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±0.41) and 400mg/kg (5.40±0.35) respectively which lower than that of control group (9.50±0.56) and is significant camparable to diazepam also (5.57±0.56).Duration of sleeping time in animals receiving 200 and 400mg/kg of ethanolic extract doses increased to 56.73±1.33 and 52.91±0.87 that was highly significant (p<0.001) compared with control group (26.95±1.18). There was a significant (p<0.001) increased in duration of sleep in diazepam group (43.96±1.04) when compared to control group.

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

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

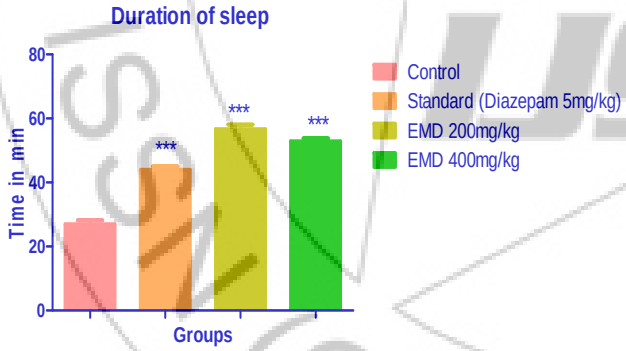


**Figure 4:** Effect of ethanolic extract of *Momordica dioica* on duration of sleep in pentobarbitone induced sleeping time in mice.

All the values are expressed as mean±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±0.35)and 400mg/kg (37.64±0.94) had significantly increased no. of hole poking in mice as compared to control group (33.23±0.95). The mice treated with standard drug diazepam produced s significant increase in no. of hole pokings by 46.21±1.11. (Table no 5)

Administration of different doses of EMD 200 (13.50±1.17) and 400mg/kg (14.67±1.14) had significantly increased duration of head dips in mice as compared to control group (8.33±0.88). The mice treated with standard drug diazepam produced s significant increase in duration of head dips by 22.50±1.25 (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).

| Treatment Groups | No. of Head Poking | Duration of head 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±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.

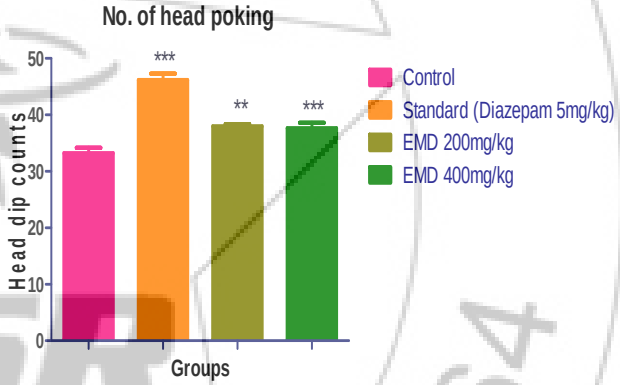


**Figure 5:** Effect of ethanolic extract of *Momordica dioica* on Hole board (No. of head poking).

All the values are expressed as mean±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.

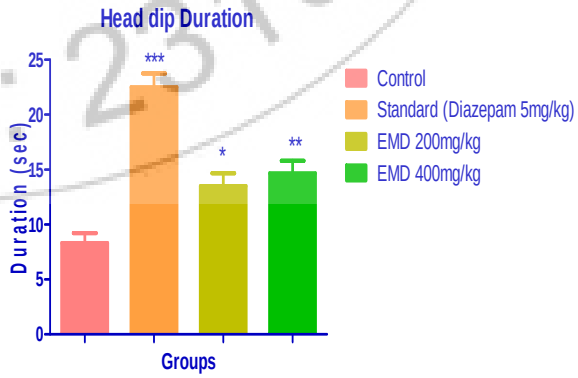


**Figure 6:** Effect of ethanolic extract of *Momordica dioica* on Hole board (duration of head dips)

All the values are expressed as mean±SEM, n=6, One way analysis of variance (ANOVA) followed by multiple comparison Dunnett's test, *p<0.05, **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 MES-induced 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[43, 44].

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 γ-amino butyric acid receptor (GABA) complex[115]. Inhibition of stimulant activity of PTZ might be responsible for antiepileptic activity of *Momordica dioica*. PTZ produces oxidative stress to neuronal cell.[48]

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 [49]. 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 released by nerve impulses. Hence, the 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)[52,53].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[53] 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[54,]

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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