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Research Article

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Evaluation of anticonvulsant activity of ethanolic extract of *Zingiber officinale* in Swiss albino rats

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ABSTRACT

Epilepsy is a serious neurological disorder associated with recurrent episodes of seizures due to the abnormal electrical activity in the brain. Ginger, the rhizome of Zingiber officinale, is one of the most widely used species of the ginger family Zingiberaceae. Zingiber officinale shows anticonvulsant activity apart from many other medicinal properties such as immuno-modulatory, anti-tumorogenic, anti-inflammatory, anti-apoptotic, anti-hyperglycemic, anti-lipidemic, carminative and anti-emetic actions. Ginger is a strong anti-oxidant agent and may prevent generation of free radicals. Maximal electroshock seizures (MES) in albino rats were used to study anticonvulsant activity of ethanolic extract of Zingiber officinale rhizome. The ethanolic extract of Zingiber officinale rhizome was administered orally in graded doses of 50 mg/kg, 100 mg/kg and 200 mg/kg in swiss albino rats and the effects were compared with phenytoin as standard and normal saline as control in MES method. The Zingiber officinale rhizome has shown significant decrease in the duration of tonic hind limb extension suggesting anticonvulsant effect. The screening results indicate that ethanolic extract of Zingiber officinale rhizome have possible anticonvulsant activity

Key words: Epilepsy, Maximal Electro Shock Seizures, Phenytoin, Swiss Albino Rats, *Zingiber officinale* Rhizome**.**

INTRODUCTION

Epilepsy is a serious neurological disorder associated with recurrent episodes of seizures due to the abnormal electrical activity in the brain. Nearly 40 million people all over the world are affected by this disease.[1] Prevalence rate of epilepsy is about 5.59 per 1000 population in India. [2] Currently, many drugs are available for treating this disorder, but these drugs have draw backs like teratogenicity and other dose-related side effects. In spite of daily treatment, nearly 30% of patients continue to have convulsions and fail to provide a complete cure.[3]

Wide range of medicinal plants have been identified by the ancient systems of medicines for treating these problems which are devoid of undesirable effects and are gaining popularity in most of the developing countries.[4] Hence, there is a need for a potent anti-epileptic agent, which is devoid of side-effects. Plants have been a principal source of traditional medicine for more than 5000 years. Plants and their phytoconstituents have important role in the development of a potent anti-convulsant agent. [5,6].

Ginger, the rhizome of *Zingiber officinale*, is one of the commonly used species of the ginger family *Zingiberaceae* and is used for various foods and beverages. Ginger has number of medicinal uses since 2,500 years in China and India for conditions such as headaches, nausea, rheumatism, and colds. [7] Ginger is used in Chinese medicine to warm the body and treat cold extremities, improve a weak and tardy pulse, and strengthen the body after blood

loss.[8] It is used for the treatment of gastrointestinal disorders and piles.[9] It is also used for the treatment of gastrointestinal disorders including gastric ulcerogenesis.[10] Ginger contains a number of active ingredients and pungent constituents. Ginger oil formed from the steam distillation of powdered ginger , contains a high proportion of sesquiterpene hydrocarbons, predominantly zingiberene.[11] Ginger's active ingredients are thought to be present in its volatile oils, which comprise about1-3% of its weight .[12] The major active ingredients in ginger oil are the sesquiterpenes: zingiberene, bisapolene, and zingiberol.[13,14] Gingerols have sedative, analgesic, antibacterial and antipyretic effects in vitro and in animals.[15,16]

EXPERIMENTAL SECTION

Collection of plant & preparation of extract

The rhizomes of *Zingiber officinale* were collected from the local market and authenticated by Professor and Head, Department of Botany, Government Degree College, Khammam.

The *Zingiber officinale* rhizomes (ginger) were cut into smaller pieces, dried under shade for 10 days and pulverized to coarse powder using a manual blender. The ginger powder was extracted with ethanol by continuous extraction in a soxhlet. After extraction the solvent is removed, typically by means of a rotary evaporator, yielding the extracted compound. The non-soluble portion of the extracted solid remains was discarded. The extract was dried under vacuum, stored at room temperature and protected from direct sunlight in the Department of Pharmacology, Mamata Medical College, Khammam.

Drugs & Instruments

1. Phenytoin (Anglo-French Drugs & Industries Ltd., Bangalore), and 0.9% normal saline (0.9% NaCl solution) were used in this study.
2. Electroconvulsiometer

Experimental animals

Swiss albino rats of either sex weighing 150 to 200 gm were obtained from NIN, Hyderabad. The animals were housed in standard cages with free access to food (standard laboratory pellet diet) and water. The animal house temperature was maintained at 23 ± 5.0^0C with a 12-h light/dark cycle. Experimental protocol was approved by Institutional Animal Ethical Committee (IAEC). The guidelines for the investigation of experimental seizures in conscious animals were followed.

Acute toxicity tests

Acute toxicity tests in albino rats have proven the LD_{50} of *Zingiber officinale* rhizome extracts to be more than 5g/kg.[15] The stomach showed no histomorphological changes in any of the dose of extract studied. Based on the results obtained from this study, the dose of ethanolic extract of *Zingiber officinale* rhizome for anti-convulsant activity was fixed to be 50mg/kg, 100mg/kg and 200mg/kg body weight.

Experimental design

After acclimatization, the animals were randomly divided into five groups of six rats each (n = 6). Group-I: Normal saline 25 ml/kg, (control), Group-II: phenytoin 25mg/kg, (standard), Group-III, IV, V: Received three graded doses of 50, 100 and 200 mg/kg, of *Zingiber officinale* rhizome extract respectively. The test samples were given orally one hour prior to induction of convulsions.

MES-Induced Seizures

Corneal electrodes were used for bilateral delivery of electrical stimulus (Maximal Electroshock Seizures, MES-150mA; 50Hz; 0.2 Sec) using electroconvulsiometer. Suppression of tonic hind limb extension was taken as a measure of efficacy and compared with the control and phenytoin group. [17,18] All precautions were taken to minimize animals suffering.

Statistical Analysis

Results were expressed as Mean ± SEM. Data were analyzed by one-way analysis of variance, followed by Dunnett's multiple comparison tests was performed using primer of biostatistics. $P < 0.05$ was considered as significant.

RESULTS

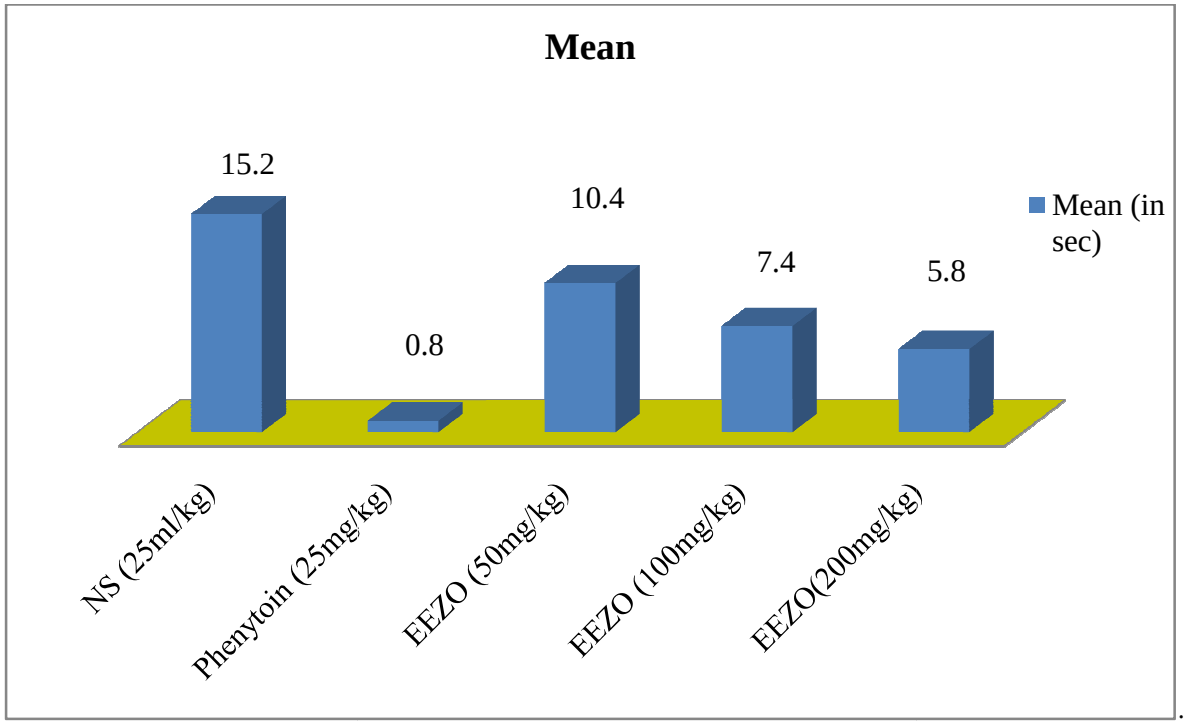
Table 1: Effect of ethanolic extract of *Zingiber officinale* in MES induced seizures in rats

S. No	Treatment Groups	Duration of tonic Extension in sec. (Mean±SEM)
1	Group I (NS- 25ml/kg)	15.2±1.1
2	Group II (Phenytoin- 25 mg/kg)	0.8±0.4 (P=0.00)**
3	Group III (EEZO-50mg/kg)	10.4±0.9 (P=0.01)**
4	Group IV (EEZO-100mg/kg)	7.4±0.8 (P=0.00)**
5	Group V (EEZO- 200mg/kg)	5.8±0.7 (P=0.00)**

*Values are expressed as Mean±SEM. NS- Normal Saline. EEZO- Ethanolic Extract of Zingiber officinale. **P<0.01 Significant compared to normal-saline treated group.*

Table: 1 Shows the reduction in the duration of hind limb extension in Phenytoin and EEZO groups on comparing with the control group ($P < 0.01$) in MES induced seizures. EEZO exhibited a significant (P<0.01) dose dependent protection against tonic extensor phase at all tested doses (50, 100 and 200mg/kg), with maximal effect seen in higher dose (200 mg/kg). There was no death seen in any of the treated groups.

Bar diagram showing the mean duration of tonic hind limb extension in seconds



DISCUSSION

Epilepsy is a CNS disorder associated with recurrent episodes of seizures due to the abnormal electrical activity in the brain. In India, 5.59 per 1000 population are affected by this disorder. The currently available drugs used for treating epilepsy are associated with many adverse effects. Hence, there is a need for a potent anti-epileptic agent, which is devoid of side-effects. Plants and their phytoconstituents have important role in the development of a potent anti-convulsant agent.

Ginger, the rhizome of *Zingiber officinale*, is one of the widely used species of the ginger family *Zingiberaceae* and is a common condiment for various foods and beverages. Ginger is used for a wide array of unrelated ailments that include arthritis, rheumatism, sprains, muscular aches, pains, sore throats, cramps, constipation, indigestion, vomiting, hypertension, dementia, fever, infectious diseases and helminthiasis. Ginger and its active compounds found to have immuno-modulatory, anti-tumorogenic, anti-inflammatory, anti-apoptotic, anti-hyperglycemic, anti-lipidemic and anti-emetic actions. Ginger is a strong anti-oxidant agent and may prevent generation of free radicals. It is considered a safe herbal medicine with only few and insignificant adverse effects.

MES-induced convulsion model is a widely used tool to screen drugs for generalized tonic-clonic seizures. MES causes several changes at the cellular level, disrupting the signal transduction in the neurons. MES causes cellular damage by facilitating the entry of Ca^{2+} into the cells in large amounts, prolonging the duration of convulsions.[19] Apart from Ca^{2+} ions, MES may also facilitate the entry of other positive ions like Na^{+}, blockade of which, can prevent the MES-induced tonic extension.[20]Currently available anticonvulsant drugs like sodium valproate and phenytoin act by modulation of these ion channels.[21] On the other hand, drugs that antagonizes NMDA receptors or potentiate opioids and GABA receptors are also reported to protect against MES-induced seizures.[22] EEZO(Ethanolic Extract of *Zingiber officinale*) exhibited a significant ($P<0.01$) dose dependent protection against tonic extensor phase at all tested doses (50, 100 and 200mg/kg), with maximal effect seen in higher dose (200 mg/kg). This observed effect suggests that the protection of EEZO was maximum at 200 mg/kg. The anti-convulsant activity can be due to the presence of various phytoconstituents like phenylpropanoid, gingerol[23]

It has been suggested that MES induced convulsions are associated with oxidative damage. [24, 25] *Zingiber officinale* also has strong antioxidant property (Kim et al., 2007).[26] . The anti-convulsant activity of *Zingiber officinale* rhizome can also be due to the antioxidant property.

CONCLUSION

The present study demonstrated that ethanolic extract of *Zingiber officinale* rhizome has dose dependent anticonvulsant activity in tested animal model. Further research is required to elucidate specific mechanism and active principles responsible for its anticonvulsant property.

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