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Research Article

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Evaluation of Antianxiety activity of Zonisamide based on the Serendipitious action in Swiss albino mice

Kanupriya J*, G. Ariharasivakumar, Srividhya V, Gopalasateeskumar K

Department of Pharmacology,
KMCH College of Pharmacy, Kovai Estate, Kalapatti Road, Coimbatore-641048, Tamil Nadu, India.
*Corresponding author: **Kanupriya J,**
KMCH College of Pharmacy,
Kovai Estate, Kalapatti Road, Coimbatore-641048, Tamil Nadu, India.
E- mail: kanujkotek@gmail.com

Abstract

Background: Anxiety is a psychological and physiological state characterised by somatic, emotional and behavioural components with displeasing feeling of fear and concern.
Aim and Objectives: In our study we have attempted to evaluate the antianxiety activity of zonisamide based on the serendipitious action in Swiss albino mice and also to study the histopathology of the brain hippocampal region.
Materials and methods: The anxiolytic activity of test drug is evaluated with three animal models, Elevated pluz maze, Light dark exploration test and Hole board apparatus. Zonisamide (25mg/kg, 50mg/kg), Diazepam(1mg/kg), 0.5% Sodium carboxymethyl cellulose were given orally to the randomly divided 4 groups of six animals each. Number of entries and time spent in the open arm in the elevated pluz maze , time spent in the light arena of the light dark arena model and the number of nose poking behaviour in the hole board apparatus. Statistical analysis was done by ANOVA.
Results: Zonisamide showed significant increase in the number of entries and the time spent in the light arena of the light dark model and elevated plus maze test. It also showed significant increase in number of nose poking in the hole board apparatus.
Conclusion: Zonisamide has a potential clinical application in the management of anxiety disorders. It shows anxiolytic activity in three models.

Keywords: Zonisamide, antianxiety, Elevated plus maze, light dark model, hole board apparatus

Introduction

Anxiety affects one eighth of the total population of the world and has become an important arena of research interest in the field of psychopharmacology.[1] Anxiety is a condition of persistent and uncontrollable nervousness, stress and worry that is triggered by the anticipation of future events, memories of past events or ruminations over the day to day events, with disproportionate fears. It is characterizied by the feeling of apprehension, insecurity, uncertainity or fear.[2]

It is one of the most common psychopharmacological disorders and represent a significant disease burden affecting between 10-30% of general population.[3]

Zonisamide (ZNS) is a sulphonamide anticonvulsant drug and used to treat seizures worldwide.[4] Zonisamide can facilitates the dopaminergic and serotonergic transmission, based on the mechanism of action it can be suggested to have efficacy in the treatment of anxiety.

Since the anxiety disorders are having a huge impact on our lives, it is most important in evaluating the alternative forms of medicines which can be used for its treatment. Hence, in this study, an effort was made to investigate the antianxiety effect of zonisamide based on the serendipitious action in animal models

Materials and Methods

Drugs used

Diazepam, Sodium carboxy methylcellulose, zonisamide

Animals

Swiss albino mice of 20-30 g body weight were obtained from Biogen Laboratories, Bangalore. All rats were housed and maintained under standard conditions of temperature (250C ± 50C), relative humidity (55 ± 10%), and 12/12 h light/dark cycle. Animals were fed with commercial pellet diet and water ad libitum freely throughout the study. Protocols for the study were approved by the Institutional Animal Ethical Committee (IAEC) for Animal Care and were in accordance with Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA) guidelines, Government of India.

Table 1: Screened animals were divided into 4 groups of 6 animals each.

Group	Number of animals	Group Specifications
Group I	**6**	**Vehicle control(0.5 % CMC)**
Group II	**6**	Diazepam (1mg/kg) i.p
Group III	**6**	Low dose of zonisamide (25mg/kg, p.o)
Group IV	**6**	High dose of zonisamide (50mg/kg, p.o)

The antianxiety property was assessed by the Light-Dark Arena model, Elevated Plus-Maze model and Hole board apparatus

Light Dark model

The apparatus consisting of an open top wooden box with two chambers of specific dimensions separated by partition wall and connected by small open door measuring 7.5 x 5 cm at the floor level in the centre of the wall.the light chamber measuring 20 x 30 x 25cm is painted white and illuminated with 100 watt bright light source located 17 cm above the box.

Each mouse is placed in the centre of the light arena of the apparatus and is allowed to explore for 5min.The total time spent in each chamber and show more locomotor activity after treatment with anxiolytics.[5]

Elevated plus maze

The plus maze apparatus consisting of two open arms (16 x 5 cm) and two closed arms (16 x 5 x 12 cm) having an open roof with a plus maze elevated (25 cm) from the floor was used to observe anxiolytic behavior of animals. The animals were fasted 18 h prior to experiment. The dose administration schedule was so adjusted that each mouse was having its turn on plus maze after 45 min of administration of dose. Each animal was placed in the centre of the elevated plus maze with its head facing the open arms.

The duration of the test period was 10 minutes, during which the following parameters were evaluated.
- The number of entries into the open arm.
- The number of entries into the closed arm.
- Time spent in the open arm.
- Time spent in the closed arm.[6]

Hole Board Apparatus

Hole board apparatus is a wooden board of the size 40×40cm. The board consists of sixteen holes with a diameter of 3cm which are distributed evenly on the board. The board is elevated to a particular height (5 cm) from the floor, so that the mouse while poking its nose into the hole does not see the bottom. The mice were grouped into four of five animals each and were trained for two consecutive days. Thirty minutes after the administration of test and standard drugs, the animals were subjected to the test for a period of six minutes and the number of counts for nose-poking of treated animals was calculated as percentage of control animals.[7]

Results

All the values were expressed as mean ± standard error mean (SEM). Intergroup difference was statistically determined by ANOVA. A 'P' value less than 0.05 was taken as the level of significance.

Light dark model

Table No.2: Effect of the test drugs in the Light and Dark arena model. Results are expressed as Mean value±SEM

Treatment	Time spent in light space	
	Before	After
Control	3.33 ± 0.615	2.833 ± 0.601
Standard	3.400 ± 0.510	8.167 ± 0.601***
Test (Low dose)	3.600 ± 0.678	5.167 ± 0.601**
Test (High dose)	3.6 12 ± 0.510	7.500 ± 0.428***

Values were mean ± S.E.M. for (n=6) expressed as the time (in sec) of 6 animals in each group. Data analysis was performed using Dunnett's test. *P < 0.05, **P < 0.01, ***P < 0.001 vs. control

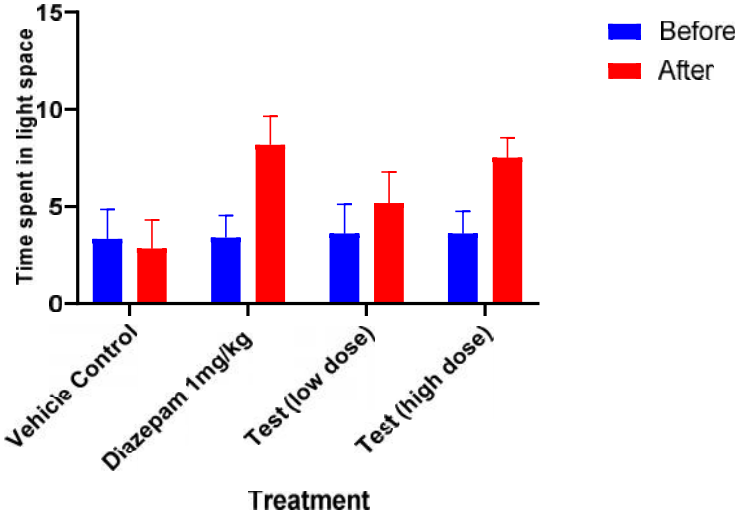

Fig no.1 Mean time spent in the light space

Elevated plus maze

Table No 3: Effect of the test drugs in the Elevated plus maze model. Results are expressed as Mean value ± SEM.

Treatment	Mean no. of entries in		Mean time spent in	
	Open arm	Closed arm	Open arm	Closed arm
Control	8.23 ±0.232	10.83± 0.591	105.500 ± 1.688	427 ± 4.773
Diazepam 1mg/kg	10.917± 0.472***	12.733± 0.411***	268.167± 2.482***	343.33± 1.667***
ZNS 25mg/kg	15.667± 0.186**	14.483± 0.347**	205.000 ± 1.592	307.500±1.945
ZNS 50 mg/kg	10.500 ± 0.619***	11.533±0.541***	222.333± 1.745***	356.167±2.358***

Values were mean ± S.E.M. for (n=6) expressed as the time (in sec) of 6 animals in each group. Data analysis was performed using Dunnett's test. * P < 0.05, ** P < 0.01, *** P < 0.001 vs. control

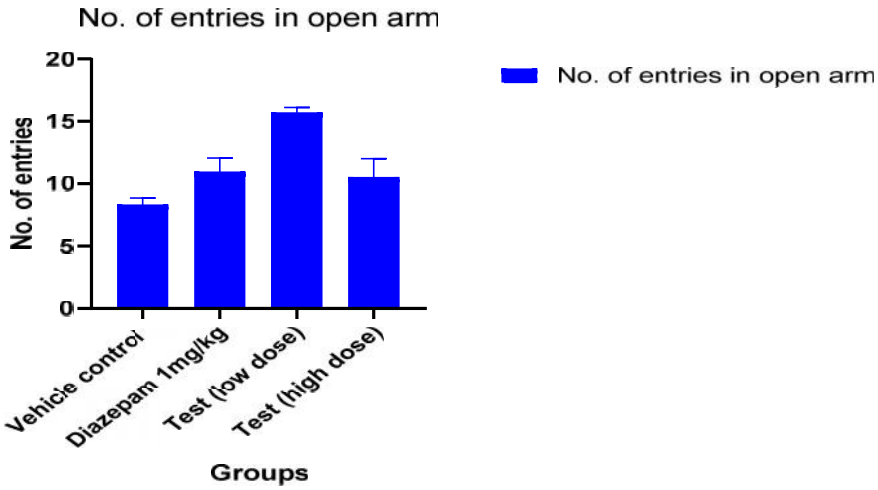

Fig no.2 Number of entries in the open arm in the elevated plus maze

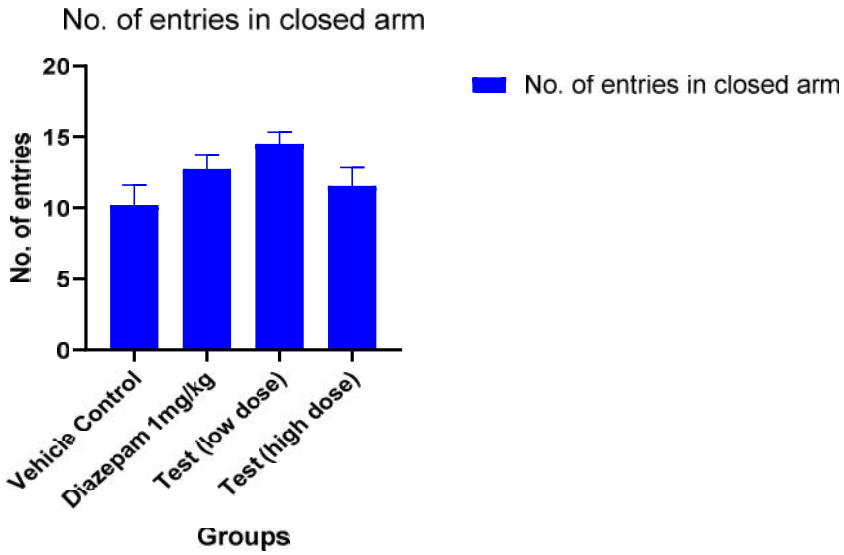

Fig no.3 Number of entries in the open arm in the elevated plus maze

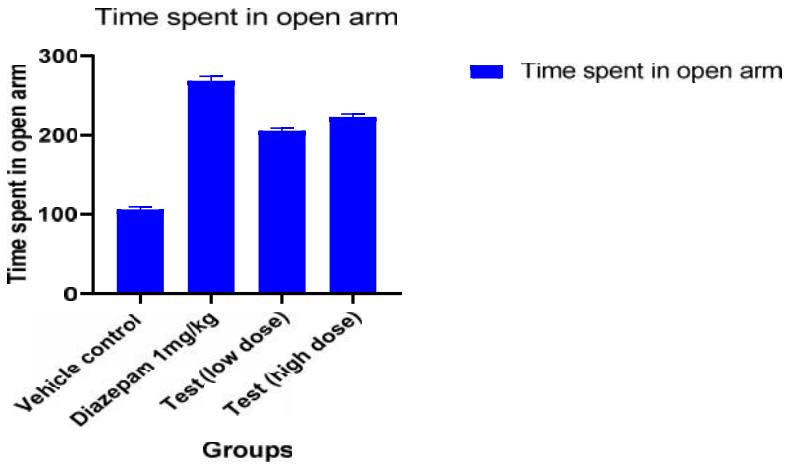

Fig no.4 Time in the open arm in the elevated plus maze

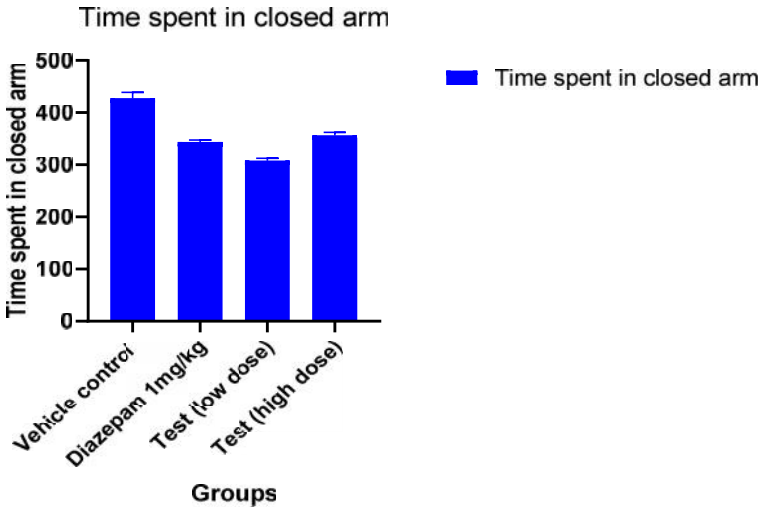

Fig no.5 Time in the open arm in the elevated plus maze

Hole Board Apparatus

Table No.4 Effect of the test drugs in the Hole Board Apparatus. Results are expressed as Mean value±SEM.

Treatment	Number of nose poking	
	Before	After
Control	36.167±4.834	35.500±4.722
Standard	37.333±2.944	7.33±1.306***
Test (Low Dose)	35.343± 4.131	21.000±3.162**
Test (High Dose)	34.333±4.761	12.500±2.345***

Values were mean ± S.E.M. for (n=6) expressed as the time (in sec) of 6 animals in each group. Data analysis was performed using Dunnett's test. *P < 0.05, **P < 0.01, ***P < 0.001 vs. control

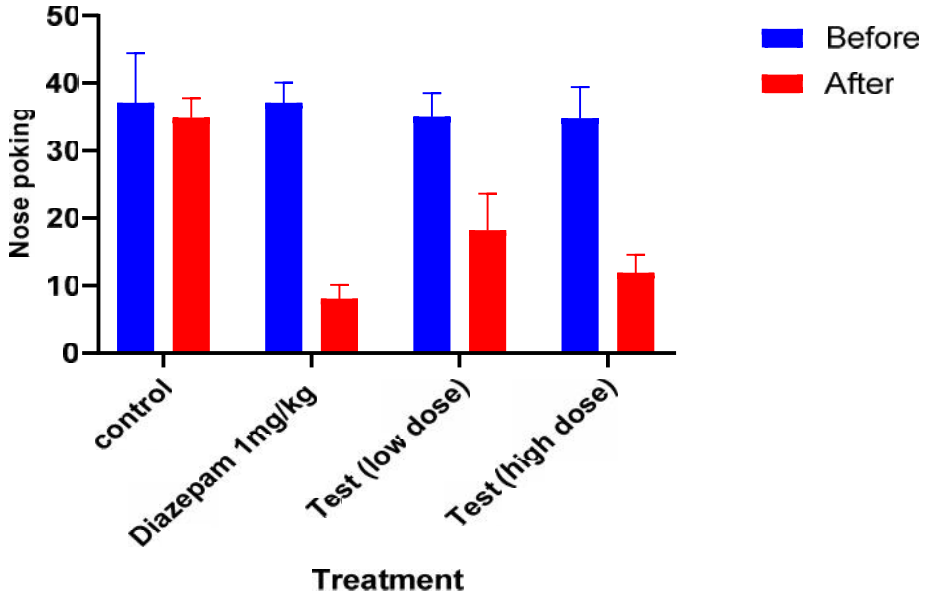

Fig No.6 Number of nose poking in the hole board apparatus

Discussion

Anxiety is an adaptive emotion that permits physiological and behavioural changes, to appropriately react to a stressful situation to resolve it by fighting or escaping.[8] The brain amygdala appears as a key in modulating fear and anxiety. In the central nervous system, the major mediators of the symptoms of anxiety disorders appear to be norepinephrine, serotonin, dopamine and gamma-amino butyric acid (GABA). Peripherally, the autonomic nervous system, especially the sympathetic nervous system, mediates many of the symptoms. The anxiolytic activity of Diazepam is due to its GABA facilitatory action through GABA-A receptor.[9]

In this study, Elevated Plus Maze model were used to assess the anxiolytic activity of test drug. Swiss albino mice naturally show aversion to light, high or open spaces, and hence spend more time in enclosed or dark spaces.

In Light Dark Model, behavioural changes showing an increase in total time spent in the light arena and is deemed as a reduction in anxiety and this forms the basis for its use in the antianxiety screening models.

In Hole board test, shown that head-dipping behavior was sensitive to changes in the emotional state of the animal, and suggested that the expression of an anxiolytic state in animals may be seen by an increase in headdipping behaviour.

Conclusion

The results obtained in this study suggest that the test drug zonisamide possesses anxiolytic activity. Thus, Zonisamide has potential clinical application in the management of anxiety disorders.

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