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EVALUATION OF ANTIEPILEPTIC ACTIVITY OF AQUEOUS EXTRACT OF AERIAL PARTS OF *ACALYPHA FRUTICOSA* IN MICE

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ABSTRACT

Objective: The aim of the present study was to investigate antiepileptic activity of aqueous extract of Acalypha fruticosa (AAF) in mice. Methods: The antiepileptic activity of AAF at 30, 100 and 300 mg/kg, p.o. was evaluated by the convulsions induced in mice by maximum electroshock (MES), Pentylenetetrazole (PTZ) and Isoniazid (INH). Statistical analysis was carried out by one-way analysis of variance (ANOVA) followed by Dunnett's test. Results: In MES method, AAF (30, 100 and 300 mg/kg) inhibited convulsions significantly but less potent than Diazepam. In PTZ method, AAF inhibited convulsions potent than Phenobarbitone sodium (PS). In INH method, AAF delayed the latency of convulsions less potent than Diazepam. Conclusion: In Present investigation, AAF showed significant dose dependent antiepileptic effect potent than PS.

KEYWORDS: *Epilepsy, Acalypha fruticosa, Pentylenetetrazole, Isoniazid.*

INTRODUCTION

The term epilepsy is of Greek origin that originally was known as "falling sickness" and means "Seizure" or "Seized" [1]. Epilepsy is a major neurological disorder and upto 5% of the world population have epilepsy in their lifetime. It affects an estimated 7 million people in India and 50 million worldwide, approximately 40% of them are women. In developed countries where drugs are easily available, epilepsy responds to treatment in up to 70% of the patients. However, in developing countries 75% of people with epilepsy do not receive effective treatment. It is estimated that up to 5% of people suffer at least one seizure in their lifetime [2]. All the currently available AED have potential for adverse effects on cognition and behavior [3]. Search for anti-epileptic agents has made man turn to alternative sources, indigenous system of medicine.

Acalypha fruticosa (Euphorbiaceae) commonly known as "Chinnichedi" and "Birch-leaved Acalypha" is a strong-smelling pubescent and bushy shrub found in India from Orissa to Karnataka, Tamil Nadu and Kerala [4].

Aerial parts of *Acalypha fruticosa* were traditionally used to treat epilepsy [5]. The aim of the present study is to evaluate the potential of aqueous extract of aerial parts of *Acalypha fruticosa* (AAF) to protect the mice from convulsions.

MATERIALS AND METHODS

Drugs and chemicals

Pentylenetetrazole (Sigma Aldrich Chemical Co.), Isoniazid (s.d. Fine-Chem. LTD), Diazepam (Ranbaxy) and Phenobarbitone sodium (Bayer AG).

Plant Collection

The aerial parts of *Acalypha fruticosa* were collected from Tirupati, Andhra Pradesh, India. The aerial parts of the plant were identified and authenticated by Botanist, Dr. K. Madhava Chetty, Assistant Professor, Department of Botany, Sri Venkateswara University, Tirupati. The plant specimen was deposited at Sri Venkateswara University Herbarium, Tirupati with voucher number 1252.

Preparation of extract

The fresh aerial parts of *Acalypha fruticosa* were collected and washed under running tap water. They were shade dried at room temperature and the dried aerial parts were made in to coarse powder. The powder was passed through a 60 No mesh sieve. The grounded powder was macerated

with chloroform water at room temperature. The solvent was then removed by filtration and fresh solvent was added to the plant material. The extraction process was twice repeated. The combined filtrates were then evaporated under reduced pressure [6].

Animals

Swiss Albino mice of either sex weighing 18-22 g were used. They were housed in standard polypropylene cages and kept under controlled room temperature (24±2^{0}C; relative humidity 60-70%) in a 12h light – dark cycle. The mice were given a standard laboratory diet and water *ad libitum.*

Qualitative analysis

The crude aqueous extract was subjected to preliminary phytochemical screening. The study was carried out by using standard procedure [7].

Acute Toxicity Study

Acute toxicity study will be performed for the extracts to ascertain safe dose by acute oral toxic class method of Organization of Economic Co-operation and Development, as per 420 guidelines (OECD) [8].

Antiepileptic activity

Maximum electroshock (MES) in mice

Five groups of six male Swiss albino mice (25 – 30) were used. The test was started one hour after oral treatment with the test compound (AAF 30, 100, 300 mg/kg, p.o.) or the vehicle or the standard (Diazepam 3 mg/kg, p.o.). An apparatus with corneal electrodes was used to deliver the stimuli. The intensity of the stimulus is dependent on the apparatus, eg: 30 mA, 50 Hz for 0.2 sec has been used. The onset and the duration of tonic hind limb extension (THLE) were recorded and percentage of inhibition of seizures relative to controls was calculated [9].

Pentylenetetrazole (PTZ) induced convulsions in mice

Control group received vehicle, test group received AAF (30, 100 and 300 mg/kg, p.o.) and standard group received Phenobarbitone sodium, (40 mg/kg, i.p.). Convulsions were induced by administering PTZ (75 mg/kg, i.p.), 1hr after AAF and 15 min after PS administration. The onset and the duration of convulsions were recorded, and percentage inhibition was calculated [10].

Isoniazid (INH) induced convulsions in mice

Control group received vehicle, test group received AAF (30, 100 and 300 mg/kg, p.o.) and standard group received Diazepam, (4 mg/kg, i.p.). Convulsions were induced by administering INH (300 mg/kg, s.c.), 1hr after drug administration. The onset time of convulsions was recorded [11].

Statistical analysis:

The data was analyzed by using one-way analysis of variance (ANOVA), followed by Dunnett's test. P <0.05 was considered as statistically significant. The data are expressed as mean ± Standard deviation.

RESULTS

Qualitative analysis

The preliminary phytochemical screening of the aqueous extract revealed the presence of alkaloids, carbohydrates, tannins, saponins and proteins as major compounds tabulated in Table 1.

Acute Toxicity Study

In acute toxicity study, mortality was found at 2 gm/kg, p.o. So, doses of 30, 100 and 300 mg/kg, p.o. were selected for the study.

Antiepileptic activity

Maximum electroshock (MES) in mice

In MES method, AAF increased the onset time and decreased the duration of tonic hind limb extension when compared to control group, which were shown in Table 2. AAF exhibited significant dose-dependent antiepileptic activity but less potent than Diazepam.

Pentylenetetrazole (PTZ) induced convulsions in mice

In PTZ method, AAF increased the onset time and decreased the duration of convulsions when compared to control group presented in Table 3. AAF exhibited significant dose-dependent antiepileptic activity. AAF at 300 mg/kg, p.o. exhibited antiepileptic activity potent than PS.

Isoniazid (INH) induced convulsions in mice

AAF at all three doses exhibited significant dose-dependent delay in latency of convulsions when compared to control but less potent than Diazepam shown in Table 4.

Table 1: Phytochemical constituents of aqueous extract of *Acalypha fruticosa*

Phytoconstituents	AAF
Alkaloids	+ ve
Steroids	- ve
Carbohydrates	+ ve
Tannins	+ ve
Flavonoids	- ve
Saponins	+ ve
Lipids	- ve
Proteins	+ ve

Table No.2: Effect of aqueous extract of *Acalypha fruticosa* on maximal electroshock induced convulsions in mice

Group (n=6)	Treatment	Onset of THLE (sec)	Duration of THLE (sec)	Percentage inhibition of convulsions
I	Distilled water	1.52±0.05	93.56 ±0.33	-
II	AAF (30 mg/kg)	2.29±0.14**	60.28±0.40**	35.57**
III	AAF (100 mg/kg)	2.51±0.32**	51.59±0.35**	44.85**
IV	AAF (300 mg/kg)	2.88±0.04**	42.22±0.22**	54.87**
V	Diazepam (3 mg/kg)	3.53±0.25**	39.59±0.35**	57.69**

AAF: Aqueous extract of *Acalypha fruticosa*; Values are mean±SD (n=6). Statistical significance was determined by ANOVA, followed by Dunnett's t test (n=6); $^{**}p < 0.01$.

Table No.3: Effect of aqueous extract of *Acalypha fruticosa* on PTZ-induced convulsions in mice

Group (n=6))	Treatment	Onset of convulsions (min)	Duration of convulsions (min)	Percentage inhibition of convulsions
I	Distilled water	3.06±0.02**0.**	22.54±0.02	-
II	AAF (30 mg/kg)	3.11±0.04**	11.23±0.03**	50.19**
III	AAF (100 mg/kg)	3.53±0.04**	9.43±0.03**	58.16**
IV	AAF (300 mg/kg)	4.05±0.03**	8.02±0.21**	64.44**
V	Phenobarbitone sodium (40 mg/kg)	6.46 ±0.02**	11.09±0.03**	50.82**

AAF: Aqueous extract of *Acalypha fruticosa*; Values are mean±SD (n=6). Statistical significance was determined by ANOVA, followed by Dunnett's t test (n=6); $^{**}p < 0.01$.

Table No.4: Effect of aqueous extract of *Acalypha fruticosa* on INH-induced convulsions in mice

Group (n=6)	Treatment	Latency of convulsions (min)
I	Distilled water	25.15±0.28
II	AAF (30 mg/kg)	28.58±0.22**
III	AAF (100 mg/kg)	30.33±0.03**
IV	AAF (300 mg/kg)	33.59±0.22**
V	Diazepam (4 mg/kg, i.p.)	63.27±0.04**

AAF: Aqueous extract of *Acalypha fruticosa*; Values are mean±SD (n=6). Statistical significance was determined by ANOVA, followed by Dunnett's t test (n=6); $^{**}p < 0.01$.

DISCUSSION

Epilepsy is a major neurological disorder and upto 5% of the world population have epilepsy in their lifetime. [2]. All the currently available AED have potential for adverse effects on cognition and behavior [3]. Search for anti-epileptic agents has

made man turn to alternative sources, indigenous system of medicine.

Acalypha fruticosa (Euphorbiaceae) commonly known as "Chinnichedi" whose aerial parts were traditionally used to treat epilepsy [5]. The preliminary phytochemical screening of the aqueous extract revealed the presence of alkaloids, carbohydrates, tannins, saponins and proteins.

Based on acute toxicity study, doses of 30, 100 and 300 mg/kg, p.o. were selected for the evaluation of antiepileptic activity. To screen the antiepileptic activity, most extensively studied, well established and simple animal seizure models viz. maximal electroshock, pentylenetetrazole and isoniazid-induced seizures in mice were selected.

The convulsions induced by MES and PTZ were effectively controlled by AAF. In INH model, AAF significantly delayed the latency of convulsions in mice but failed to protect the mice against mortality.

CONCLUSION

Normally, antiepileptic drugs may act by modifying inhibitory neurotransmission through effects on GABA(A) receptors [12]. Here PTZ act as GABA antagonist and INH act as GABA synthesis inhibitor [9]. Maximum protection of mice from convulsions was observed in PTZ model. So, AAF may be a GABA agonist and the antiepileptic effect may be due to enhanced GABAergic neurotransmission. The antiepileptic activity may be due to the phytoconstituent/s present in the extract which is responsible for the enhanced GABAergic neurotransmission. Further studies are necessary to identify and reveal the active phytoconstituent/s responsible for the antiepileptic effect.

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