# Phytochemical Screening and Pharmacological Evaluation of Momordia Dioica Ethanolic Extract for Anticonvulsant and Antidepressant Activity

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Abstract: Momordica dioica is traditionally used as astringent, febrifuge, antiseptic, anthelmintic, spermicidal. also used in bleeding piles, urinary infection and as a sedative. Studies indicate that it possesses antioxidant, hepatoprotective, antibacterial, antiinflammatory, anti-lipid peroxidative, hypoglycemic and analgesic properties. Momordica dioica ethanolic extract was tested for anticonvulsant and antidepressant action at 200 and 400mg/kg doses by using a different models of convulsion and depression in mice and results were compared with those standard and control groups. Sensitive mice which showed expected standard responses to MES, PTZ and INH were stimuli divided into four groups of 6 mice in each. The anticonvusant drug phenytoin 25mg/kg and diazepam was used as a standard. The important parameters studied were seizure latency, tonic hind limb flexion, tonic hind limb extension and percentage protection against mortality (only in MES model). In PTZ and INH model the parameters were selected for the study jerking movement, clonic convulsion and extensor then in INH latency of seizure and time taken for death was done. The ethanolic extract of Momordica dioica is likely to be of safe in the management of convlsions. The antidepressant activity of the ethanolic extracts of Momordica dioica revealed significant depression pattern in test for pentobarbitone induced sleeping time and exploratory activity in mice.

Keywords: Anticonvulsant, Antidepressant, Momordica dioica, ethanolic extract, Isoniazid, Pentelynetetrazole.

#### 1. Introduction

The word "epilepsy" is derived from a Greek word meaning, "a condition of being overcome, seized, or attacked." The word epilepsy means nothing more than a tendency to have seizures.<sup>1</sup> More than a century ago, John Hughlings Jackson, the father of modern concepts of epilepsy proposed that seizures were caused by "occasional, sudden, excessive, rapid and local discharges of gray matter," a generalized convulsion resulted when normal brain tissue was invaded by the seizure activity initiated in the abnormal focus.<sup>2</sup>

Epilepsy is a brain disorder that causes people to have recurring seizures.<sup>3</sup> When nerve cells in the brain fire electrical impulses at a rate of up to four times higher than normal, this causes a sort of electrical storm in the brain, known as a seizure<sup>4</sup> characterized by paroxysmal transient disturbances of brain function that may be manifested as episodic impairment or loss of consciousness, abnormal motor phenomena, psychic or sensory disturbances, or perturbation of the autonomic nervous system.<sup>5</sup>

The prevalence of epilepsy is approximately 1% of the population, both in the United States and internationally.<sup>6</sup> Epilepsy is the fourth most common neurological disorder in the U.S. after migraine, stroke, and Alzheimer's disease. Its prevalence is greater than autism spectrum disorder, cerebral palsy, multiple sclerosis and Parkinson's disease combined.<sup>7</sup>

The use of plants for treating various diseases predates human history and forms the origin of much of the modern medicine The modern antiepileptic drug (AED) era spanning a period of more than 150 years from the first use of bromide in 1857 to 2008 has seen the introduction into clinical practice of a diverse group of effective and safe drugs.<sup>8</sup>

Medicinal herbs and plant extracts are now generally considered as effective medicines to be respected, appreciated and they play a major role in modern pharmacy. World Health Organization estimated that about 80% of the world's population relies on herbs for their primary healthcare needs. In the present study, Argyreia nervosa is used to study the anticonvulsant activity in mice. Various parts of the plant have been explored for central nervous depressant activity, nootropic activity, aphrodisiac activity, activity, immunomodulatory anticonvulsant activity, antioxidant activity, analgesic activity, anti-inflammatory activity, hypoglycemic activity, hepatoprotective activity, antibacterial activity, antifungal activity and many other activities.9

#### 2. Materials and Methods

#### 2.1 Chemicals and Reagents

The drugs used were diazepam (DZ) (Ranbaxy Lab. Ltd., Thane), phenytoin (Zydus Neuroscience, Ahmedabad) and Phenytoin (Radicura Pharmaceuticals, New Delhi). Phenobarbitone and were purchased from Sigma Aldrich, USA. Other chemicals used for extraction and phytochemical investigation were of analytical grade from S.D. Fine Chemicals, Mumbai, India.

#### **2.2 Plant Material and Extraction**

The *Momordica dioica* leaves was collected during the march 2013 from Sri Venkateshwara University, Tirupati, India. The plant was authenticated by Dr. K. Madhava Chetty, Department of Botany and voucher specimen of the plant were preserved at institute herbarium library. Leaves was separately washed, wiped-dry, and subsequently reduced to a coarse powder. About 100 g of the plant powder were separately extracted for 24 h with 90% ethanol with intermittent vigorous shaking. The extracts were filtered, concentrated with a rotary evaporator and dried over a water bath at 45°C. The residue from the plant parts were used for experimental analysis

#### **2.3 Experimental Animals**

Wistar albino male mice (18-22 g) and rats (180-220) was obtained from the central animal house of Sigma Institute of Clinical Research and administration Pvt Ltd Hyderabad. The animals were housed at room temperature (22-28 °C) for 12 hr dark and 12 hr light cycle and given standard laboratory feed and water *ad-libitum*. The study was approved and conducted as per the norms of the Institutional Animal Ethics Committee (769/2010/CPCSEA).

#### 2.4 Acute Oral Toxicity Study

#### 2.4.1 Procedure

Acute toxicity studies were performed according to OECD-423 guidelines category IV substance (acute toxic class method). Albino mice (n=3) of either sex selected by random sampling technique were employed in this study. The animals were fasted for 4 hrs with free access to water only. The ethanolic extract of *Momordica dioica* was administered orally with a maximum dose of 2000 mg/kg body weight. The mortality was observed for three days. If mortality was observed in2/3 or 3/3 of animals, then the dose administered was considered as a toxic dose. However, if the mortality was observed only one mouse out of three animals then the same dose was repeated again to confirm the toxic effect. If mortality was not observed, the procedure was then repeated with higher dose (Organization for economic Co-operation and development, 2001)

#### 2.4.2 Preliminary Phytochemical Studies

Ethanolic extract of the plant of *Momordica dioica* were subjected to chemical tests for the identification of their active constituents.

2.4.3 Phytochemical screening of ethanolic extract of *Momordica dioica*.

Phytoconstituents	Presence or Absence
Carbohydrates	+
Glycosides	+
Fixed oils and fats	-
Gums and Mucilage	-
Protein and Amino Acids	+
Saponins	+ + +
Tannins	+
Phytosterols	+ +
Flavonoids	+ +
Alkaloids	+ + +

#### 2.5 Assessment of Anticonvulsant activity by MES Model

#### 2.5.1 Maximal electroshock induced seizures (MES)

Tonic convulsions of the hind extremities of male mice were induced by passing alternating electrical current (50 Hz, 60 mA, 0.2 s) through ear clip electrodes by a Rodent shocker generator (Inco Electroconvulsometer model# 100-3). For each experiment, one group served as the control (3% tween 80, 10 mL/kg, p.o.) and one group as the standard (Phenytoin, 25 mg/kg, p.o.). The test extract, *Momordica dioica* was also administered at various doses (200 and 400 mg/kg, p.o.).The number of animals protected from tonic hind limb extension seizure and the latency of onset were determined in each dose group. Percentage protection against mortality was also calculated.

## 2.5.2 Assessment of Anticonvulsant activity by PTZ Model

#### Pentylenetetrazole (PTZ) induced convulsions :

The mice were randomly divided into four groups containing six mice in each group as follows: **Group I:** Control (Vehicle p.o.); **Group II:** Standard (Diazepam (5 mg/kg, i.p.) **Group III:** EMD (200 mg/kg, p.o.); **Group IV:** EMD (400mg/kg p.o.)

Swiss albino male mice  $(25 \pm 2 \text{ g})$  were used. Vehicle, extract or the standard drug (diazepam 5 mg/kg) were administered by intraperitoneal route. PTZ 80 mg/kg was injected intraperitoneally to all mice after 45 minutes of vehicle or extract and 30 min after the standard drug. Immediately after PTZ administration mice were placed individually and observed for onset time of convulsion, duration of clonus and recovery/death (% recovery or % survival).

#### 2.5.3 Isoniazid induced convulsions

Albino mice (18-22 g) of male sex were divided into 04 groups of 06 mice in each was fasted overnight prior to the test but water was supplied ad libitum. Group I was maintained as control which was given with distil water (10 ml/kg p.o.) once daily for 7 days. Group II was administered with diazepam (5 mg/kg i.p.) alone on 1<sup>st</sup> day only; 30 min after administration (diazepam) INH 300mg/kg i.p was administered. Groups III, and IV were treated with different

doses of EMD (200 and 400 mg/kg p.o.) respectively once daily for 7 days. On 7<sup>th</sup> day 60 min after distil water and extract administration into the respective groups, INH was administered. The following parameters were recorded during test session of initial, 30 min. Latency (onset of clonus), and time taken for death.

#### 2.6 Antidepressant Activity

#### 2.6.1 Pentobarbitone Induced Sleeping Time

Mice of either sex will be randomly allocated to the different control and test groups. They will be treated with ethanolic extract of *Momordica dioica* and pentobarbitone sodium (40 mg/kg, i.p.) will be administered 30 min later. The control group receive 10 ml/kg normal saline, i.p. 15 min before pentobarbitone. For positive control group; pentobarbitone (40 mg/kg, i.p.) will be administered 15 min after chlorpromazine hydrochloride (1 mg/kg, i.m.). Onset of sleep will be taken as the time when mice accept the decubitodorsal position for three consecutive trials. Conversely, the duration will be considered complete when mice do not accept the decubito dorsal position for three consecutive trials.

#### 2.6.2 Exploratory Activity- Hole Board Test

#### a) Apparatus and Experimental Design

The hole-board apparatus consisted of a wooden, grey box, measuring  $68 \text{ cm} \times 68 \text{ cm}$ . The walls were 40 cm high, and the box was raised 28 cm above the ground on a metal stand. Four holes (4 cm in diameter) were cut into the floor of the apparatus; each hole was 28 cm from a corner of the box along the diagonal from the corner to the centre. The floor of the box was marked out into four outer areas and one central area using black masking tape. The central area was delineated by four lines of tape each 20 cm from one of the walls, while the four outer areas were marked out by diagonal lines of tape running from the corners of the floor to the corners of the central square. The four holes were thus located at the corners of the central square. The apparatus was located in a small testing room with dimmed white lighting. The stand of the apparatus was open on all sides, allowing the floor or objects to be dimly lit. In the hole board test, a paradigm involving novelty and uncertainty is employed. Head-dipping is generally considered to provide a measure of exploitation that was distinct from motor activity. Twenty four mice (n=24) were divided into four (n=6 per group). The animals were placed on board (40 X 40) with 16 holes (symmetrically distributed in four rows) 1-hr after oral administration of vehicle (normal saline) or different doses of extract (200mg/kg and 400mg/kg). The frequency of head dips into the holes during 5 min was registered immediately after the administration of the extract samples at different doses used and duration was also recorded.

They are expressed as mean total number of head dips: **Group I:** Control (Vehicle p.o.); **Group II:** Standard (Diazepam 1 mg/kg, p.o) **Group III:** EMD (200mg/kg, p.o) **Group IV:** EMD (400mg/kg p.o)

#### b) Statistical analysis

Data were analysed by PrismGraphPad® version 5.0 software and presented as mean $\pm$ SEM values. The statistical tests used were one-way analysis of variance (ANOVA) followed by Dunnett's multiple comparison test. The levels of statistical significance ranged from p<0.05 to p<0.001.

#### 3. Results

#### 3.1 Acute toxicity study

There was no mortality amongst the graded dose groups of mice up to a dose of 2000 mg/kg for duration of 24 h. This finding probably suggests that the ethanol extract is relatively safe or non-toxic in mice at the doses used for this study.

#### 3.2 Phytochemical Screening

Phytochemical screening of the ethanolic extract of *Momordica dioica* (EMD) showed that the crude extract contained small quantities of alkaloids, flavonoids, saponins and large amounts of cardiac glycosides, triterpenoids, phenolic compounds and tannins.

#### 3.3 Assessment of Anticonvulsant Activity by MES model

Maximal electroshock produced hind limb tonic extension seizures (HLTE) in all the animals used. The vehicle-treated mice showed tonic hind limb extsension for a duration of  $32.5 \pm 0.61$  sec. standard drug phenytoin 25 mg/kg showed significant reduction in the duration ( $20\pm 3.77$ ) of HLTE and extract EMD treated group 200mg/kg only showed significant reduction in duration of HLTE and there was no significant reduction of HLTE in 200mg/kg dose of extract animals.EMD (200 mg/kg) significantly reduced the onset of latency, but did not alter the incidence of seizures elicited by maximal electroshock to any significant extent. EMD at doses of 200 and 400 mg/kg, respectively, protected 50% and 66% of mice and significantly reduced the duration of the seizures. The standard antiepileptic drug, Phenytoin protected 83% of mice against seizures and significantly reduced the duration of the seizures. However, phenytoin completely inhibited the MES-induced tonic seizures in all the animals used (Table 1). The onset of clonus of EMD is represented in figure no 1.

<b>Table 1:</b> Effect of ethanolic extract of <i>Momordica dioica</i> on
maximal electroshock induced seizures in mice:

Treatment	Latanav	Duration of	Duration	0/ protoction
Treatment	Latency	Duration of	Duration	76 protection
Group	Onset of	tonic	Of tonic	Against
	Clonus	Flexion	extension	mortality
Control	2.6	$11.6 \pm 0.76$	$225 \pm 0.61$	0
	$\pm 0.335$	$11.0 \pm 0.70$	$52.5 \pm 0.01$	0
Standard				
Phenytoin	$3 \pm 0.11*$	$0.33 \pm 0.20$ ***	$20 \pm 3.77*$	83
25mg/kg)				
EMD	$25 \pm 0.22*$	$7.2 \pm 1.45*$	10.2 + 2.52*	((
(200mg/kg)	$2.3 \pm 0.22$	$7.5 \pm 1.45$	$19.5 \pm 2.55$	00
EMD	$1.0 \pm 0.22*$	5 2 + 1 40**	22.2 + 4.24*	50
(400mg/kg)	$1.9 \pm 0.33^*$	$5.5 \pm 1.40^{**}$	$22.3 \pm 4.24^{*}$	50

All the values are expressed as mean $\pm$ SEM, n=6, One way analysis of variance (ANOVA) followed by multiple comparison Dunnett's test, \*p<0.05, \*\*p<0.01 and \*\*\*p<0.001 as compared to control group.



Jerks 100 80-90 60-90 40-20-0-0-Groups



Figure 1: Effect of ethanolic extract of *Momordica dioica* on latency of onset of clonus on maximal electroshock induced seizures in mice.

All the values are expressed as mean $\pm$ SEM, n=6, One way analysis of variance (ANOVA) followed by multiple comparison Dunnett's test, \*p<0.05 as compared to control group.

#### 3.4 Chemically-induced seizures

# **3.4.1 Effect of ethanolic extract of** *Momordica dioica* on PTZ induced seizures in mice:

In vehicle treated group myoclonic jerks followed by tonic clonic seizure and death was observed after i.p. injection of PTZ. All the animals died in vehicle control group. EMD in a dose of 200 mg/kg and 400 mg/kg increased latency for onset of myoclonic jerks and seizures as well as decreased incidence, total duration of seizure and mortality, though effect was statistically significant in a dose of 200 (p<0.05) and 400 mg/kg (P< 0.001) as compared to vehicle control group. Diazepam completely prevented incidence of tonic clonic convulsions and mortality as compared to vehicle control group.(Table no 2, Fig no 2)

**Table 2:** Effect of ethanolic extract of *Momordica dioica* on PTZ induced convulsions

Treatment Groups	Onset time in seconds (mean±SEM)		
	Jerks	Clonus	Extensor
Control	43.01 ±0.77	$72.45 \pm 0.54$	$264.4 \pm 0.73$
Standard (Diazepam 5mg/kg)	82.96±0.98***	91.59±2.311***	303.3 ±3.37***
EMD 200mg/kg	45.31±1.31ns	77.53±0.81*	273.0±1.02*
EMD 400mg/kg	61.09±1.15***	86.28±0.96***	282.1± 1.98***

All the values are expressed as mean $\pm$ SEM, n=6, ns= not significant, One way analysis of variance (ANOVA) followed by multiple comparison Dunnett's test, \*p<0.05, \*\*p<0.01, \*\*\*p<0.001 as compared to control group.

All the values are expressed as mean±SEM, n=6, ns= not significant, One way analysis of variance (ANOVA) followed by multiple comparison Dunnett's test, \*\*\*p<0.001 as compared to control group.

# **3.4.2** Effect of ethanolic extract of *Momordica dioica* on onset of latency on Isoniazide induced seizures in mice.

Isoniazid (300 mg/kg i.p.) elicited tonic-clonic convulsions followed by onset of latency and mortality in mice. Mice treated with EMD (200 and 400mg/kg) and diazepam significantly delayed (P<0.001) onset of convulsion as compared to INH control mice (Table no 3). There was significant delayed in the mortality (P<0.001) in extract EMD and diazepam treated mice as compared to INH control treated mice (Figure no 3).

Table 3:	Effect of	ethanolic	extract	of Momo	rdica dioica	on
	flatana	I	المستر الرئيسي	1 :		

onset of latency of Isomazia induced seizures in fince.			
Treatment Groups	Onset of Latency	Time taken for death	
Control (INH 300mg/kg i.p)	13.58±0.52	21.17±1.44	
Standard (Diazepam 5mg/kg)	23.67±0.66***	45.00±0.57***	
EMD 200mg/kg	18.67±0.66***	32.33±0.84***	
EMD 400mg/kg	21.17±0.60***	39.17±0.83***	

All the values are expressed as mean $\pm$ SEM, n=6, One way analysis of variance (ANOVA) followed by multiple comparison Dunnett's test, \*p<0.05, \*\*\*p<0.001 as compared to control group.



Figure 3: Effect of ethanolic extract of *Momordica dioica* on onset of latency on Isoniazid induced seizures in mice

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All the values are expressed as mean±SEM, n=6, One way analysis of variance (ANOVA) followed by multiple comparison Dunnett's test, \*\*\*p<0.001 as compared to control group.

### **3.4.3** Effect of ethanolic extract of *Momordica dioica* on pentobarbitone induced sleeping time in mice.

The Time between injection of pentobarbitone and onset of sleep in all treated groups (onset of latency time) presented in (table 4). Ethanolic extract of *Momordica dioica* in the doses of 200 and 400mg/kg shortened the onset of latency time of sleep to 200 ( $6.34\pm0.41$ ) and 400mg/kg ( $5.40\pm0.35$ ) respectively which lower than that of control group ( $9.50\pm0.56$ ) and is significant camparable to diazepam also ( $5.57\pm0.56$ ).Duration of sleeping time in animals receiving 200 and 400mg/kg of ethanolic extract doses increased to  $56.73\pm1.33$  and  $52.91\pm0.87$  that was highly significant (p<0.001) compared with control group ( $26.95\pm1.18$ ). There was a significant (p<0.001) increased in duration of sleep in diazepam group ( $43.96\pm1.04$ ) when compared to control group.

Table -	4: Effect of ethanolic extract of Momordica dioica on
	pentobarbitone induced sleeping time in mice

1	10	
Treatment Groups	Onset of Sleep	Duration of sleep
Control	9.50±0.56	26.95±1.18
Standard (Diazepam 5mg/kg)	5.57±0.25***	43.96±1.04***
EMD 200mg/kg	6.34±0.41***	56.73±1.33***
EMD 400mg/kg	5.40±0.35***	52.91±0.87***

All the values are expressed as mean $\pm$ SEM, n=6, One way analysis of variance (ANOVA) followed by multiple comparison Dunnett's test, \*\*\*p<0.001 as compared to control group.



**Figure 4:** Effect of ethanolic extract of *Momordica dioica* on duration of sleep in pentobarbitone induced sleeping time in mice.

All the values are expressed as mean $\pm$ SEM, n=6, One way analysis of variance (ANOVA) followed by multiple comparison Dunnett's test, \*\*\*p<0.001 as compared to control group.

# 3.4.4 Effect of ethanolic extract of *Momordica dioica* on Hole board (No. of head poking and duration of head dips).

Administration of different doses of EMD 200  $(38.00\pm0.35)$  and 400 mg/kg  $(37.64\pm0.94)$  had significantly increased no. of hole poking in mice as compared to control group  $(33.23\pm0.95)$ . The mice treated with standard drug

diazepam produced s significant increase in no. of hole pokings by  $46.21\pm1.11$ . (Table no 5)

Administration of different doses of EMD 200 ( $13.50\pm1.17$ ) and 400mg/kg ( $14.67\pm1.14$ ) had significantly increased duration of head dips in mice as compared to control group ( $8.33\pm0.88$ ). The mice treated with standard drug diazepam produced s significant increase in duration of head dips by  $22.50\pm1.25$  (Figure no 5, 6).

**Table 5:** Effect of ethanolic extract of *Momordica dioica* on Hole board (No. of head poking and duration of head dips)

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Treatment Groups	No. of Head	Duration of head	
	Poking	Dips	
Control	33.23±0.95	8.33±0.88	
Standard (Diazepam 5mg/kg)	46.21±1.11***	22.50±1.25***	
EMD 200mg/kg	38.00±0.35**	13.50±1.17*	
EMD 400mg/kg	37.64±0.94***	14.67±1.14**	

All the values are expressed as mean $\pm$ SEM, n=6, One way analysis of variance (ANOVA) followed by multiple comparison Dunnett's test, \*p<0.05, \*\*p<0.01, \*\*\*p<0.001 as compared to control group.



Figure 5: Effect of ethanolic extract of *Momordica dioica* on Hole board (No. of head poking).

All the values are expressed as mean $\pm$ SEM, n=6, One way analysis of variance (ANOVA) followed by multiple comparison Dunnett's test, \*\*p<0.01, \*\*\*p<0.001 as compared to control group.





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All the values are expressed as mean $\pm$ SEM, n=6, One way analysis of variance (ANOVA) followed by multiple comparison Dunnett's test, \*p<0.05, \*\*p<0.01, \*\*\*p<0.001 as compared to control group.

### 4. Conclusion and Discussion

It can be concluded from the study that the anticonvulsant and antidepressant effects of the ethanolic Momordica dioica may be via non-specific mechanisms. However, extensive studies are needed to evaluate the precise mechanism(s), active principles, and the safety profile of the plant as a medicinal remedy for convulsive and depression disorders The results of the present study indicate that ethanol extract of Momordica dioica (EMD) possesses anticonvulsant activity in mice. GABA is the major inhibitory neurotransmitter in the brain while glutamic acid is an excitatory neurotransmitter in the brain. The inhibition of GABA neurotransmitter and the enhancement of the action of glutamic acid have been shown to be the underlying factors in epilepsy $^{41,42}$ . Our study shows that the ethanol extract of Momordica dioica protected some of the animals against seizures induced by maximal electroshock, PTZ and INH also delayed the latency of the seizures.

In the present study maximal electroshock produced seizures in all the animals used. Antiepileptic drugs that block MESinduced tonic extension are known to act by blocking seizure spread. Moreover, drugs that inhibit voltage-dependent Na+ channels, such as phenytoin can prevent MES-induced tonic extension<sup>43, 44</sup>.

PTZ induced seizure is commonly used model for screening of drugs effective in absence seizures. In present study EMD in the dose of 200 and 400mg/kg increased latency of onset of first myoclonic jerk, onset of clonus and decreased total mortality though it was statistically significant in the dose of 400 mg/kg it produced statistically significant (P < 0.001) protective effect. Combination of therapeutic dose of diazepam 5mg/kg with EMD showed significant (P < 0.05) antiepileptic activity as compared to vehicle control group.. PTZ is a CNS stimulant which acts by inhibiting chloride channels of  $\gamma$ -amino butyric acid receptor (GABA) complex<sup>115</sup>. Inhibition of stimulant activity of PTZ might be responsible for antiepileptic activity of *Momordica dioica*. PTZ produces oxidative stress to neuronal cell.<sup>48</sup>

Isoniazid is used widely for the treatment and chemoprophylaxis of Tuberculosis, but can have serious effects on the central nervous system causing seizures and comas <sup>49</sup>. The factor responsible for INH-induced epileptic seizure is the decrease of GABA below a critical level in some neurons. Perhaps the decrease in the amount of GABA stored presynaptically causes a reduction in the amount of GABA receptors are regulated at the level of maximal sensitivity in order to maximize the action of GABA. Diazepam treated group showed 100% protection of the animals. INH-induced epileptic seizure in mice significantly delayed the onset of seizures. The test drug treated groups showed protection of the animals suggesting that ethanolic extract of *Momordica dioica*. leaves has antiepileptic activity.

In the present study, we studied antidepressant activity of the ethanolic extract of Momordica dioica, in mice. We used two animal models, pentobarbitone induced sleeping and exploratory activity for antidepressant study.Diazepam which belongs to the benzodiazepine group is a central nervous system depressant used in the management of sleep disorders such as insomnia. Benzodiazepines have a binding site on GABA receptor type-ionophore complex (GABAA)<sup>52,53.</sup>They decrease activity, moderate excitement and calm the recipient. Substances like diazepam (the reference drug used in this study) reduce onset of and increase duration of barbiturate-induced sleep and reduce exploratory activity possessing potentials as sedative<sup>53</sup> EMD after oral administration of 200 and 400 mg/kg doses produced sedative effect similar to that observed with 5 mg/kg diazepam. Diazepam is a very well-known anxiolytic benzodiazepine which produces not only anxiolytic-like effect, but also important sedative action It is possible that the tranquillizing activity of EMD is mediated by GABAergic system, since it can produce profound sedation in mice<sup>54,</sup>

The inhibitory action of GABA consists in the opening of chloride channels to allow hyper polarization of the membrane, leading to CNS depression and resulting in sedative and hypnotic activity. Glutamate and GABA are quantitatively the most important excitatory and inhibitory neurotransmitters, respectively, in the mammalian brain. Thus, receptors for these two neurotransmitters are regarded as the important targets for psychotropic drugs. In the test of pentobarbital-induced sleeping in mice, the potentiated effect of EMD in mice was represented. It not only prolonged the sleeping time, but also decreased the latency of falling asleep and increased the sleep onset. Since the effect of barbiturates on the CNS involves activating of the inhibitory GABA ergic system, the result of the present study suggests that some ingredients in EMD produce facilitation of this inhibitory system.

Depressive disorders accompany most of the clinical condition including cardiovascular disorders, thyroid disorders and post partum condition. In view of this there is an urgent need of a drug that can overcome both these symptoms. Various plant based products identified to possess neuropharrmacological properties. Which might prove useful as a therapeutic agent in these disorders. The hole board test provides a simple method for measuring the response of animal to an unfamiliar environment and is widely used to assess the emotionality, anxiety and/or responses to stress in animals. The extract of EMD was observed to have a significant effect on a hole poking and duration of time, which further justifies its depressive effect.

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