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STUDY OF THE ANTICONVULSANT ACTIVITY OF ETHANOLIC EXTRACT OF RHIZOMES OF *ZINGIBER OFFICINALE* IN EXPERIMENTAL ANIMALS

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Anticonvulsant property, *Zingiber officinale*, Maximal electroshock seizures, Epilepsy

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ABSTRACT: Objective: To evaluate the anticonvulsant property of *Zingiber officinale* as well as its interaction with conventional anticonvulsant drug using Maximal electroshock seizures (MES) model and to evaluate possible mechanism involved in its action. **Method:** The present study was done after getting ethical clearance. The rhizomes of ginger were authenticated and extraction of dried rhizomes was done by using Soxhlet apparatus to obtain its ethanolic extract. Animals were divided into 4 groups using Phenytoin (25 mg/kg) as the standard drug. The alcoholic extract of *Zingiber officinale* was given at the doses of 200 mg/kg and 100 mg/kg. The test samples will be given one hour prior to induction of convulsions. **Results:** In MES model, the alcoholic extract of *Zingiber officinale* at the doses of 200 mg/kg and 100 mg/kg p.o significantly reduced the duration of tonic hind limb extension (THLE) in mice ($P<0.05$) in a dose dependent manner as compared to the vehicle control. The extract at a dose of 200 mg/kg body weight is found to be effective nearly similar to that of standard drug Phenytoin. **Conclusion:** The ethanolic extract of *Zingiber officinale* showed significant anticonvulsant activity in Maximal electroshock seizures (MES) model.

INTRODUCTION: 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 [1]. Although probably a native of Asia, *Z. officinale* has become naturalized in many countries and is now widely distributed throughout tropical and subtropical parts of the world. Ginger has been cultivated for thousands of years for medicinal purposes and as a spice. It is used extensively in traditional medicine to treat cold, fever, headache, nausea, and digestive problems and is also used in western herbal medical practices for the treatment of arthritis, rheumatic disorders, and muscular discomfort [2].

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The main constituents of ginger are the gingerols, shogaols, paradols, and zingerone [3]. The major gingerol and shogaol components present in the rhizome of ginger are 6-gingerol and 6-shogaol, respectively. The main aroma defining component is zingiberol, whereas others such as gingediol, monoacyldigalactosyl-glycerol, diarylheptanoids, and phytosterols have also been identified [4].

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 [5]. Prevalence rate of epilepsy is about 5.59 per 1000 population in India [6]. 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 [7]. 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 [8]. Plants and their phytoconstituents have important role in the development of a potent anticonvulsant agent [9, 10].

So the present study was done to evaluate different pharmacological actions of *Zingiber officinale* including anticonvulsant activity due to involvment of different active ingredients so as to minimize the side effects of synthetic drugs and to promote the use of a novel natural medicinal plant.

MATERIALS AND METHODS: The present study was conducted in the Department of 1) Pharmacology, Gauhati Medical College and 2) Hospital. 3)

Ethical Review: The protocol was submitted to the Animal Ethics Committee, GMCH and the study was conducted after obtaining permission from the Institutional Animal Ethics Committee (MCI 05/2015/48).

Experimental Animals:

Inclusion Criteria: Adult male Swiss albino mice weighing 25-30 g was used in the study. The animals were fed on commercial rodent pellets and water *ad libitum* during the study. The animals were housed in plastic cages at a controlled temperature of 24 ± 1 ºC and 12 h light and dark cycle. Before conducting the experiment all animals were acclimatized to laboratory condition for 7 days. All experiments were done after following the guidelines on ethical standards for investigation of experimental pain in animals and the guideline for the investigation of experimental seizures in conscious animals.

Exclusion Criteria:

- Female Swiss albino mice
- Neonate albino mice
- Albino mice with signs of disease

Collection of Plant and Preparation of Extract: The rhizomes of *Zingiber officinale* was collected from the local market and authenticated by Professor and Head, Department of Botany, Gauhati University. 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 apparatus. 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, Gauhati Medical College and Hospital.

Acute Toxicity Study: Acute toxicity study was carried out according to OECD 425 guidelines.

Reagent and Instrument:

- Phenytoin
- 0.9% normal saline (0.9% NaCl solution)
- Electroconvulsiometer

Experimental Design:

To Demonstrate Anticonvulsant Effect: After acclimatization, animals were randomly divided into 4 groups of six mice each (n = 6).

Group I: Normal saline 25 ml/kg (control).
Group II: Phenytoin 25 mg/kg (standard) [11].
Group III: 100 mg/kg p.oof *Zingiber officinale* rhizome extracts [11].
Group IV: 200 mg/kg p.oof *Zingiber officinale* rhizome extracts [11].

MES (Maximal Electroshock Seizures) Induced Seizures: The test samples were given one hour prior to induction of convulsions. Corneal electrodes were used for bilateral delivery of electrical stimulus using electro convulsiometer (MES-150mA; 50Hz; 0.2 Sec).The animals were observed closely for 2 min. Suppression of tonic hind limb extension was taken as a measure of efficacy and compared with the control and Phenytoin group [12, 13]. Following parameters were seen:

Duration of observed tonic hind limb extension seizure (THLE) was recorded in each dose group[14, 15]. The number of animals protected from tonic hind limb extension seizure (*i.e.* abolition of tonic hind limb extension within 10 sec after delivery of the electroshock was considered as protected rat) [14, 15] and was calculated in each group by-

Percentage protection (%) = No. of animals with THLE lasting less than 10 sec / Total no. of animal ×100

Anticonvulsant activity was expressed as the percentage of inhibition of convulsion compared with control animals. All precautions were taken to minimize animals suffering.

RESULTS AND OBSERVATION: The data obtained were analyzed and presented using appropriate statistical method.Results were expressed as Mean ± SEM. Data was analyzed by one-way analysis of variance, followed by Dunnett's multiple comparison tests which was performed using primer of biostatistics. *P* <0.05 was considered as significant.

Anticonvulsant Activity: In the present study, standard anticonvulsant drug Phenytoin at the dose of 25 mg/kg significantly reduced the duration of tonic hind limb extension (P<0.05) as compared to the vehicle control group. In MES model, the extract shortened the duration of tonic hind limb extension in comparison with control and exhibited a dose dependent anticonvulsant activity. As shown in the **Table 1**, the alcoholic extract of *Zingiber officinale* at the doses of 200 mg/kg and 100 mg/kg significantly reduced the duration of tonic hind limb extension (THLE) in mice (P<0.05) as compared to the vehicle control. The extract at a dose of 200 mg/kg body weight is found to be effective nearly similar to that of standard drug Phenytoin **Fig. 1**. Anticonvulsant activity was expressed as the percentage of inhibition of convulsion compared with control animals which was maximum for Phenytoin followed by *Zingiber officinale* extract at a dose of 300 mg/kg. As shown in **Table 2**, Phenytoin offered 100% protection followed by *Zingiber officinale* 200 mg/kg which offered 66.7% protection. Abolition of tonic hind limb extension within 10 sec after delivery of the electroshock was considered as protected rat in all the groups.

TABLE 1: EFFECTS OF *ZINGIBER OFFICINALE* ON DURATION OF THLE AND PERCENTAGE OF INHIBITION OF CONVULSION IN MES INDUCED SEIZURES USING MICE

Group no.	Group	Dose (mg/kg)	Duration of THLE (Sec)	Percentage of inhibition of convulsion (%)	Mice convulsed / mice used
I	Control- Normal saline	25 ml/kg	36.66 ± 0.49	-	6/6
II	Standard drug- Phenytoin	25 mg/kg	4.50 ± 0.56**	87.7%	0/6
III	Test drug- *Zingiber officinale*	100 mg/kg	15.17 ± 1.76**	59.6%	4/6
IV	Test drug- *Zingiber officinale*	200 mg/kg	10.67 ± 0.75**	71.0%	2/6

Values represented as Mean ± S.E.M. (n=6), ** P<0.05 *vs.* control (group 1)

TABLE 2: EFFECTS OF *ZINGIBER OFFICINALE* ON PERCENTAGE OF PROTECTION IN MES INDUCED SEIZURES USING MICE

Group no.	Group	Dose (mg/kg)	Percentage protection (%)	Mice protected*/ mice used
I	Control- Normal saline	25 ml/kg	0%	0/6
II	Standard drug- Phenytoin	25 mg/kg	100%	6/6
III	Test drug- *Zingiber officinale*	100 mg/kg	33.3%	2/6
IV	Test drug- *Zingiber officinale*	200 mg/kg	66.7%	4/6

*Abolition of tonic hind limb extension within 10 sec after delivery of the electroshock was considered as protected rat.

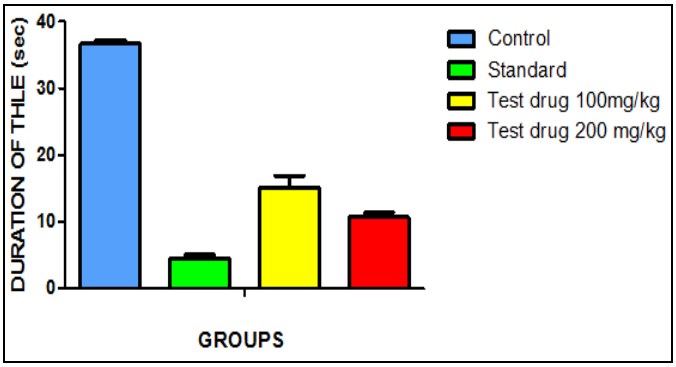

FIG. 1: EFFECTS OF *ZINGIBER OFFICINALE* ON DURATION OF THLE

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 [1]. There are a number of synthetic anticonvulsant drugs currently available for use in the management, control and treatment of individuals with epilepsy.

However, most of the synthetic drugs are not only inaccessible and unaffordable, but also possess many toxic adverse effects. Therefore, there is a

great need for the development of cheap, effective and safe anticonvulsant agents from plants and other sources.

Plants and their phytoconstituents have important role in the development of 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 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 [1].

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.[16] 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 [17]. Currently, available anticonvulsant drugs like sodium valproate and phenytoin act by modulation of these ion channels [18]. On the other hand, drugs that antagonizes NMDA receptors or potentiate opioids and GABA receptors are also reported to protect against MES-induced seizures [19]. EEZO (Ethanolic Extract of *Zingiber officinale*) exhibited a significant ($P<0.05$) dose dependent protection against tonic hind limb extension seizure at all tested doses (100 and 200 mg/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 [20]. It has been suggested that MES induced convulsions are associated with oxidative damage [21, 22]. *Zingiber officinale* also has strong antioxidant property (Kim *et al*., 2007). The anti-convulsant activity of *Zingiber officinale* rhizome can also be due to the antioxidant property.

CONCLUSION: From the above study we can conclude that the plant extract of *Zingiber officinale* showed significant dose dependent anticonvulsant activity in MES induced seizures, thus making it a novel promising medicinal plant with diverse effect on central system which is devoid of side effects of conventional antiepileptic drugs. However further research is required to elucidate specific mechanism and active principles responsible for its anticonvulsant property.

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CONFLICT OF INTEREST: No conflict of interest.

REFERENCES:

1. Venkatanarayana N: Evaluation of anticonvulsant activity of ethanolic extract of *Zingiber officinale* in Swiss albino rats. J Chem Pharm Res 2013; 5(9): 60-64.
2. White B: Am Fam Physician: Ginger: an overview 2007; 75(11): 1689-91.
3. Langner E, Greifenberg S and Gruenwald J: Ginger: history and use. Adv Ther 1998; 15(1): 25-44.
4. Jiang H, Xie Z, Koo HJ, McLaughlin SP, Timmermann BN and Gang DR: Metabolic profiling and phylogenetic analysis of medicinal *Zingiber species*: tools for authentication of ginger (Zingiber officinale Rosc.). Phytochemistry 2016; 67: 232-244.
5. Ngo Bum E, Taiwe GS, Moto FC, Ngoupaye GT, Vougat RR and Sakoue VD: Antiepileptic medicinal plants used in traditional medicine to treat epilepsy, clinical and genetic aspects of epilepsy. In: Zaid Afawi 2015. 307-700-0. Available from: http://www.intechopen.com/books/clinical-and-genetic-aspectsofepilepsy/antiepileptic-medicinal-plants-used-in-traditional-medicine-to-treat-epilepsy. Croatia.
6. Kumar D, Singh J, Baghotia A and Kumar S: Anti-convulsant effect of the ethanol extract of *Caesalpinia pulcherrima* (L.) Sw., Fabaceae, leaves. Available from: http://www.scielo.br/pdf/rbfar/2010 nahead/aop1410.pdf.
7. Anonymous: Neurological disorders: Public health challenges. Switzerland: World Health Organization 2016.
8. Umachigi SP, Kumar GS, Jayaveera , Kishore KD, Ashok KC and Dhanapal: Afr J Tradit Complement Altern Med 2017; 4(4): 481-487.
9. Hegde K, Thakker SP, Joshi AB and Shastry CS, Chandrasekhar KS: Tropical J Pharm Res 2009; 8(2): 117-125.
10. Available from: http://www.cdc.gov/nccdphp/publications/aag/pdf/epilepsy.pdf

11. Hosseini A, Mirazi N: Acute Administration of ginger extract on timed intravenous PTZ infusion seizure model in mice. Epilepsy Res march 2014; 108(3): 411-9
12. Mahendran S, Thippeswamy BS, Veerapur VP and Badami S: Anticonvulsant activity of embelin isolated from Embeliaribes. Phytomedicine 2011; 18(2-3): 186-88.
13. Goyal M, Nagori BP and Sasmal D: Sedative and anticonvulsant effects of an alcoholic extract of *Capparis deciduas*. J Nat Med 2009; 63(4): 375-379.
14. Swinyard EA and Woodhead J: Experimental detection, quantification and evaluation of anticonvulsants in antiepileptic drugs. Ravenpress, New York 2015: 111-126.
15. Ngo Bum E, Dawack DL, Schmutz M, Rakotonirina A, Rakotonirina SV, Portet C, Jeker A, Olpe HR and Herrling P: Anticonvulsant activity of *Mimosa pudica* decoction. Fitoterapia 2014; 75: 310-315.
16. Inan SY and Buyukafsar K: Br J Pharmacol 2008; 155(1): 44-51.
17. Bum EN, Nkantchoua GN, Njikam N, Taiwe GS, Ngoupaye GT and Pelanken MM: Int J Pharmacol 2010; 6(2): 123-128.
18. Rang HP, Dale MM, Ritter JM and Moore PK: Pharmacology, Philadelphia, Churchil Livingstone, Elsevier Science Ltd., Edition 5th, 2013.
19. Manocha A, Sharma KK and Mediratta PK: Indian J Pharmacol 2017; 29(3): 194-197.
20. Nikaljee AG: IJRPS 2015; 2(3): 1-13.
21. Rauca C, Zerbe R and Jantze H: Brain Res 1999; 847(2): 347-351.
22. Rola R, Swiader M and Czuczwar SJ: Pol J Pharmacol 2012; 54(5): 521-524.

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