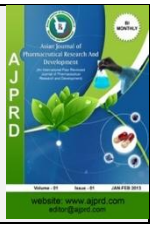

Open Access Research Article

Evaluation of Antiepileptic Activity of Ficusracemosa in Chemicals Induced Epilepsy in Mice

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A B S T R A C T

Objective: To Evaluvate of Antiepileptic Acivity of Ficus Racemosa Extract Against Chemicals Induced epilepsy in mice, ficusracemosa is also used as antihyperglycemic, antiinflammatery , hepatoprotective action. **Method :** Anticonvulsant activity of three distinct dose levels of ethanolic extract of Ficus racemosa (100, 200, and 400 mg/kg) was tested in Swiss albino mice in seizures induced by Pentylenetetrazol (PTZ). Statistical analysis was carried out by one-way analysis of variance followed by Dunnett's test. **Results**: The presence of , flavonoids, were detected in the bark of Ficus racemosa. The extract dose-dependent effect in the delay of the onset of seizures and reduction in the duration of seizure. **Conclusion :** The ethanolic extract of Ficus racemosa exhibited significant and dose-dependent antiepileptic activity, which may be due to the presence of antioxidant principles like flavanoidsa nd other phytoconstituent produce protective activity against PTZ.

Keywords: Pentelynetetrazole, Anticonvulsant activity, diazepam, *Ficus racemosa* bark.

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INTRODUCTION:

Epilepsy is a chronic disorder of central nervous system, Epilepsy are disorders characterized by paroxysmal, abnormal, excessive or synchronous neuronal activity in the brain with 5-10% of the population. There are many antiepileptic agents available for treatment but associated with side-effects such as depression, ischemia, impaired cognition and motor disability. This made man to search for alternative medicine from natural source.

Medicinal plants used for the therapy of epilepsy in traditional medicine have been shown to anticonvulsant activities. which can be much cheaper and less time-consuming. Several useful medicines derived from plants have been discovered from scientific investigation of traditional claim.

Ficus racemosa is also known as F. Glomerata. Ficus racemosa has various synonyms like Udumbara (U gular etc. It is used in treatment of burning sensation and obesity, anti-ulcer antipyretic antidiabetic diuretic, like astringent, and useful in vaginaldisorder Epilepsy is the term used for a group of disorders characterized by recurrent spontaneous seizures and involves hyperexcitable neurons. It is assumed that there is an imbalance between inhibitory GABA-mediated and excitatory glutamate-mediated neurotransmission. It is commonly associated with the brain.

The seizure activity during epilepsy decreases the antioxidant defense mechanism in the brain and increases the amount of free radicals, which further induces the oxidative stress. Free radicals (FR) can be defined as molecules or molecular fragments that contain one or more unpaired electrons. These free radicals were involved in causation of lipid peroxidation, brain edema and epilepsy.

Material and Methods:

Drug andchemicals

The standard drugs of Diazepam were obtain form (Ranbaxy), Pentylenetetrazole obtained from (OZONE® INTERNATIONAL (INDIA) , All other chemicals used were of analytical grade.

Plant collection:

The bark of ficusracemosa plant were collected and shade dried and made in coarse powder

After collection Ficus racemosa bark were cleaned, washed to remove any dirt, dust and foreign particles. Botanical identity of plant specimen was authenticated by Dr. S. A. Mohite, Head, Department of Botany, Lal Bahadur Shastri College, Satara (MS), India. A voucher specimen of the bark has been deposited in the department for future reference .The bark were coarsely powdered and further utilized for preparation of ethanol extract.

Plant Extraction:

The ethanol extraction of bark of Ficus racemosa was carried out by soxhlet apparatus. The bark were crushed and ground to powder and placed into extractor. The ethanol was poured on powder with three cycles. After that extraction process was started and continued till appearance of solvent in syphon tube turns brown to clear. Then brown colored solvent mixture from round bottom flask was collected and evaporated with the help of rotary evaporator to get a solid residue. The residue was placed in a vacuum desiccator and was further used for the experiments.

Pharmacological Investigation:

Experimental Animals: Adult Swiss albino mice (25-30 g) were used for this study. The animals were housed at 24°C ± 2°C and relative humidity 55 ± 5 with 12:12 h light and dark cycle. They were provided food and water *ad libitum*. The experimental protocol was approved by the Institutional Animals Ethics Committee of Yashoda College of Pharmacy, Satara , Maharashtra.

Acute toxicity study:

The acute oral toxicity was performed as per the Organization for economic co- operation and development (OECD) guideline 423.[14]Acute toxicity study was performed in Swiss albino mice. The animals were grouped with three numbers in each were administered orally with the ethonolic extract of Ficus racemosa was given to animals with starting dose 300mg/kg in 0.1% CMC for first According to observations of first group, study was carried out further on next group with dose 2000 mg/kg. From obtained results it was clear that no death as well as no toxicological signs in animals so, for confirmation of safety of extract study was repeated with dose 2000mg/kg on third group. After administration of extract, animals were observed carefully for first 30 min. and periodically for 24 h with special attention during first four hours. Animals were further observed daily for subsequent 14 days. Effects such as changes in skin fur, eyes and mucous membranes were observed daily. Animals were further observed for salivation, diarrhea, tremors, lethargy, convulsions, sleep, and coma. The parameters like body weight, food, and water intake were checked periodically every two days[20].

Evaluation of antiepileptic activity:

PTZ-induced convulsions in mice

Swiss mice of either sex were randomly divided in to Five different groups of six mice each. Group I received the vehicle, Group II received the standard drug, Diazepam at the dose of 5 mg/kg, i.p. Group III, IV and V received EEFR at the doses of 100, 200 and 400 mg/kg, p.o. respectively. Group I mice were administered with PTZ (80mg/kg, i.p.) 1 h after vehicle. Group

II mice received PTZ 30 min after Diazepam (5 mg/kg, i.p.). Group III,IV and V mice received different doses of plant extracts, p.o. 1 h before PTZ. Onset time as well as duration of convulsions were recorded [12].

Statistical analysis

The data were analyzed using one-way analysis of variance, followed by Dunnett's test. $P < 0.05$ was considered as sta1tistically significant. The data are expressed as mean ± standard deviation.

RESULT:

Preliminary phytochemicalinvestigation

Table 1.Shows the findings of qualitative analysis of Preliminary phytochemical screening of Ethanolic extract of ficusracemosa bark indicated the presence of steroids, triterpenoids, polyphenolics, coumarins, flavonoids and tannins, while alkaloids and saponins were absent.

Table 1. Qualitative analysis of the phytochemicals inextracts of *Ficus racemose bark*

Phytoconstituent	EEFR
Alkaloid	-
Carbohydrate	+
Protein	_
Steroid	+
Flavonoid	+
Tannin	_
Saponin	_
Lipid	+

+ indicating Positive , - indicate negative and EEFR indicate Ethanolic Extract of ficus Racemosa

PHARMACOLOGICAL INVESTIGATIONS

Acute toxicitystudy

The acute toxicity study began with a 300mg/kg starting dose. During a 14-day observation period, oral administration of a 300 mg/kg dosage of ethanol extract of *ficusracemosa bark* caused no significant toxicity.

From above results it is clear that given dose was safe and hence further study was performed by administering 2000mg/kg dose of extract to next group of animals. There were no indicators of toxicity and mortality [Table 2.], as well as the animals' morphological characteristics and general appearance did not change. There was no salivation, diarrhoea, tremors, convulsions, lethargy or unusual behavior observed during study in treatment group. For further confirmation of results effect was checked by giving same dose (2000mg/kg) to another group of three animals and results parameters were normal. The oral LD_{50}could be over 2000mg/kg body weight. As a result, greater dose testing of the extracts may not be necessary, and the extracts were practically non-toxic.

Table 2: Effect of *Ficus racemosa bark* extract for sign of toxicity and mortality (n = 3).

Group	Treatment	Sign of toxicity (ST/NB)	Mortality (D/S)
Normal Control	Vehicle	0/3	0/3
Aqueous extract	2000 mg/kg	0/3	0/3
Alcoholic extract	2000 mg/kg	0/3	0/3

STs = Sign of toxicity, NB = Normal behaviour, D = Died, S = Survived.

Table 3: Effects of ficus racemose bark extract dose 2000mg/kg on morphological characteristics and general appearance in mice (n=3)

Sr. No.	Response	Before	After
1.	Alertness	Normal	Normal
2.	Touch response	Normal	Normal
3.	Torch response	Normal	Normal
4.	salivation,	Normal	Normal
5.	Diarrhoea	Absent	Absent
6.	Tremors	Absent	Absent
7.	Convulsions	Absent	Absent
8.	Lethargy	Absent	Absent
9.	Skin fur	Normal	Normal
10.	Pinna reflux	Normal	Normal
11.	Corneal reflux	Present	Present
12.	Pupils	Normal	Normal
13.	Lacrimation	Normal	Normal
14.	Gripping strength	Normal	Normal
15.	Urination	Normal	Normal
16.	Hyper activity	Absent	Absent

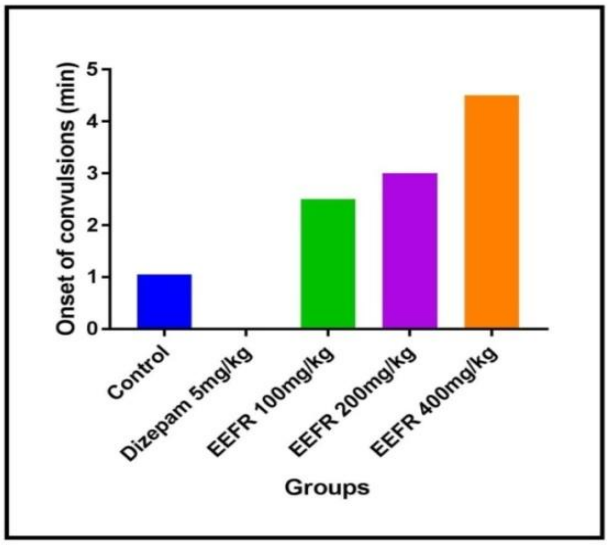
PTZ induced Epilepsy

The average time of onset, duration of convulsions and percentages of inhibition of convulsions were presented in table. 3 EEFR treated mice not only exhibited delay in the onset time of convulsions at the doses of 100, 200 and 400 mg/kg, p.o. but also showed reduced duration of convulsions when compared with the control group mice. All the three doses of EEFR afforded significant protection in a dose-dependent manner against convulsions induced by PTZ ($P < 0.01$). Animals pretreated with EEFR at all the three doses exhibited significant antiepileptic activity and more percentage of inhibition of convulsions when compared with Diazepam treated animals.

Table 3: Anticonvulsant effect ethanolic extracts of Ficus racemosa on PTZ-induced convulsions in mice.

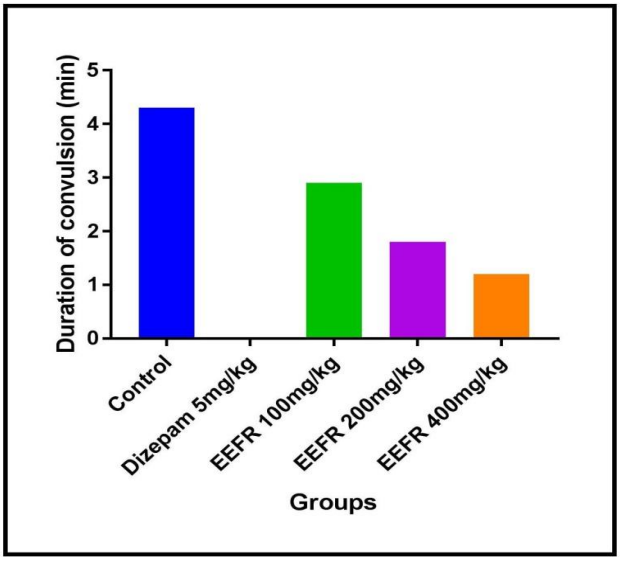
Experimental Group	Dose	Onset of convulsion(min)	Duration of convulsion(min)	Mortility	% Protection
Control	Vehicle	1.05.±0.12	.4.30 ± 0.20	6/6	0%
Standard (Diazepam)	5mg/kg	0.000.±0.00	0.00.±0.00**	0/6	100%
EEFR	100mg/kg	2.5.±0.17	2.9 ±0.40	4/6	33.33%
EEFR	200 mg /kg	3.1.±0.22	1.8± 0.03	3/6	50%
EEFR	400mg /kg	4.5.±0.25	1.2.± 0.004	2/6	66.66%

Value are mean ± SEM ;n= 6; ANOVA followed by Dunnets test. Where *p< 0.05 **p<0.01 and***P<0.001



Graph 1.:Effect of EEFR on onset of convulsions in PTZ induced convulsions

Values represent mean ± SEM; n=6; Analysis was performed using one way ANOVA followed by Duneet multiple comparison test; p value less than 0.05 was considered as statistically significant. [a]p<0.05, [b]p<0.01, [c]p<0.001; [##]Data compared with control



Graph 2 : Effect of EEFR on Duration of convulsions in PTZ induced convulsions

Values represent mean ± SEM; n=6; Analysis was performed using one way ANOVA followed by Duneet multiple comparison test; p value less than 0.05 was considered as statistically significant. [a]p<0.05, [b]p<0.01, [c]p<0.001; [##]Data compared with control.

DISCUSSION:

Epilepsy is one of the chronic and most common neurological disorders. The basic and major mechanisms associated with epilepsy are increased synaptic connectivity of neurons (such as excitatory glutaminergic neurons), (weakening of potassium channels and/or inure persistent sodium channels, changes in voltage-gated ion channels), perturbance in synaptic receptors (suppressed GABAergic receptor altered nicotinic receptors), decrease in inhibitory neurotransmission (decreased GABA levels), enhanced excitatory neurotransmission (enhanced glutamate levels. [29]

In this study, anticonvulsant activity of bark extracts of Ficus racemosa PTZ-induced convulsions in Swiss albino mice.

PTZ is a potent GABA receptor antagonist, it is well known to decrease the GABA levels, and density of GABA A receptors in various parts of the brain, this leads to continuous stimulation of cortical neurons and results in convulsions similar to absence seizures is human Hence, if thought that the agents which enhance GABA levels, GABA-A receptor agonists (like diazepam), the agents behave like GARBA are thought to be useful in abolishing PTZ-induced convulsions [6].

The reports on chemical constituents of EEFR have shown the presence of antioxidant and chemopreventive principles namely, racemosic acid, bergenin, tannins, kaempferol, rutin, bergapten, psoralenes, coumarin and phenolic glycosides antioxidant used in Parkinson's ,epilepsy, Alzheimer [26][1] .

PTZ-induced convulsions in mice are a suitable model for petit mal epilepsy. PTZ is GABA antagonist. This assay has been used primarily to evaluate AED. Drugs which antagonize PTZ- induced seizures are generally useful in petit mal epilepsy. It has been indicated that PTZ- induced seizures can be prevented by drugs that reduce T-type Ca^{2+} currents, such as ethosuximide and also by drugs that enhance $GABA_A$ receptor-mediated inhibitory neurotransmission, such as benzodizepine .

It is also found that many flavonoids could act as benzodiazepine-like molecules in the central nervous system and modulate GABA-generated chloride currents in animal models of anxiety, sedation and convulsion [34][4] .

The average time of onset, duration of convulsions and percentages of inhibition of convulsions were presented in EEFR treated mice not only exhibited delay in the onset time of convulsions at the doses of 100, 200 and 400 mg/kg, p.o. but also showed reduced duration of convulsions when compared with the control group mice. All the three doses of EEFR afforded significant protection in a dose-dependent manner against convulsions induced by PTZ ($P < 0.01$). Animals pretreated with EEFR at all the three doses exhibited significant antiepileptic activity and more percentage of inhibition of convulsions when compared with Diazepam treated animals. convulsion were induced the all animals by given PTZ 80 mg/kg i.p. 100% mortality was observed in control groups. Diazepam at the dose of 5 mg/kg p.o. significantly delayed onset of convulsion and decreased duration of convulsion and also delayed onset of convulsions and decreased duration of convulsions and also prototected 100% mortality rate.

CONCLUSION:

Based on the above investigations, it may be concluded that the ethanolic extract of bark of ficusracemos *a* exhibited significant antiepileptic activity. The presence of flavanoids may partially contribute the significant

activity of EEFR by enhanced GABAergic neurotransmission which responsible for the antiepileptic effect.

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