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Akhtar Ali
Resident, Department of Pharmacology, Dr. S.N. Medical College Jodhpur, Rajasthan, India

Kamal Kishore Khichi
Associate Professor, Department of Pharmacology, Dr. S.N. Medical College, Jodhpur, Rajasthan, India

Anusuya Gehlot
Sr. Professor, Department of Pharmacology, Dr. S.N. Medical College Jodhpur, Rajasthan, India

Rajkumar Rathore
Professor, Department of Pharmacology, Dr. S.N. Medical College, Jodhpur, Rajasthan, India

Correspondence
Kamal Kishore Khichi
Associate Professor, Department of Pharmacology, Dr. S.N. Medical College, Jodhpur, Rajasthan, India

A study on albino rat for anticonvulsant properties of *Cuminum cyminum*: An experimental study

Akhtar Ali, Kamal Kishore Khichi, Anusuya Gehlot and Rajkumar Rathore

Abstract
Aim: To evaluate the Anticonvulsant property of *Cuminum cyminum* in albino rats.
Methodology: This experimental study conducted on albino rats by MES method. Adult albino rats of either sex (100-150g) were divided into three groups for each parameter under study. Group I consisting of six animals, served as control and received distilled water. Group II subdivided into three groups II-A, II-B, II-C, consisting of six animals each, received *Cuminum cyminum* in three doses of 300mg, 750 mg, 1000mg per orally respectively. Group III subdivided into three groups III-A, III-B, III-C, consisting of six animals each, received the Phenytoin in three doses per orally.
Result: *Cuminum cyminum* decreased extension period. Although the extension period was not significant [$P > 0.05$] in 300 mg per kg dose, while the extension period was highly significant [$P < 0.001$] in higher doses (750, 1000mg per kg).
Conclusion: *Cuminum cyminum* is having Anticonvulsant property in the albino rat. However further study needed to find out its mechanism of actions and chemical constitutes responsible for these activities.

Keywords: *Cuminum cyminum*, anticonvulsant property, albino rat, phenytoin

Introduction
The use of plants as a source of medicinal agents lies deep in the roots of antiquity. No one will ever know what led primitive human being emerging from ancestral origin to select certain plant material for the treatment of human suffering. There was a conscious realization that certain roots, leaves, barks, fruits, seeds, and even plant exudations had some beneficial actions. The routes of many of the modern therapeutic agents can be traced back to the plants used in ancient societies. In countries like India, China and Greek, with well-developed indigenous systems of medicine have a sound theoretical basis. Their use got incorporated into the material medical of these systems of medicine.
Cuminum cyminum (Jeera) has been one of the common constituents of home-based spices. Jeera is a widely distributed plant and used in all parts of the world as a spice. Its importance has already been recognized several thousand years ago in ancient India. It was regarded as one of the important foodstuff and medicinal plant.
Cuminum cyminum is a grassy plan with the white or pink floor. It is a herbaceous annual plant, with a slender branched stem 20-30 cm tall. Leaves are 5 cm long, thread-like leaflets. The flowers are small pink in umbels. Fruits are lateral fusiform or ovoid 4-5 mm long, containing a single seed. Cumin seeds are similar to fennel seeds in appearance but are smaller and darker in color. Cultivation of cumin requires a long, hot summer of 3-4 months, with a day time temperature around 30^0 Celsius [1, 2]. It is drought tolerant and it is mostly grown in Mediterranean climates.
Several medicinal and therapeutic indications of *Cuminum cyminum* have been described in Indian ancients scriptural book Ayurveda as well as in ancient Iranian medica book which involved antiinflammatory, anticonvulsive, antihyperlipidemic and antidiabetic property [3, 4].
The period from 1951-1975 may be considered as the golden period of research in modern medicine. The use of plant products was gradually overtaken by that of synthetic drugs and the microbial products until about the mid of the 1970s. Thereafter, due to a variety of reasons, a reappraisal of modern medicine versus those of traditional medicine gradually set in. The main

reasons for this were the undesirable side effects of a number of modern drugs; some therapeutic gaps with modern drugs, non-availability and unaffordable costs of allopathic drugs and easy acceptability to Ayurvedic and alternative medicine. So In the present study, we are illustrating the Anticonvulsant property of *Cuminum cyminum.*

Methodology

The present study was conducted in the Department of Pharmacology, Dr. S. N. Medical College, Jodhpur, (Rajasthan). Ethical approval was taken prior to the starting of study from the institutional ethical committee and from institutional animal ethical committee. All guidelines were strictly followed during the study.

Experimental Animals

The albino rates were used as experimental animals. Adult albino rats of either sex (100-150g) were divided into three groups for each parameter under study. Group I consisting of six animals, served as control and received distilled water. Group II subdivided into three groups II-A, II-B, II-C, consisting of six animals each, received *Cuminum cyminum* in three doses of 300mg, 750 mg, 1000mg per orally respectively. Group III subdivided into three groups III-A, III-B, III-C, consisting of six animals each, received the standard drug in three doses per orally.

In this preliminary study, parameter like Anticonvulsant properties was study, in the above-mentioned animal groups.

Drugs under study with doses

A) Test drugs for all experiments

- *Cuminum cyminum* 300 mg per kg
- *Cuminum cyminum* 750 mg per kg
- *Cuminum cyminum* 1000 mg per kg

B) Standard drugs for antiepileptic activity

- Phenytoin 25 mg per kg
- Phenytoin 40 mg per kg
- Phenytoin 50 mg per kg

Preparation of drug solution by hot continuous extraction method

We have collected aqueous extract of *Cuminum cyminum* through soxhlet apparatus by hot continuous extraction method. The use of commercially available Soxhlet apparatus is a convenient way to prepare crude plant extract.

Mode of administration

Cuminum cyminum & the standard drugs were administered orally by feeding needle, in various doses in the in-vivo experiment, half an hour before the actual procedure.

Experimental setup of Anticonvulsant properties

Electrically induced seizures- There is three major types of electrically induced seizure models:

1. Threshold models
2. Maximal electroshock seizure test (MES)
3. Focal electrical stimulation such as kindling

These models are used for screening of drugs with efficacy against generalized tonic-clonic and focal epilepsy [5]. We have conducted our experiment with MES method on albino rats.

Maximal Electroshock Seizure test (MES)

Meritt and Putname (1938) developed the MES test and discovered the antiepileptic effect of diphenylhydantoin using this test. This model is useful for screening of drugs effective against primary and secondary generalized seizures [6]. Drugs effective against generalized tonic-clonic seizures have increased this threshold.

Apparatus - Techno Electroconvulsiometer

Wood bury *et al*., Davenport vo 1952 designed and used the new electroshock seizure apparatus and analysis of factor, altering seizure threshold and pattern. It provides 50 H_Z alternative current stimulus 50 milliamperes for the 2-millisecond duration, 250-volt amplitude through ear-clip electrode in rats. A pair of ear-clip electrodes applied on external pinnas of rats.

Conduct of experiment

After connecting the instrument to an electrical outlet turn the norms marked, duration- 0.2 sec., 50 milliamperes current, respectively. This setting on the machine will deliver an electrical current adequate for inducing convulsions in albino rats. Ear-clip electrode was connected to the external ear of the rat. The electroshock convulsiometer was activated by turning the switch to on and red light indication showing that the machine is on. Thirty minutes after administered test drug (*Cuminum cyminum*) and standard drug (phenytoin) per orally test was conducted [7].

Rats from each group were placed on the experimental table and their responses to the electroshock were observed for a period of 10-15 minutes.

Different stages of seizure are as following-

1. Tonic flexion phase
2. Tonic extension Phase
3. Clonic convulsion
4. Stupor
5. Recovery or Death

These stages were noted and also noted the time, within second; spend by the rat in each phase of convulsion. The endpoint of this experiment is convulsion. Reduction or complete abolition of tonic extension phase was considered as an anticonvulsive activity of the test drug.

Results

Anticonvulsant activity of *Cuminum cyminum* (jeera) was evaluated from "Maximal Electro Shock method". Three orally administered doses of 300, 750, 1000 mg per kg of *Cuminum cyminum* were tested against convulsions. Test drug was compared with phenytoin which was used as a standard drug. *Cuminum cyminum* decreased extension period. Although the extension period was not significant [$P > 0.05$] in 300 mg per kg dose, while the extension period was highly significant [$P < 0.001$] in higher doses (750, 1000mg per kg). Extension period was decreased by -3%, 5%, 25% respectively with all the three doses of *Cuminum cyminum*. Phenytoin has highly significant the extension period [$P < 0.001$] in all the three doses. Extension period was decreased by 41%, 45% and 43% respectively with all the three doses of *Cuminum cyminum*.

- Group one was compared with groups II-A, II- B, II-C.
- Groups III-A, III-B, III-C were compared with groups II-A, II-B, II-C respectively.

"Student's t-test" was used to compare different groups.

Table1: Effect of *Cuminum cyminum* and phenytoin on Anticonvulsant Activity

Group	Treatment	Oral Dose mg /kg	Flexion Period			Extension Period		
			Mean ± S.E.	Percent Reduction %	'P' Value	Mean ± S.E.	Percent Reduction %	'P' Value
I	Control	Distilled water	3.25±0.07			10.28 ±0.08		
II-A	*Cuminum cyminum*	300	3.25±0.07	0	> 0.05	10.61±0.02	-3	> 0.05
II-B	*Cuminum cyminum*	750	3.15±0.04	12	> 0.05	09.65±0.04	5	< 0.001
II-C	*Cuminum cyminum*	1000	2.79±0.05	14	<0.001	07.61±0.15	25	< 0.001
III-A	Phenytoin	25	2.16±0.07	33	<0.001	06.20±0.06	41	< 0.001
III-B	Phenytoin	40	1.96±0.05	46	<0.001	05.30±0.07	45	< 0.001
III-C	Phenytoin	50	1.45±0.03	48	<0.001	04.30±0.07	43	< 0.001

Each group consist of 6 animals, n=6

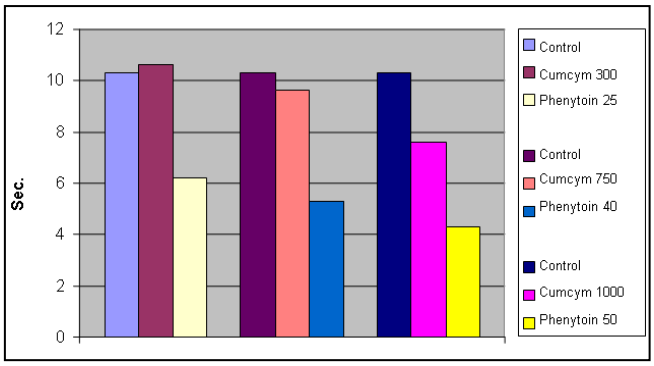

Fig 1: Effect of *Cuminum cyminum* and Phenytoin on Anticonvulsant Activity in Albino rats (mean extension period) (Cumcym = *Cuminum cyminum*)

Discussion

Epilepsy is a common disorder with an incidence of approximately 0.3% -0.5% in different populations throughout the world and prevalence of 5-10 persons per 1000. The characteristic event in epilepsy is the seizure. Currently available antiepileptic drugs act by modulating GABA or glutamate transmission or by modulating sodium and calcium ion channels. Drug therapy of epilepsy is an empirical therapy and does not correct the underlying pathology.

In our study, we found that the effectivity of *Cuminum cyminum* was not significant in a lower dose (300 mg per kg) while significant in higher doses (750, 1000 mg per kg) as an anticonvulsant agent. Phenytoin was highly significant even with the higher doses of the *Cuminum cyminum* as an anticonvulsant.

In support of our study, Janahmadi *et al.* have demonstrated that essential oil of *Cuminum cyminum* (1% & 3 %) dramatically decreased the frequency of spontaneous activity induced by Pentylenetetrazol in a time and concentration-dependent manner [8]. In addition, it has shown protection against PTZ induced epileptic activity by increasing the duration, decreasing the amplitude of after hyperpolarization potential (AHP) following the action potential, The peak of action potential and inhibition of firing rates. These membrane effects suggest a cellular mechanism by which the essential oil of *Cuminum cyminum* can inhibit the PTZ induced epileptic activity. Other hands Sayyah *et al.* demonstrated in an animal model that anticonvulsant activity of the fruit essential oil of Cumins against seizures induced by MES and PTZ in mice. The essential oil-suppressed tonic seizures and mortality, induced by MES and PTZ in a dose-dependent manner [9].

Conclusion

In our study, we demonstrated that *Cuminum cyminum* is having antiepileptic activity property in the albino rat. However further study needed to find out its mechanism of actions and chemical constitutes responsible for these activities.

Limitation of study

This study has its limitation especially experiment is conducted only on Techno Electro-convulsiometer and the solvent is being recycled, the extract that collects in the lower container is continuously being heated and may suffer thermal degradation reactions. To overcome this limitation need further study with more advanced test and extract without heat degradation.

Acknowledgments

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Conflict of Interest

The authors declare that no conflict of interest, financial or otherwise exists.

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