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Evaluation of Anticonvulsant Activity of Hydro Ethanolic Extract of *Coccinia grandis* in Mice

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Abstract **Original Research Article**

Background: Hydro ethanolic extract of Coccinia grandis leaves was assumed to have anticonvulsant activity. ***Objective:*** To evaluate the anticonvulsant activity of Coccinia grandis by using some animal models like maximal electric shock model, pentylenetetrazole induced seizures, Isoniazid induced seizures. ***Materials and Methods:*** Various equipment and apparatus were used in the present study. Hydroethanolic extract of Coccinia grandis was done by Soxhlet apparatus. Phytochemical investigation of the leaf extract of Coccinia grandis was performed. Anticonvulsant activity was determined by using different animal models like maximal electric shock model, pentylenetetrazole induced seizures, Isoniazid induced seizures. ***Results:*** Anticonvulsant activity was determined by using different animal models like Maximal electric shock model, pentylenetetrazole induced seizures & Isoniazid induced model. Percentage of protection, Duration of hind limb tonic extension (HLTE), Latency of onset of convulsions were taken as a indication of anticonvulsant activity. Phenytoin and Diazepam showed significant anticonvulsant activity. In the present study the test samples exhibited significant ($P < 0.0001$) anticonvulsant activity and antioxidant activity at a dose of 200,400mg/kg. It may due to the presence of alkaloids, Phenols, carbohydrates, glycosides, saponins and flavonoids terpenoids. ***Conclusion:*** In present study leaves of Coccinia grandis extract was collected and anticonvulsant activity was examined in a doses of 200mg/kg, 400mg/kg. The results clearly shown that the low dose 200mg/kg of plant extract shown appropriate anticonvulsant activity and the high dose 400mg/kg shown specific anticonvulsant activity when compared to control and standard groups.

Keywords: Coccinia grandis, Maximal electric shock, pentylenetetrazole & Isoniazid.

INTRODUCTION

Epilepsy is defined as a group of disorders in which there are recurrent episodes of altered cerebral functions [1]. Epilepsy is a neurological disorder characterised by recurrent unprovoked seizures. Epilepsyis the second most common disorder of the central nervous system after stroke and up to 5% of worldpopulation develops epilepsy in their lifetime. Present therapy of epilepsy with modern antiepileptic drugs is highly correlate with side effects, dose-related and chronic toxicity, as well as teratogenic effects, andapproximately 30% of the patients continues to have seizures with current antiepileptic drugs therapy [2].

Traditional ideology is believed to be an important source of chemical substances with potential therapeutic effects. Some herbs may useful to increase brain levels, binding of nerve transmitter gamma amino butyric acid (GABA), which quiets nerve activity. Chemical compounds identified from traditional medicinal plants are presenting an exciting opportunity for the providing new types of therapeutics. This has advance the global effort to harness and harvests those medicinal plants that carry substantial amount of potential phytochemicals showing multiple beneficial effects in convulsion.

Coccinia grandis(Ivy gourd) belonging to Cucurbitaceae family, used as vegetable and grown throughout India and some of Asian countries. Ivy plant has been used in traditional medicine as household remedy for various diseases [3]. Every part of the plant exhibits pharmacological activity and finds application in treating various ailments in traditional Ayurvedic, The preliminary phytochemical screening of leaves Coccinia grandis showed the presence of carbohydrates, alkaloids, proteins, amino acids, tannins and phenolics compounds, flavonoids, saponins. Many of these compounds have been reported for hepatoprotective

activity. Therefore, there is possibility that ethanolic extract of Coccinia grandis leaves may possess the anticonvulsant activity.

The Coccinia grandis leaves were collected from local region of vizianagaram district; the leaves were verified and authenticated by Dr.M.V.Suresh BabuM.Sc.Ph.D, Department of Botany, Government Degree College, Rajampet, Kadapa, A.P, India.

Extraction in Soxhlet apparatus [4]

The plant leaves were shade dried and powdered. The powdered plant leave material was placed in a thimble present in the central compartment, with siphoning device side arm which was connected to the lower compartment. The solvent vapor which was generated by heating the reservoir gets condensed and was allowed to drip back onto the porous sample cup. The liquid condensate that drips onto sample performs the extraction which then passed through the container and back into the reservoir. The cycle was repeated continuously and can be sustained as long as needed. As it progresses, the species was concentrated in the reservoir. The powdered plant leaves material was subjected to successive extraction, 70% ethanol and water (70:30) (500ml/ 100g of dried powder) for 18hrs, the extract solutions obtained were collected separately and concentrated using rotary evaporator. The yield were stored in air tight container and placed in refrigerator.

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 feeded food and water ad libitum. The animals were acclimatized before the study. The animals were accommodate in sanitized polypropylene cages containing sterile paddy husk as bedding.

All experiments and protocols described in present study were approved by the institutional animal ethical committee (IAEC) of Annamacharya College of Pharmacy, Rajampet, Kadapa and with permission from committee for the purpose of control and supervision of experiments on animals (CPCSEA Reg No. AEC/ANCP/2018-19/11& dated-03/12/2018), Ministry of social justice and empowerment, government of India.

1. Maximal Electroshock Model (MES) - induced seizures [5]

Seizures were induced in mice by electroshock of 50 mA for 0.2 sec. by means of an electro-convulsometer over a pair of ear clip electrodes. All the test groups were compared with the control group. Characteristic hind limb extension followed by clonic phase, a tonic flexor phase, a tonic extensor phase with protected from hind limb tonic extension seizure (HLTE) and the time spent in this position were determined for each dose group [5].

Evaluation

Characteristic hind limb extension followed by clonic phase, a tonic flexor phase, a tonic extensor phase with protected from hind limb tonic extension seizure (HLTE) and the time spent in this position were determined for each dose group [5].

2. Pentylenetetrazole (PTZ) - induced seizures

Group I served as normal control group. Groups III, and IV served as test groups treated with the extract 200 and 400 mg/kg, p.o. The Coccinia grandis leaf extract was administered 60 min before the subcutaneous injection of PTZ (80 mg/kg). Group II received diazepam (2.0 mg/kg, i.p.) as a reference standard. The animals were observed for onset of convulsion upto 30 min after PTZ. Hind limb extension was taken as tonic convulsion [6].

Evaluation

The onset of tonic convulsion and the number of animals convulsing or not convulsing within the investigation period were recorded. The ability of the plant extract to prevent or delay the onset of the hind limb extension exhibited by the animals was taken as an indication of anticonvulsant activity.

3. Isoniazid induced convulsions [7]

Group I served as normal control group.Groups III, and IV served as test groups treated with the extract 200 and 400 mg/kg, p.o. The Coccinia grandis leaf extract was administered 30 min before then the oral dosing of INH (300 mg/kg BW) to induce clonic seizures and mice were observed for onset of convulsions. Group II received diazepam (2.0 mg/kg,i.p.)as a reference standard [7].

Evaluation

The onset of tonic convulsion and the number of animals convulsing or not convulsing within the investigation period were recorded.

- Thiobarbituric acid reactive substance (TBARS)
- Reduced glutathione (GSH)

STATISTICAL ANALYSIS

All the values are expressed as mean ± SEM. Statistical differences between means were determined by oneway ANOVA followed by Dunnett. S post hoc test. $p<0.05$ was considered as significant [5].

RESULTS

The preliminary phytochemical analysis showed the presence of carbohydrates, alkaloids, proteins, amino acids, tannins and phenolics compounds, flavonoids, saponins, terpenoids.

1. Maximal electric shock model (MES)

The mice treated with normal saline showed tonic hind limb extension for duration of 19.17 ±0.74

sec, low dose and high dose of HEECG (hydro ethanolic extract of Coccinia grandis)13.67± 0.33 , 10.83± 0.30 respectively. The HEECG at doses of 200 and 400 mg/kg respectively protected 66.66% and 83.33 % of mice and significantly reduced the duration of the seizures when compared to control. However, phenytoin completely abolished the MES-induced tonic seizures in all the animals.

2. Pentylenetetrazole (PTZ) induced seizures

The HEECG at doses of 200 and 400 mg/kg protected 50% and 83.33 % of mice and Low dose, high dose of HEECG 158.3 ± 0.33, 170.7 ± 0.66sec significantly delays the myoclonic jerks and 622 ± 0.96, 704.8±0.47 sec delays the clonic seizures when compared to control.

3. Isoniazid induced convulsions

The mice treated with normal saline showed onset of convulsions 45.18± 0.87 minutes, low dose and high dose of HEECG 72±0.36, 84.21±0.51respectively. The HEECG at doses of 200 and 400 mg/kg respectively protected 50% and 83.33 % of mice and significantly delayed the onset of convulsions when compared to control.

Table-1: Effect of HEECG on MES induced Seizures

Groups	Treatment & Dose	% of protection	Duration of HLTE (sec)
Control	Normal saline	0	19.17 ±0.74
Standard	Phenytoin 25mg/kg	100	0.50±0.22***
Test- low dose	HEECG 200mg/kg	66.66	13.67±0.33***
Test- High dose	HEECG 400mg/kg	83.33	10.83±0.30***

All values are expressed as mean ± SEM (n=6) by one way ANOVA followed by dunneet's method*** P< 0.0001 Vs Control.

Maximal Electric Shock (MES)

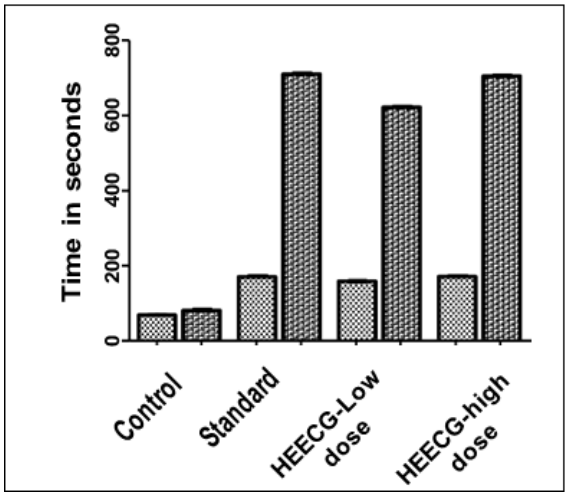


Table-2: Effect of HEECG on PTZ Induced seizures

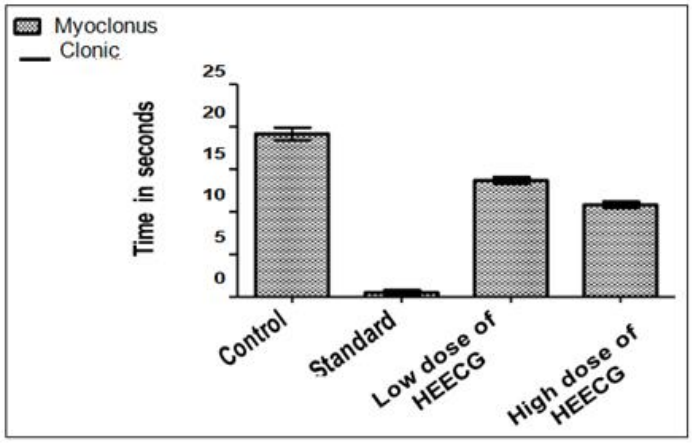
Groups	Treatment& Dose	% of Protection	Onset of myoclonus(sec)	Onset of clonic seizures (sec)
control	Normal saline 10mg/kg	0	68 ±0.93	81 ± 1.06
standard	Diazepam (2.0 mg/kg)	66.66	170 ±2.30	710 ± 1.69***
Test–low dose	HEECG 200mg/kg	50	158.3 ±0.33	622 ± 0.96***
Test–high dose	HEECG 400mg/kg	66.66	170.7 ±0.66	704.8±0.47***

All values are expressed as mean ± SEM (n=6) by one way ANOVA followed by dunneet's method*** P< 0.0001 Vs Control.

Table-3: Effect of HEECG on Isoniazid induced Seizures

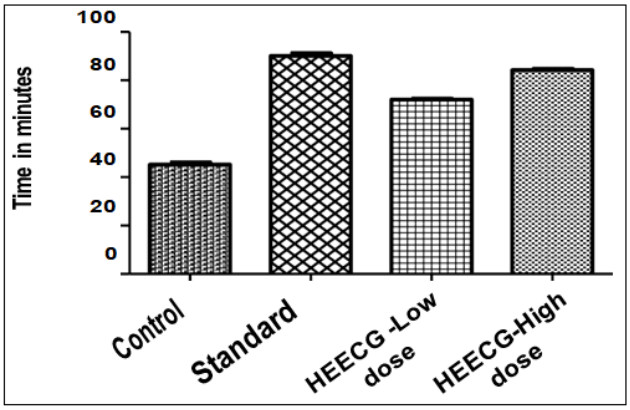
Groups	eatment& Dose	% of Protection	Onset of convulsions (minutes)
Control	Normal saline 10mg/kg	0	45.18± 0.87
Standard	Diazepam (2.0 mg/kg)	83.33	90.05±0.98***
Test low dose	HEECG 200mg/kg	50	72±0.36***
Test High dose	HEECG 400mg/kg	83.33	84.21±0.51***

Pentylenetetrazole induced seizures



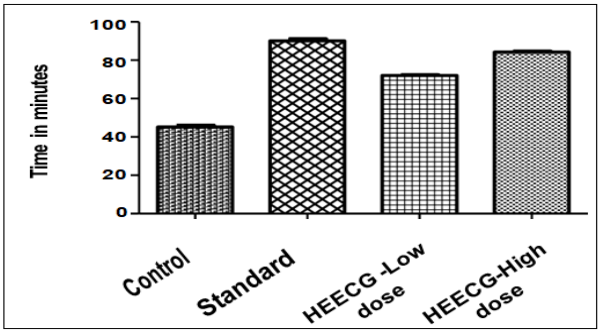
GROUPS

ISONIAZID INDUCED CONVULSIONS



Treatment groups

ISONIAZID INDUCED CONVULSIONS

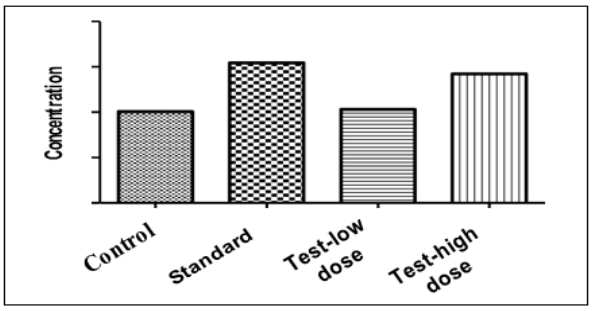


Treatment groups

GSH

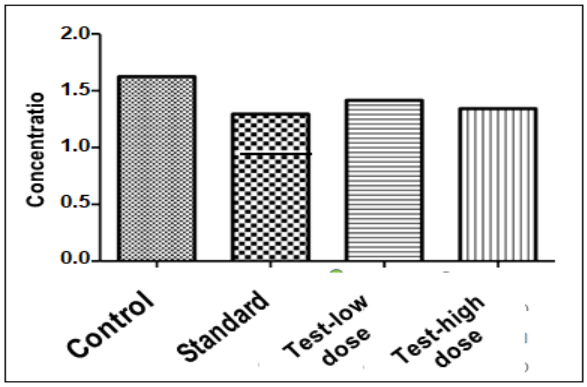
EFFECT OF Coccinia grandis –TBARS GSH IN BRAIN

Effect of HEECG on TBARS& GSH



Groups

TBARS



Groups

Groups	Treatment& Dose	TBARS	GSH
Control	Normal saline 10mg/kg	1.625±0.02	4.030±0.02
Standard	Phenytoin	1.295±0.004***	6.175±0.05***
Test–low dose	HEECG 200mg/kg	1.417±0.005***	4.125±0.01***
Test–high dose	HEECG 400mg/kg	1.342±0.002***	5.691±0.07***

DISCUSSION

All values are expressed as mean ± SEM (n=6) by one way ANOVA followed by dunneet's method*** P< 0.0001 Vs Control Coccinia grandis leaves extract at a doses of 200mg/kg (1.417± 0.005) and 400mg/kg (1.342±0.002) ***P< 0.0001 significantly reduces the levels of TBARS when compared with control (1.625±0.02). And 200mg/kg (4.125± 0.01) and 400mg/kg (5.691±0.07) ***P< 0.0001 significantly rises the levels of GSH when compared with control (4.030± 0.02).

The present study shows that the hydro ethanolic extract of Coccinia grandis (HEECG) protected some of the animals against seizures induced by maximal electrical shock (MES) and decreases the tonic hind limb extension low dose and high dose of HEECG 13.67± 0.33, 10.83± 0.30 seconds, as compared with the results of Jiban Debnath *et al*. [4, 2]. Antiepileptic drugs which inhibit voltage-dependent Na+ channels, such as phenytoin can prevent MES-induced tonic extension [5].

In PTZ model, percentage of protection from seizures and duration of onset of myoclonus and clonic seizures was delayed in low dose and high dose of HEECG compared with the results of Latha S *et al*. [6] Diazepam, a standard antiepileptic drug is believed to produce their effects by enhancing GABA mediated opening of chloride channel on GABA-A receptor leading to more chloride ion entering the neuron which in turn decreases the neuronal activity in the brain [5].

In isoniazid model, percentage of protection from seizures and duration of onset of convulsions was delayed in low dose and high dose of HEECG compared with the results of N. Vanaja *et al*. [7]. In the present study diazepam shown to antagonize the seizure

induced by isoniazid, pentylenetetrazole which is regarded as a GABA-synthesis inhibitor. The extract was also shown to delay the latency of isonizid induced seizures, suggesting that the extract exhibiting anticonvulsant affect, probably by openingthe chloride channels associated with GABA receptors [5].

Phytochemical compounds present in Hydro ethanolic extract of Coccinia grandis revealed the presence of flavonoids, tannins, terpenoids, alkaloids, steroids, phenols and saponins. It has been reported that alkaloids, flavonoids, saponins and terpenoids have antiepileptic activity and antioxidant activity [3, 6]. 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 convulsion [9].

CONCLUSION

In this study leaves of Coccinia grandis extract was collected and anticonvulsant activity was examined in a dose of 200mg/kg, 400mg/kg by Maximal electric shock model, Pentylenetetrazole (PTZ) - induced seizures and Isoniazid induced model. Due to the presence of alkaloids, flavonoids, saponins and terpenoids it possesses antiepileptic activity and Antioxidant activity.

Based on the results of the present study, it may conclude that hydroethanolic extract of Coccinia grandis leaves possess significant anticonvulsant property against the MES and Pentylenetetrazole (PTZ) - induced seizures, Isoniazid induced seizures. Further studies are recommended to know exact mechanism and to isolate the active compound responsible for this pharmacological activity.

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