

## ANTICONVULSANT EFFECTS OF NIFEDIPINE ON MES INDUCED SEIZURES

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### ABSTRACT

**Objective:** To evaluate the anticonvulsant activity of Nifedipine against MES induced seizures.

**Methods:** The study was induced by techno electroconvulsometer. The animals were treated with Nifedipine (100 µg/100 g i. p. and 200 µg/100 g i. p.) and MES was induced 2 h after the administration of the drug, and duration of various phases was noted. Duration of THLE was taken as an index for antiepileptic activity.

**Results:** Nifedipine when administered in a dose of 100 µg/100 g ip, did not produce any changes in any phases of the MES induced seizure. But in a dose of 200 µg/100 g ip, it significantly reduced the duration of THLE.

**Conclusion:** Nifedipine has a significant action against MES induced seizures suggesting an important role of CCBs as future, promising antiepileptic drug.

**Keywords:** Calcium channels, MES seizures, Nifedipine, THLE, Anticonvulsants

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### INTRODUCTION

Epilepsy is one of the most common afflictions of a man with a prevalence of approximately 1% of the total population. Anticonvulsant drugs act after binding to specific sites within the brain like gamma amino butyric acid, excitatory amino acids and benzodiazepine receptors.

Voltage-gated calcium channels mediate calcium influx that controls both neuronal excitabilities and regulates calcium sensitive intracellular signaling pathways. Previous studies have already shown some alterations in Ca<sub>v</sub> 3.2 (gene encoding T type Ca<sup>++</sup>channels), which may induce altered biophysical properties or increase channel expression [1-4]. The Ca<sub>v</sub>2.1 encodes for both P and Q type calcium channels and these channels are highly expressed presynaptically where they are critically involved in neurotransmission and synaptic efficacy and therefore have a great influence on neuronal excitability [5, 6]. Studies have also been carried out on genetic epilepsy-prone rats (GEPRs), and in them induction of secondary tonic-clonic seizure have shown an increase in Ca<sub>v</sub> 1.3 (L type) and Ca<sub>v</sub> 2.3 (R type) protein level, in neurons, [7] further supporting the role of calcium ions in epileptogenesis. Thus it may be concluded that calcium current may contribute to epileptogenesis by undergoing burst in pacemaker cells, enhancing postsynaptic excitatory responses in dendrites and somatic nerve cells, and, providing post burst re-excitation. [8] Through intensive research, it has also been highlighted that calcium is also involved in neuronal injury which is caused as a result of repeated seizures. [9] Accumulated evidence shows a clear correlation of calcium channel expression with the development and maintenance of seizures. Thus the present study was undertaken to evaluate the anticonvulsant activity of NIFEDIPINE, which is a dihydropyridine calcium channel blocker, on MES induced seizure.

### MATERIALS AND METHODS

#### Animals

Adult, healthy swiss albino mice, aged 6-8 w of either sex weighing 20-30 g were used. They were housed under standard laboratory conditions [controlled temperature (around 22±/2 °C) and humidity (50%) colony room] for one week before experiments were started and were kept in groups of 3-4 in per polypropylene cages. Animals were allowed standardized diet and water ad libitum, except for the period of experimentation.

#### Drugs and chemicals

1. Nifedipine (JB chemicals, Mumbai)–it was dissolved in propylene glycol, just before use.
2. Propylene Glycol (Hi Media, Mumbai)–This solvent was used to dissolve the Nifedipine and it served as solvent control in Nifedipine treated animals.

#### Method

The present study was undertaken to see the antiepileptic activity of Nifedipine, which is a DHP calcium channel blocker, against MES induced seizure.

The animals were grouped in three groups, each group comprising of 10 animals.

Maximal electroshock seizure was induced by Techno-electro convulsometer (50 mAmp, 0.1 sec duration) through ear electrodes, via small alligator pinnal clips. Duration of various phases of maximal electroshock seizure (tonic flexion, tonic extension, tonic convulsion, post-tetanic depression) was noted with the help of stopwatch.

In the first phase, the animals were treated with Nifedipine (100 µg/100 g ip). MES was induced by techno-electro convulsometer, 2 h after the administration of the drug, and various duration were noted.

In the second phase, the animals were treated with Nifedipine (200 µg/100 g ip). MES was induced by techno-electro convulsometer, 2 h after the administration of the drug, and various duration were noted.

Propylene glycol (0.2 ml/100 g ip) treated animals served as solvent control.

The result were statically analyzed by paired student's' test. P values<0.05 were considered significant.

The anticonvulsant effects of Nifedipine were evaluated in the maximal electroshock (MES) seizure test.

### OBSERVATION AND RESULTS

The present study was undertaken to explore the anticonvulsant effect of Nifedipine, a calcium channel blocker, against MES induced seizure. The experimental study was conducted in mice. Each study was conducted with a control group treated with propylene glycol.

The abolition or reduction of the duration of the tonic extension was considered as an index for antiepileptic activity.

#### MES seizure test

When administered in a dose of 100 µg/100g i. p., Nifedipine did not produce any significant change in any phase (tonic flexion, tonic extension, clonic convulsion, posttetanic depression) of MES induced

seizures ( $p>0.05$ ). When administered in a dose of 200µg/100g i. p., Nifedipine significantly reduced the duration of tonic hind limb extension ( $p<0.001$ ), but failed to produce any significant change in any other phase of MES induced seizures ( $p>0.05$ ).

The tonic hindlimb extensor component was found to be reduced significantly in animals pretreated with Nifedipine. On the basis of these observations, Nifedipine appeared to have a potent antiepileptic effect.

**Table: Effect of Nifedipine on the duration of various phases of MES induced seizures**

No.	Dose of drug	TF	THL	CC	PTD
1.	Control	3.3±0.82	13.9±1.19	9.0±0.81	6.0±0.94
2.	N (100 µg/100g)	3.1±1.01	13.7±1.03	8.9±1.02	5.6±1.05
3.	N (200 µg/100g)	3.2±0.99	4.7±0.76	8.8±1.02	5.8±1.03

N = Nifedipine, TF = tonic flexion, THLE = tonic flexion leg extension, CC = clonic convulsion, PTD = post tetanic depression, Values are given as mean±SEM (n = 10).

#### DISCUSSION

The current experimental study has been planned with an objective to study the antiepileptic effects of Nifedipine on MES induced seizures. From the experimental results, it was found that Nifedipine do have a significant anticonvulsant action. This anticonvulsant action may be based on the facts that, during the episode of epileptic attack there is ischemia and excitation which can cause damage in the hippocampus and cerebellar cortex [10]. Epileptic depolarization in single motor and hippocampal neurons and focal epileptic discharges in neuronal cortical preparations have also been described to be decreased by calcium channel blockers and hence CCBs prevents cell damage [11]. The anticonvulsant effect of Nifedipine may also be correlated with the increase in local blood flow due to vasodilatation [12], and all these effects of Nifedipine may be due to central blockade of calcium entry through dihydropyridine L-type calcium channels [13]. It has been established that even small alterations in the biophysical properties of presynaptic calcium channels could have a significant impact on the firing properties of nerve cells and neuronal networks with the potential to lead to epileptic seizure activity [14-16]. The fact that CCBs do not directly inhibit neurotransmitter release, except, in the situation of ischemia and excitation, can encourage the use of these drugs as non-sedative anticonvulsants without the risk of a catastrophic effect on neurotransmission [17]. The considerable effect is still going on towards developing new and selective calcium channel blocking compounds aimed at the treatment of epilepsy [18]. In conclusion, as we already know that many of the currently used antiepileptic drugs have been shown to block the calcium channels and the present study also demonstrated that Nifedipine (calcium channel blocker) has anticonvulsant action, calcium channels are more commonly viewed as attractive targets for novel epileptic therapies.

#### AUTHORS CONTRIBUTIONS

All the author have contributed equally

#### CONFLICT OF INTERESTS

Declared none

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