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EVALUATION OF NOOTROPICACTIVITY OF NEWLY SYNTHESIZED GABA DERIVATIVE IN MICE

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Abstract:

Objective*: This study was aimed to "Evaluate the Nootropic activity of newly synthesized GABA derivative in Mice"*

Methodology*: The activity of the Test drug studied using the Actophotometer test model in swiss albino mice. Learning and memory parameters were evaluated using Open field test. The Test drug was administered in dose of50mg/kg body weight i.p. to the respective groups. Piracetam (200mg/kg,i.p.) was used as astandard nootropic agent.*

Results*: It was observed Test drug at a dose of 50mg/kg (i.p.) was administered and subjected to locomoter activity in Actophotometer Test, exhibited a significant behavioral activity in Actophotometer test and Open field test. Its effect is clearly seen by the decreased in motility rate i.e., response to the decreased in activity is said to be depressant, anxiolytic and inhibitory effects on the CNS.*

Conclusion*:N-plthaloyl GABA derivativehas inhibitory effects which may be processed by the GABAnergic action of the drug. Enhancement of GABA by the drug under study may prove to be a useful memory restorative agentinthe treatment of dementia seen in Alzheimer's disease. Hence, further studies are required to know the exact mechanism.*

Key Words: *N-pthaloyl GABA, Alzheimer's disease, Picrotoxin, Nootropic.*

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INTRODUCTION:

"Nootropic" is the name given to any chemical substance that can improve brain function withoutnegatively affecting the brain. Supplements that fall into this category are known to enhancecognitive abilities such memory formation and recall, learning, logical reasoning, creative thinking,concentration, motivation mood and mental energy. Memory is one of the activities of the human mind much studiedby the experimental and cognitive psychologists. It is undoubtedly one ofthe oldest topics and most important human faculties. Our daily lifeconsists of momentary experiences that may have little relation to otherexperiences. But we must remember these thoughts so as to be able torelate our experiences and form concepts and impressions tocommunicate with others. Without memory, there would be no learningfrom experiences, no intellectual functioning, and no development oflanguage. We can even reflect the impression of our various experiences,for the very notion of the 'self depends on the sense of continuity thatonly memory can bring. So, there would be no development of any of thequalities that are generally associated with being human.

Memory is a key process in understanding behaviour because itforms the very basis of all learning. The question of how the brain"remembers" past experiences has preoccupied researchers sincephysiological brain research began, because the answer always seemed too close but still too tantalizingly out of reach. Thompson (1986), quotesthat 'This is a field into which only geniuses or idiots go'.But now theresearchers have been able to put together enough pieces of puzzle so thatat least a clear picture is beginning to emerge. Some of the work done by the "geniuses and idiots" is beginning to reveal "the biological residue ofmemory that come from a life time of experience".

Memory is ability of an individual to record events, information and retains them over short or long periods of time and recalls the same whenever needed. Age, stress and emotions are conditions that may lead to memory loss, amnesia, anxiety, high blood pressure, dementia, to more ominous threat like schizophrenia and Alzheimer's diseases. (joshi H, Parle M. Nootropic activity calcyces of Hibiscus sabdariffa Linn. IJPT 2006; 5:15-20)

Alzheimer's disease (AD) is a progressive neurodegenerative brain disorder that occurs gradually and results in memory loss, unusual behavior, personality changes and ultimately death.2 It is an incurable, progressive brain disorder that causes dementia and abnormal phosphorylation of the intracellular tau proteins, causing abnormalities of microtubule assembly and collapse of the cytoskeleton affected, particularly pyramidal cells of the cortex and sub cortex.

Dementia is a common and disabling disorder in the elderly. Because of the worldwide aging phenomenon, existing in both developed and developing countries, dementia has a growing public health relevance. Results from 36 prevalence and 15 incidence studies have been examined. The incidence varies from 0.8 to 4.0 per 1000 person years in people aged 60 to 64 years, and increases to 49.8 to 135.7 per 1000 person years when the population was older than 95 years.The international comparison allows the following conclusions: (i) both prevalence and incidence show little geographical variation, as differences between countries seem to reflect methodological rather than real differences [the low prevalence of dementia in Africa needs to be confirmed by incidence data]; (ii) both incidence and prevalence figures increase with age even in the advanced ages; (iii) regarding dementia types, most of the inconsistency in results from different studies is due to vascular dementia rather than to Alzheimer's disease (AD); (iv) it is still unclear if the reported higher frequency of vascular dementia in Asian populations is due to differential distribution of genetic and/or environmental factors, or due to methodological differences; (v) different dementia types might have different age distributions(Dr Laura Fratiglioni, et al 1999).

Dementia is described as a syndrome due to chronic or progressive disease of the brain, leading to disturbance of multiple functions of higher cortical centers including memory, orientation, and comprehension, calculation, learning capacity, language and judgment without altering consciousness.It is a neurodegenerative disease that primarily affects the elderly population, and is estimated to account for 50-60% of dementia cases in persons over 65 years of age.(Joshi H, Parle M 2006)

Amnesia also known as amnesic syndrome, is a deficit in memory caused by brain damage disease, or psychological trauma(Joshi H, Parle M 2006). Amnesia can also be caused temporarily by the use of various sedatives and hypnotic drugs. Essentially, amnesia is loss of memory. The memory can be either wholly or partially lost due to the extent of damage that was caused (Kshirsagra S N. et al). There are two main types of amnesia: retrograde amnesia and anterograde amnesia. Retrograde amnesia is the inability to retrieve information that

was acquired before a particular date, usually the date of an accident or operation(Rao N V et al 2008). In some cases the memory loss can extend back decades, while in others the person may lose only a few months of memory. Anterograde amnesia is the inability to transfer new information from the short-term store into the long-term store. People with this type of amnesia cannot remember things for long periods of time. These two types are not mutually exclusive. Both can occur within a patient at one time. Case studies, such as that of patient R.B., show that both types of amnesia can occur simultaneously.

MATERIALS AND METHODS:

Chemicals and Drugs

Test drug i.e., N-Phenyl pthalidomide gama-amino butyramide was received from Dr.Habib udddin (Principal and administrator of Adept pharma).

Baclofen (tablet), Piracetam (ampule), Zolpidem (tablet), Pregabaline (tablet), Atropine (eye drops), Picrotoxin was brought from SRL chem. Hyderabad, Distilled water& DMSO (Dimethyl Sulphoxide).

INSTRUMENTATION:

Actophotometer

Animals:

Albino mice (25-35g) of either sex bred from Centralized Experimental Animal Shadan Educational Society (SES) House facility of the institute were used. The animals were housed under standard conditions, maintained on a 12 h light/dark cycle and had free access to food and water up to the time of experimentation. The animals were acclimatized to the laboratory environment 1 h before the experiments. Animals were randomly distributed into groups of 6animals each. Each animal was used only once. All experiments were conducted during the light period (09.00-16.00 h). All the protocols were approved by the Institutional Animal Ethics Committee (IAEC) and conducted according to the guidelines of CPCSEA (Committee for the Purpose of Control and Supervision of Experiments on Animals).

Nootropic studies of N-pthaloyl GABA derivative:

Open Field Test:

Locomotor activity was qualified for 3 minutes in a circular open field. With base made up of thermacol of around 150cm circumference,and the side walls are made by firm wire mesh.Each mouse was gently placed in the centre, the activity was scored as line crossing from the centre to its periphery as horizontal or vertical movements. Rears or lifting of limbs was limbs was scored when a mouse raised its front paws from the floor or against the walls.

Statistical Analysis:

Statistics were performed using Graphpad Prism verion 6 and graphs were plotted.

The Data obtained in vivo experiment is expressed as Mean +SEM, analysed using ANOVA and compared by Tukey's posttest. Values of $P<0.05$ was considered to be significant.

Calculations were performed using sigma plot 13.0 version and graphs were plotted.

RESULTS AND DISCUSSION:

Table No. 1

5.1 Nootropic Effect of Test Drug and Test Drug with Antagonist Atropine and PicrotoxinIn Open Field (Horizontal)

		Motility Rate				
		Before Treatment	After Treatment			
Tratment	**Dose(mg/kg)**	**0mins**	**30mins**	**60mins**	**90mins**	**120mins**
Test Drug	50mg/kg(i.p.)	7.20± 1.15*	2.20± 0.37*	1.00± 0.44	1.40± 0.67	1.60± 0.50*
Test +Atropine	10mg/kg(i.p.)	3.80± 0.86**	0.80± 0.37	0.80± 0.37	1.40± 0.60	1.00± 0.31*
Test +Picrotoxin	0.8mg/kg(i.p.)	3.80± 0.86**	0.60± 0.40	0.60± 0.40	0.40± 0.24	0.80± 0.37

All the values are expressed as Mean ± SEM (n=6)*P<0.05, **P<0.01, ***P<0.001 were considered as significant. One way ANOVA followed by Tukey's post test.

Graph No. 1

5.1.1 Nootropic Effect of Test Drug In Open Field (Horizontal)

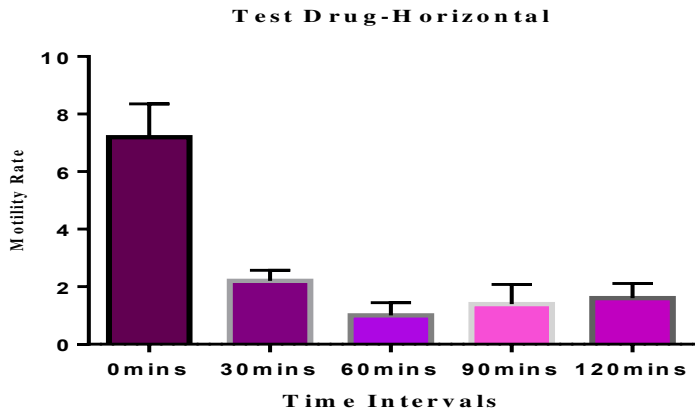


Table No. 2

5.2 Nootropic Effect of Test Drug and Test with Antagonist Atropine and Picrotoxin In Open Field (Vertical)

		Motility Rate				
		Before Treatment	After Treatment			
Tratment	Dose(mg/kg)	0mins	30mins	60mins	90mins	120mins
Test Drug	50mg/kg(i.p.)	9.40± 1.36**	2.60± 1.07	1.20± 0.37*	1.40± 0.74	1.40± 0.50
Test +Atropine	10mg/kg(i.p.)	5.60±1.43**	2.60±0.24***	1.40± 0.50*	0.40± 0.24	1.20± 0.37*
Test +Picrotoxin	0.8mg/kg(i.p.)	8.40± 1.80**	1.20± 0.58	1.40± 0.50	0.40± 0.24	0.40± 0.24

All the values are expressed as Mean ± SEM (n=6)*P<0.05, **P<0.01, ***P<0.001 were considered as significant. One way ANOVA followed by Tukey's post test.

Table No. 3

5.3 Nootropic Effect of Test Drug and Test with Antagonist Atropine and Picrotoxin In Open Field (Grooming)

		Motility Rate				
		Before Treatment	After Treatment			
Tratment	Dose(mg/kg)	0mins	30mins	60mins	90mins	120mins
Test Drug	50mg/kg (i.p.)	2.80± 0.80**	0.60± 0.40	0.80± 0.37	0.20± 0.20	0.80± 0.37
Test +Atropine	10mg/kg(i.p.)	3.60± 0.92**	1.20± 0.58	0.40± 0.40	1.00± 0.54	0.80± 0.37
Test +Picrotoxin	0.8mg/kg(i.p.)	4.20± 1.20**	0.60± 0.40	0.60± 0.24	0.40± 0.24	0.80± 0.37

All the values are expressed as Mean ± SEM (n=6)*P<0.05, **P<0.01, ***P<0.001 were considered as significant. One way ANOVA followed by Tukey's post test.

Table No. 4

5.4 Nootropic Effect of Test Drug and Test with Antagonist Atropine and Picrotoxin In Open Field (Lifting of Limbs)

		Motility Rate				
		Before Treatment	After Treatment			
Tratment	Dose(mg/kg)	0mins	30mins	60mins	90mins	120mins
Test Drug	50mg/kg (i.p.)	11.7± 0.85***	2.25± 0.47**	0.50± 0.28	1.00± 0.40	1.00± 0.40
Test +Atropine	10mg/kg(i.p.)	3.40± 0.50**	0.80± 0.58	1.00± 0.44	0.20± 0.20	2.00± 0.70*
Test +Picrotoxin	0.8mg/kg(i.p.)	2.80± 0.58**	0.60± 0.24	1.00± 0.44	0.40± 0.24	1.00± 0.31*

All the values are expressed as Mean ± SEM (n=6)*P<0.05, **P<0.01, ***P<0.001 were considered as significant. One way ANOVA followed by Tukey's post test.

Graph No. 2

5.4.3 Nootropic Effect of Test Drug with Antagonist Picrotoxin In Open Field (Lifting of Limbs)

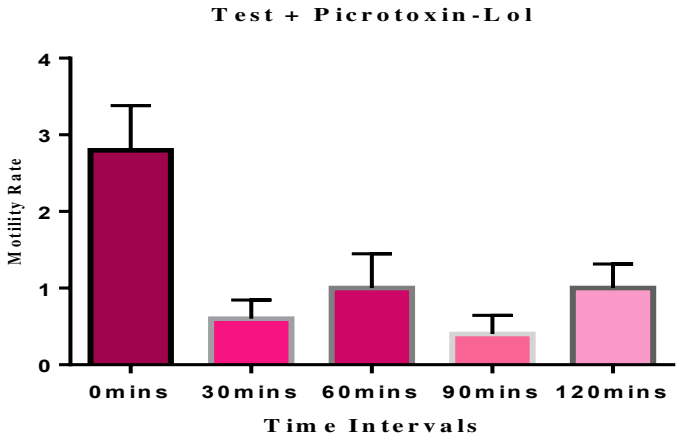


Table No. 5

5.5 Nootropic Effect of Baclofen and Baclofen with Antagonist Atropine and Picrotoxin In Open Field (Horizontal)

		Motility Rate				
		Before Treatment	After Treatment			
Tratment	Dose(mg/kg)	0mins	30mins	60mins	90mins	120mins
Baclofen	1.25mg/kg (oral)	7.16± 1.16***	6.33± 1.78**	0.66± 0.33	1.00± 0.44	3.33± 1.20*
Baclofen+Atropine	10mg/kg(i.p.)	8.75± 1.25**	3.00± 0.40**	2.50± 1.04	4.75± 1.25*	2.50± 0.64*
Baclofen +Picrotoxin	0.8mg/kg(i.p.)	6.00± 1.08**	2.25± 0.75	3.50± 1.50	2.25± 0.47**	0.50± 0.28

All the values are expressed as Mean ± SEM (n=6)*P<0.05, **P<0.01, ***P<0.001 were considered as significant. One way ANOVA followed by Tukey's post test.

Graph No. 3

5.5.1 Nootropic Effect of Baclofen In Open Field (Horizontal)

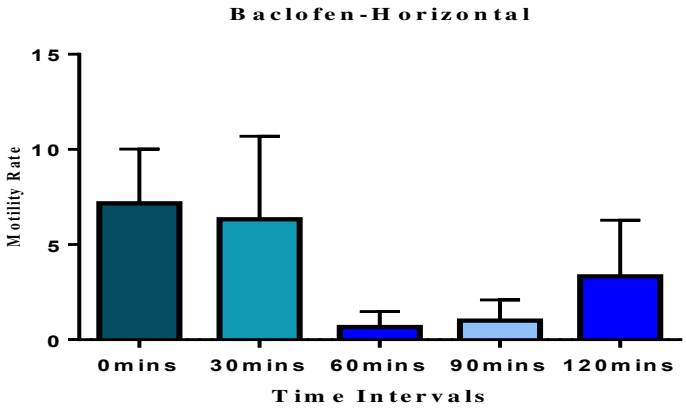


Table No. 6

5.6 Nootropic Effect of Baclofen with Antagonist Atropine and Picrotoxin Open Field (Vertical)

		Motility Rate				
		Before Treatment	After Treatment			
Tratment	Dose(mg/kg)	0mins	30mins	60mins	90mins	120mins
Baclofen	1.25mg/kg (oral)	10.00± 1.31***	6.83± 1.32**	3.167± 0.47***	3.00± 0.44***	3.33± 0.42***
Baclofen+Atropine	10mg/kg(i.p.)	4.75± 1.60*	3.75± 1.10*	2.50± 0.50**	2.75± 0.47**	1.00± 0.40
Baclofen +Picrotoxin	0.8mg/kg(i.p.)	6.50± 1.50**	3.25± 0.25***	6.50± 1.19**	4.00± 1.68	3.33± 0.88

All the values are expressed as Mean ± SEM (n=6)*P<0.05, **P<0.01, ***P<0.001 were considered as significant. One way ANOVA followed by Tukey's post test.

Table No. 7

5.7 Nootropic Effect of Baclofen and Baclofen with Antagonist Atropine and Picrotoxin In Open Field (Grooming)

		Motility Rate				
		Before Treatment	After Treatment			
Tratment	Dose(mg/kg)	0mins	30mins	60mins	90mins	120mins
Baclofen	1.25mg/kg (oral)	3.66± 0.61***	2.83± 0.60**	1.16± 0.16***	1.00± 0.36*	2.50± 0.56**
Baclofen+Atropine	10mg/kg(i.p.)	2.50± 1.04	2.50± 0.95	2.25± 0.47**	2.00± 0.91	1.50± 0.28*
Baclofen +Picrotoxin	0.8mg/kg(i.p.)	3.25± 0.62**	0.50± 0.28	0.75± 0.47	0.50± 0.28	1.00± 0.40

All the values are expressed as Mean ± SEM (n=6)*P<0.05, **P<0.01, ***P<0.001 were considered as significant. One way ANOVA followed by Tukey's post test.

Table No. 8

5.8 Nootropic Effect of Baclofen and Baclofen with Antagonist Atropine and Picrotoxin In Open Field (Lifting of Limbs)

		Motility Rate				
		Before Treatment	After Treatment			
Tratment	Dose(mg/kg)	0mins	30mins	60mins	90mins	120mins
Baclofen	1.25mg/kg (oral)	9.33± 0.98***	7.66± 0.80***	1.50± 0.71	1.50± 0.42**	1.66± 0.66
Baclofen+Atropine	10mg/kg(i.p.)	3.50± 3.50*	5.25± 2.09	2.50± 1.19	3.75± 1.10*	1.00± 0.40
Baclofen +Picrotoxin	0.8mg/kg(i.p.)	7.00± 0.40***	3.00± 1.08	2.50± 1.50	1.75± 0.62	1.00± 0.40

All the values are expressed as Mean ± SEM (n=6)*P<0.05, **P<0.01, ***P<0.001 were considered as significant. One way ANOVA followed by Tukey's post test.

Graph No. 4

5.8.3 Nootropic Effect of Baclofen with Antagonist Picrotoxin In Open Field (Lifting of Limbs)

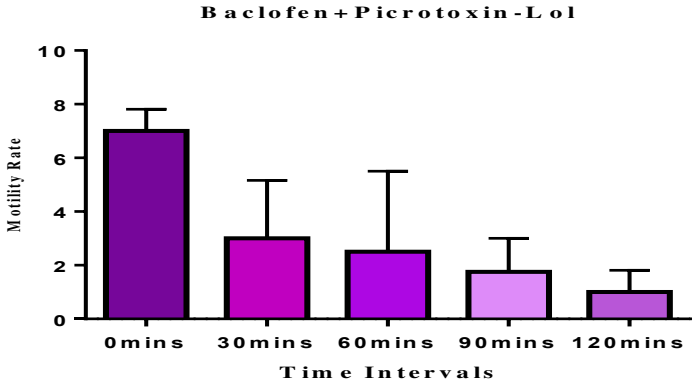


Table No. 9

5.9 Nootropic Effect of Zolpidem and Zolpidem with Antagonist Atropine and Picrotoxin In Open Field (Horizontal)

		Motility Rate				
		Before Treatment	After Treatment			
Tratment	Dose(mg/kg)	0mins	30mins	60mins	90mins	120mins
Zolpidem	1.5mg/kg (oral)	9.66 ± 1.22***	8.33± 0.66***	5.167± 1.10**	4.50± 1.38*	4.33± 1.28**
Zolpidem+Atropine	10mg/kg (i.p.)	2.00± 1.00	0.66± 0.33*	0.0 ± 0.0	1.00± 0.57	0.66± 0.33*
Zolpidem+Picrotoxin	0.8mg/kg(i.p.)	4.66± 1.85	0.66± 0.33*	1.00± 0.57	1.00± 0.57	0.66± 0.33

All the values are expressed as Mean ± SEM (n=6)*P<0.05, **P<0.01, ***P<0.001 were considered as significant. One way ANOVA followed by Tukey's post test.

Graph No. 5

5.9.1 Nootropic Effect of Zolpidem In Open Field (Horizontal)

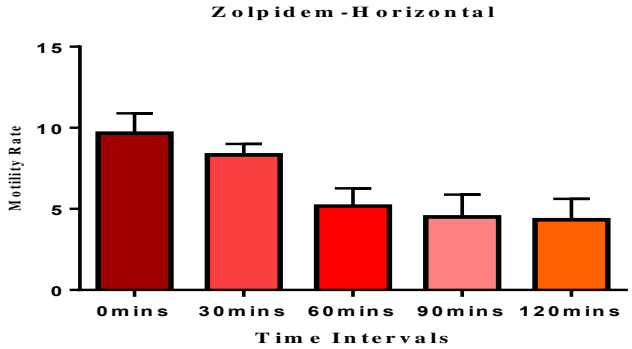


Table No. 10

5.10 Nootropic Effect of Zolpidem and Zolpidem with Antagonist Atropine and Picrotoxin In Open Field (Vertical)

		Motility Rate				
		Before Treatment	After Treatment			
Tratment	Dose(mg/kg)	0mins	30mins	60mins	90mins	120mins
Zolpidem	1.5mg/kg (oral)	9.83± 1.74**	6.83± 1.22**	7.50± 0.88***	5.66± 1.17**	5.83± 0.98***
Zolpidem+Atropine	10mg/kg (i.p.)	3.00± 0.57***	2.66± 0.33**	3.33 ±0.33***	2.66 ±0.33**	1.33 ±0.33
Zolpidem+Picrotoxin	0.8mg/kg (i.p.)	4.00±0.57*	1.66 ±0.66	2.00±0.57	2.00±0.57	0.66±0.33

All the values are expressed as Mean ± SEM (n=6)*P<0.05, **P<0.01, ***P<0.001 were considered as significant. One way ANOVA followed by Tukey's post test.

Table No.11

5.11 Nootropic Effect of Zolpidem and Zolpidem with Antagonist Atropine and Picrotoxin In Open Field (Grooming)

		Motility Rate				
		Before Treatment	After Treatment			
Tratment	Dose(mg/kg)	0mins	30mins	60mins	90mins	120mins
Zolpidem	1.5mg/kg (oral)	3.00± 0.57**	1.83± 0.70*	2.33± 0.42**	1.50 ± 0.42**	2.50± 0.61**
Zolpidem+Atropine	10mg/kg (i.p.)	3.66± 1.45	1.66± 0.66	1.33± 0.33*	2.33± 0.66	1.33± 0.33*
Zolpidem+Picrotoxin	0.8mg/kg (i.p.)	1.66± 1.20	0.33± 0.33	0.33± 0.33	1.00± 0.57	0.66± 0.33

All the values are expressed as Mean ± SEM (n=6)*P<0.05, **P<0.01, ***P<0.001 were considered as significant. One way ANOVA followed by Tukey's post test.

Table No.12

5.12 Nootropic Effect of Zolpidem and Zolpidem with Antagonist Atropine and Picrotoxin In Open Field (Lifting of Limbs)

		Motility Rate				
		Before Treatment	After Treatment			
Tratment	Dose(mg/kg)	0mins	30mins	60mins	90mins	120mins
Zolpidem	1.5mg/k (oral)	8.33± 1.05***	3.66± 0.88**	3.33± 1.14*	3.50± 1.05**	3.83± 1.24**
Zolpidem+Atropine	10mg/kg (i.p.)	4.33± 0.88*	3.00± 0.57*	3.33± 0.88	4.33± 2.33	3.00± 0.57*
Zolpidem+Picrotoxin	0.8mg/kg (i.p.)	2.66± 0.88	2.66± 1.764	1.33± 1.33	0.66± 0.33	1.00± 0.57

All the values are expressed as Mean ± SEM (n=6)*P<0.05, **P<0.01, ***P<0.001 were considered as significant. One way ANOVA followed by Tukey's post test.

Graph No. 6

5.12.3 Nootropic Effect of Zolpidem with Antagonist Picrotoxin In Open Field (Lifting of Limbs)

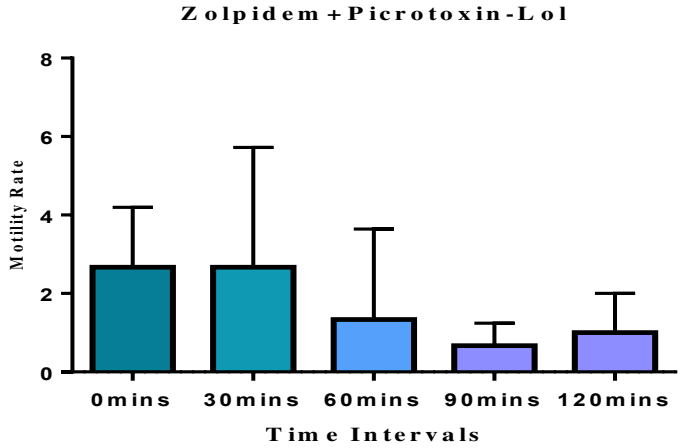


Table No.13

5.13 Nootropic Effect of Pregabalinand Pregabalin with Antagonist Atropine and Picrotoxin In Open Field (Horizontal)

		Motility Rate				
		Before Treatment	After Treatment			
Tratment	Dose(mg/kg)	0mins	30mins	60mins	90mins	120mins
Pregabalin	3mg/kg (oral)	6.33± 0.88***	6.00± 0.73***	5.16± 0.94**	3.66± 1.28*	1.83± 0.79
Pregabalin+Atropine	10mg/kg (i.p.)	4.33± 1.20	2.66± 0.33**	3.33± 0.88	3.66± 0.88	2.00± 0.57
Pregabalin+Picrotoxin	0.8mg/kg (i.p.)	5.66± 1.45*	1.33± 0.88	4.66± 0.66**	2.33± 0.66	1.66± 0.33*

All the values are expressed as Mean ± SEM (n=6)*P<0.05, **P<0.01, ***P<0.001 were considered as significant. One way ANOVA followed by Tukey's post test.

Graph No. 7

5.13.1 Nootropic Effect of Pregabalin In Open Field (Horizontal)

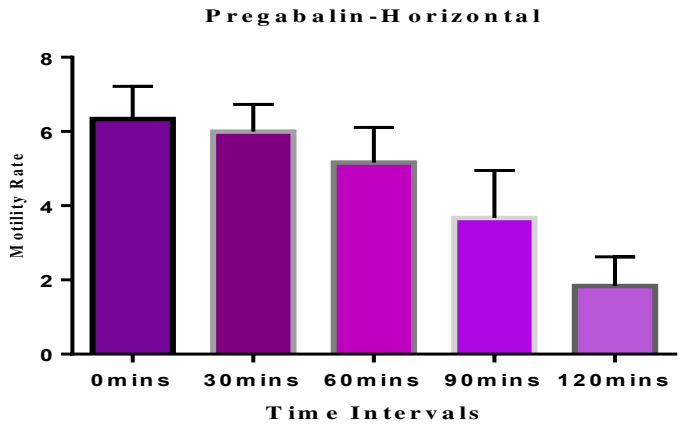


Table No.14

5.14 Nootropic Effect of Pregabalin and with Antagonist Atropine and Picrotoxin In Open Field (Vertical)

		Motility Rate				
		Before Treatment	After Treatment			
Tratment	Dose(mg/kg)	0mins	30mins	60mins	90mins	120mins
Pregabalin	3mg/kg(oral)	8.00± 1.03***	6.167± 0.60***	6.00± 1.23**	5.33 ± 0.80***	3.16± 0.30***
Pregabalin+Atropine	10mg/kg (i.p.)	2.33± 0.33**	5.00± 0.57**	2.00± 0.57	3.00± 0.57*	2.00± 0.57
Pregabalin+Picrotoxin	0.8mg/kg (i.p.)	5.00± 1.15*	3.33± 0.33**	6.66± 0.88**	1.66± 0.88	1.00± 0.57

All the values are expressed as Mean ± SEM (n=6)*P<0.05, **P<0.01, ***P<0.001 were considered as significant. One way ANOVA followed by Tukey's post test.

Table No.15

5.15 Nootropic Effect of Pregabalin and Pregabalin with Antagonist Atropine and Picrotoxin In Open Field (Grooming)

		Motility Rate				
		Before Treatment	After Treatment			
Tratment	Dose(mg/kg)	0mins	30mins	60mins	90mins	120mins
Pregabalin	3mg/kg (oral)	2.00 ± 0.73*	1.16± 0.47	1.50± 0.34**	1.83± 0.70*	1.50± 0.34**
Pregabalin+Atropine	10mg/kg (i.p.)	5.00± 1.15*	2.00± 1.15	1.66± 0.33*	2.66± 0.88	1.00± 0.57
Pregabalin+Picrotoxin	0.8mg/kg (i.p.)	3.33± 0.88	0.66± 0.33	1.00± 0.57	0.66± 0.33	0.66± 0.33

All the values are expressed as Mean ± SEM (n=6)*P<0.05, **P<0.01, ***P<0.001 were considered as significant. One way ANOVA followed by Tukey's post test.

Table No.16

5.16 Nootropic Effect of Pregabalin and Pregabalin with Antagonist Atropine and Picrotoxin In Open Field (Lifting of limbs)

		Motility Rate				
		Before Treatment	After Treatment			
Tratment	Dose(mg/kg)	0mins	30mins	60mins	90mins	120mins
Pregabalin	3mg/kg (oral)	6.66± 0.80***	5.50± 0.84***	5.50± 0.56 ***	5.66± 1.22**	4.33± 0.98**
Pregabalin+Atropine	10mg/kg (i.p.)	4.00± 1.15	3.66± 0.88	2.00± 0.57	3.66± 1.20	2.33± 0.88
Pregabalin+Picrotoxin	0.8mg/kg (i.p.)	7.00± 0.57**	3.33± 1.45	4.00± 1.15	2.33± 0.33**	1.33± 0.33*

All the values are expressed as Mean ± SEM (n=6)*P<0.05, **P<0.01, ***P<0.001 were considered as significant. One way ANOVA followed by Tukey's post test.

Graph No. 8

5.16.3. Nootropic Effect of Pregabalin with antagonist Picrotoxin In Open Field (Lifting of limbs)

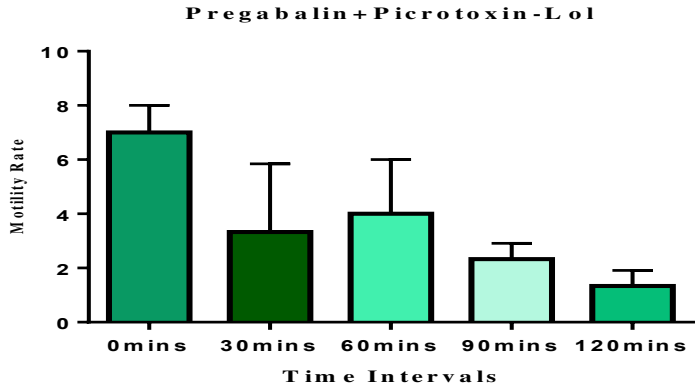


TABLE NO.17

5.17 Nootropic Effect of Piracetam and Piracetam with Antagonist Atropine and Picrotoxin In Open Field (Horizontal)

		Motility Rate				
		Before Treatment	After Treatment			
Tratment	Dose(mg/kg)	0mins	30mins	60mins	90mins	120mins
Piracetam	200mg/kg (i.p.)	4.50± 0.76**	5.16± 1.07**	6.83± 1.13***	6.66± 1.45**	3.83± 0.47***
Piracetam +Atropine	10mg/kg(i.p.)	3.20± 0.86**	1.80± 0.58*	1.40± 0.40*	1.20± 0.58	0.40± 0.24
Piracetam +Picrotoxin	0.8mg/kg(i.p.)	3.00± 0.57*	0.33± 0.33	1.00± 0.57	0.66± 0.33	0.66± 0.33

All the values are expressed as Mean ± SEM (n=6)*P<0.05, **P<0.01, ***P<0.001 were considered as significant. One way ANOVA followed by Tukey's post test.

Graph No. 9

5.17.1. Nootropic Effect of Piracetam In Open Field (Horizontal)

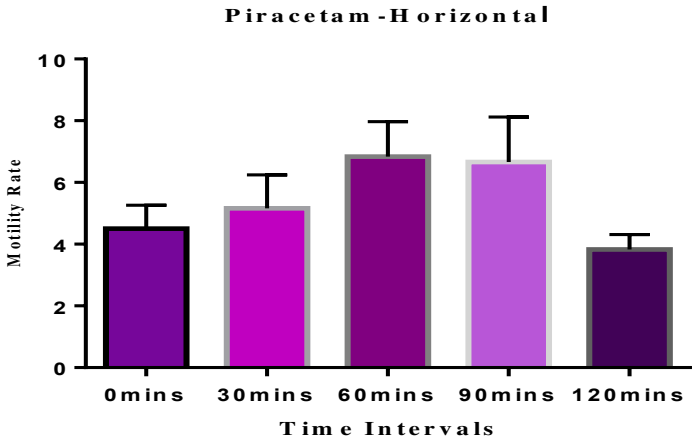


TABLE NO.18

5.18 Nootropic Effect of Piracetam and Piracetam with Antagonist Atropine and Picrotoxin In Open Field (Vertical)

		Motility Rate				
		Before Treatment	After Treatment			
Tratment	Dose(mg/kg)	0mins	30mins	60mins	90mins	120mins
Piracetam	200mg/kg (i.p.)	5.66± 0.88***	5.83± 0.79***	6.33± 0.88***	6.50± 0.99***	4.00± 0.36***
Piracetam +Atropine	10mg/kg(i.p.)	4.20± 0.80**	2.40± 0.40**	3.00± 0.54**	3.60± 0.60**	1.20± 0.37*
Piracetam +Picrotoxin	0.8mg/kg(i.p.)	7.33± 0.66**	3.33± 0.33**	2.33± 0.66	2.33± 0.66	1.00± 0.57

All the values are expressed as Mean ± SEM (n=6)*P<0.05, **P<0.01, ***P<0.001 were considered as significant. One way ANOVA followed by Tukey's post test.

TABLE NO.19

5.19 Nootropic Effect of Piracetam and Piracetam with Antagonist Atropine and Picrotoxin In Open Field (Grooming)

		Motility Rate				
		Before Treatment	After Treatment			
Tratment	Dose(mg/kg)	0mins	30mins	60mins	90mins	120mins
Piracetam	200mg/kg (i.p.)	2.50±0.88*	3.50± 0.84**	3.16± 0.47***	1.33± 0.33**	1.16± 0.30**
Piracetam +Atropine	10mg/kg(i.p.)	1.60± 0.60*	1.00± 0.31*	2.20± 0.58**	2.00± 0.44**	1.20± 0.37*
Piracetam +Picrotoxin	0.8mg/kg(i.p.)	2.33± 0.33**	1.00± 0.57	0.66± 0.33	0.33± 0.33	0.66± 0.33

All the values are expressed as Mean ± SEM (n=6)*P<0.05, **P<0.01, ***P<0.001 were considered as significant. One way ANOVA followed by Tukey's post test.

TABLE NO.20

5.20 Nootropic Effect of Piracetam and Piracetam with Antagonist Atropine and Picrotoxin In Open Field (Lifting of limbs)

		Motility Rate				
		Before Treatment	After Treatment			
Tratment	Dose(mg/kg)	0mins	30mins	60mins	90mins	120mins
Piracetam	200mg/kg (i.p.)	7.66± 1.02***	7.16± 1.01***	6.66± 0.76***	7.50± 0.99***	4.50± 0.76**
Piracetam +Atropine	10mg/kg(i.p.)	7.00± 1.30**	5.20± 1.71*	5.20± 1.06**	3.40± 1.03*	1.80± 0.37**
Piracetam +Picrotoxin	0.8mg/kg(i.p.)	4.00± 0.57*	1.33± 0.33*	1.00± 0.57	0.66± 0.33	1.33± 0.33*

All the values are expressed as Mean ± SEM (n=6)*P<0.05, **P<0.01, ***P<0.001 were considered as significant. One way ANOVA followed by Tukey's post test.

Graph No. 10

5.20.3. Nootropic Effect of Piracetam with Antagonist PicrotoxinIn Open Field (Lifting of limbs)

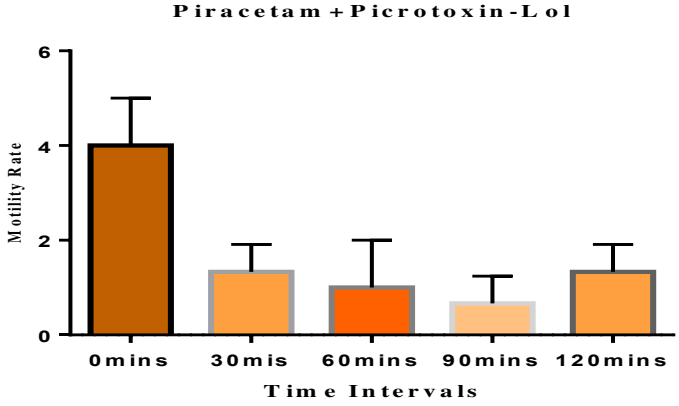


TABLE NO.21

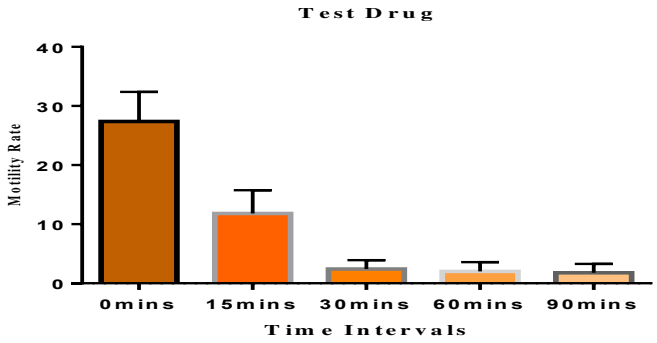
5.21Nootropic Effect of Test and Testwith Antagonist Atropine and Picrotoxin on Actophotometer Test in Mice

		MOTILITY RATE				
		Before Treatment	After Treatment			
Treatment	DOSE (mg/kg)	0mins	15mins	30mins	60mins	90mins
Test Drug	50mg/kg (i.p.)	27.40± 2.227***	11.80 ±1.77**	2.40± 0.67**	2.00± 0.70*	1.80± 0.66
Test + Atropine	10mg/kg (i.p.)	45.25± 5.406**	5.750± 0.85**	2.250± 0.75	2.250± 0.62*	0.75± 0.25
Test +Picrotoxin	0.8mg/kg (i.p.)	45.20± 2.478***	31.00± 2.16***	8.00± 0.70***	3.00± 1.14	0.60± 0.40

All the values are expressed as Mean ± SEM (n=6)*P<0.05, **P<0.01, ***P<0.001 were considered as significant. One way ANOVA followed by Tukey's post test.

GRAPH NO. 11

5.21.1 Nootropic Effect of Test Drug on Actophotometer Test in Mice



GRAPH NO. 12

5.21.3 Nootropic Effect of Test Drug with Antagonist Picrotoxin on Actophotometer Test in Mice

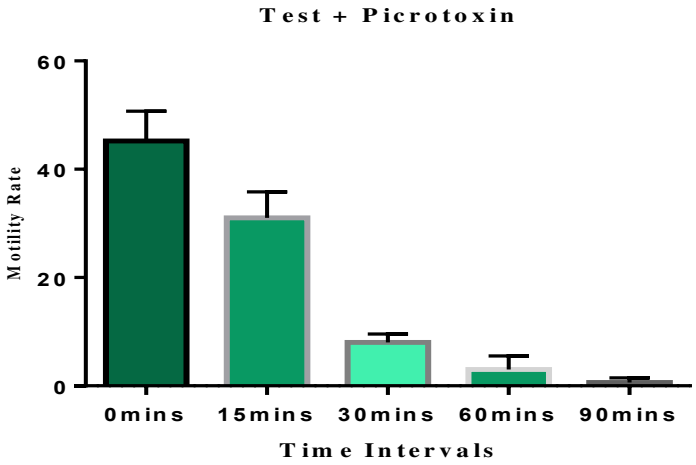


TABLE NO.22

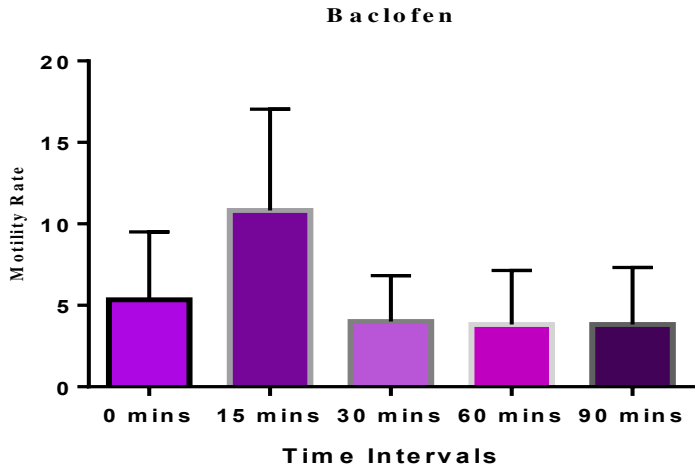
5.22NOOTROPIC EFFECT OF BACLOFENAND BACLOFEN WITH ANTAGONIST ATROPINE AND PICROTOXIN ON ACTOPHOTOMETER TEST IN MICE

		MOTILITY RATE				
		Before Treatment	After Treatment			
Treatment	DOSE (mg/kg)	0mins	15mins	30mins	60mins	90mins
Baclofen	1.25mg/kg (i.p.)	5.33± 1.70**	10.83± 2.53**	4.00± 1.15**	3.83± 1.35*	3.83± 1.42*
Baclofen + Atropine	10mg/kg (i.p.)	23.50± 2.72**	20.75± 4.88*	11.75± 2.42**	17.75± 2.097**	14.00± 2.48**
Baclofen +Picrotoxin	0.8mg/kg (i.p.)	21.25± 4.95**	15.25± 2.25**	4.00± 1.68	9.00± 0.91**	6.25± 1.25**

All the values are expressed as Mean ± SEM (n=6)*P<0.05, **P<0.01, ***P<0.001 were considered as significant. One way ANOVA followed by Tukey's post test

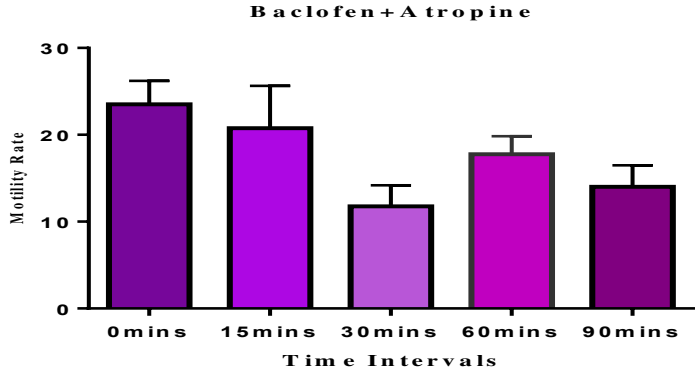
GRAPH NO. 13

5.22.1 Nootropic Effect of Baclofen on Actophotometer Test in Mice



GRAPH NO. 14

5.22.2 Nootropic Effect of Baclofen with Antagonist Atropine on Actophotometer Test in Mice



GRAPH NO. 15

5.22.3 Nootropic Effect of Baclofen with Antagonist Picrotoxin on Actophotometer Test in Mice

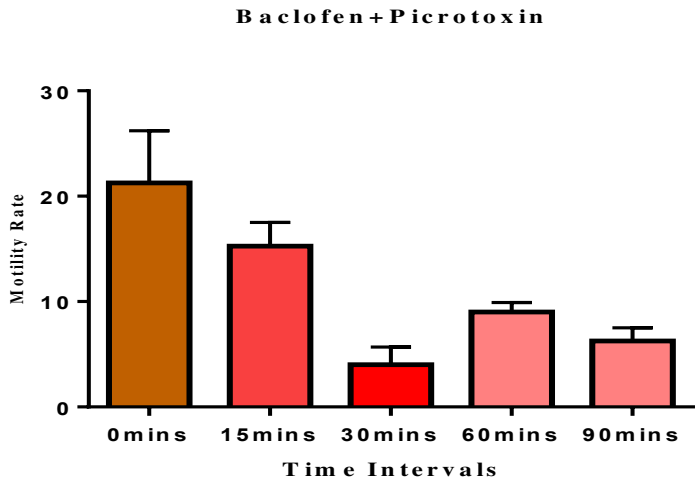


TABLE NO.23

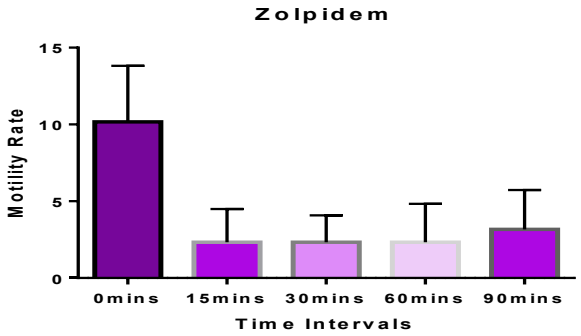
5.23NOOTROPIC EFFECT OF ZOLPIDEM AND ZOLPIDEM WITH ANTAGONIST ATROPINE AND PICROTOXIN ON ACTOPHOTOMETER TEST IN MICE

		MOTILITY RATE				
		Before Treatment	After Treatment			
Treatment	DOSE (mg/kg)	0mins	15mins	30mins	60mins	90mins
Zolpidem	1.5mg/kg (oral)	10.17± 1.49***	2.33± 0.88*	2.33± 0.71*	2.33± 1.02*	3.16± 1.04**
Zolpidem + Atropine	10mg/kg (i.p.)	54.67± 11.57*	14.33± 5.92	18.00± 7.50	18.00± 5.00	14.33± 4.33
Zolpidem+Picrotoxin	0.8mg/kg (i.p.)	49.00±12.29	3.00± 1.52	5.00± 2.51	5.66± 3.71	8.33±7.35

All the values are expressed as Mean ± SEM (n=6)*P<0.05, **P<0.01, ***P<0.001 were considered as significant. One way ANOVA followed by Tukey's post test.

GRAPH NO. 16

5.22.1. NOOTROPIC EFFECT OF ZOLPIDEM ON ACTOPHOTOMETER TEST IN MICE



GRAPH NO.17

5.22.3. NOOTROPIC EFFECT OF ZOLPIDEM WITH ANTAGONIST PICROTOXIN ON ACTOPHOTOMETER TEST IN MICE

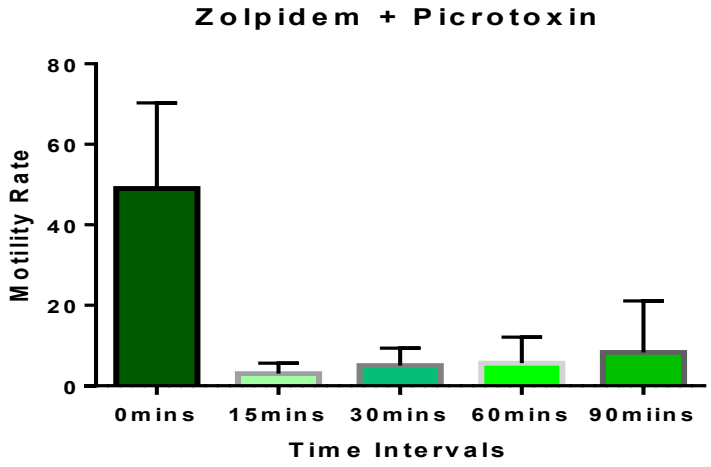


TABLE NO.23

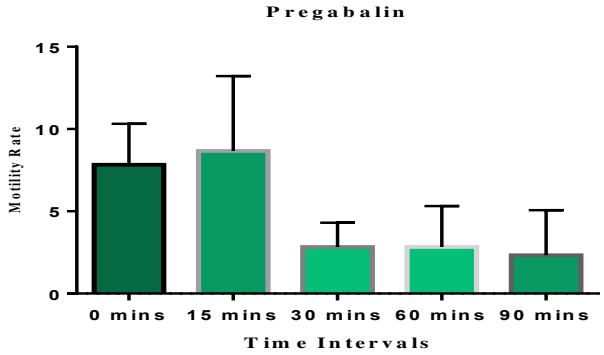
5.23NOOTROPIC EFFECT OF PREGABALIN ON AND PREGABALIN WITH ANTAGONIST ATROPINE AND PICROTOXIN ACTOPHOTOMETER TEST IN MICE

		MOTILITY RATE				
		Before Treatment	After Treatment			
Treatment	DOSE (mg/kg)	0mins	15mins	30mins	60mins	90mins
Pregabalin	3mg/kg (i.p.)	7.83± 1.01***	8.66± 1.85**	2.83± 0.60**	2.83± 1.01*	1.66± 0.49**
Pregabalin+Atropine	10mg/kg (i.p.)	23.00± 6.55	14.00± 2.64*	12.00± 5.56	11.33± 5.23	16.00± 7.00
Pregabalin +Picrotoxin	0.8mg/kg (i.p.)	27.33± 6.98	15.00± 7.63	19.00± 5.77	23.00± 4.50*	12.67± 2.96

All the values are expressed as Mean ± SEM (n=6)*P<0.05, **P<0.01, ***P<0.001 were considered as significant. One way ANOVA followed by Tukey's post test.

GRAPH NO.18

5.23.1. NOOTROPIC EFFECT OF PREGABALIN ON ACTOPHOTOMETER TEST IN MICE



GRAPH NO.19

5.23.3. NOOTROPIC EFFECT OF PREGABALIN WITH ANTAGONIST PICROTOXIN ON ACTOPHOTOMETER TEST IN MICE

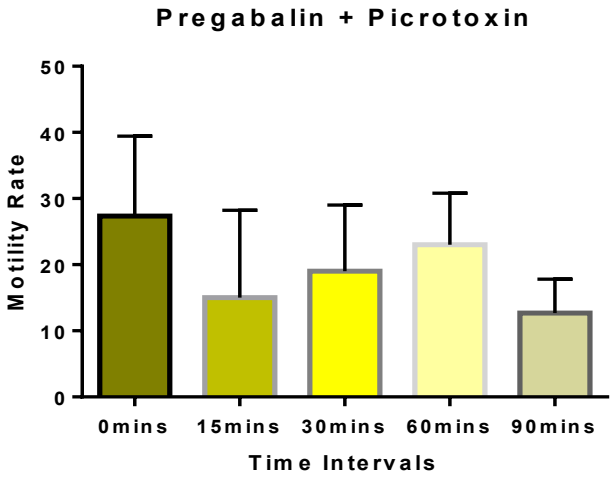


TABLE NO.24

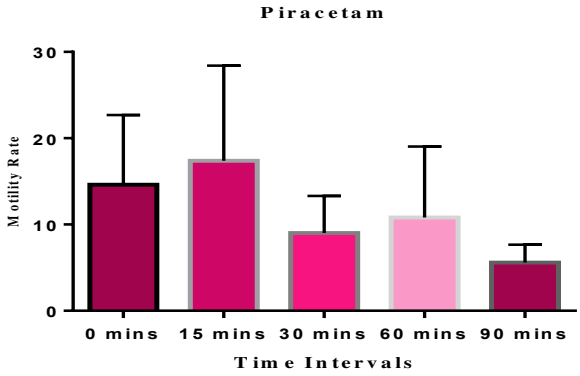
5.24 NOOTROPIC EFFECT OF PIRACETAM AND PIRACETAM WITH ANTAGONIST ATROPINE AND PICROTOXIN ON ACTOPHOTOMETER TEST IN MICE

		MOTILITY RATE				
		Before Treatment	After Treatment			
Treatment	DOSE (mg/kg)	0mins	15mins	30mins	60mins	90mins
Piracetam	200mg/kg (i.p.)	14.60± 3.61**	17.40± 4.92*	9.00± 1.92**	10.80± 3.68*	5.60± 0.927**
Piracetam +Atropine	10mg/kg (i.p.)	55.60± 7.95**	48.40± 8.77**	32.00± 6.30**	30.20± 5.161**	27.60± 3.723***
Piracetam +Picrotoxin	0.8mg/kg (i.p.)	19.67 ± 2.333	3.000 ± 0.5774	0.3333 ± 0.3333	2.333 ± 1.453	1.667 ± 1.202

All the values are expressed as Mean ± SEM (n=6)*P<0.05, **P<0.01, ***P<0.001 were considered as significant. One way ANOVA followed by Tukey's post test

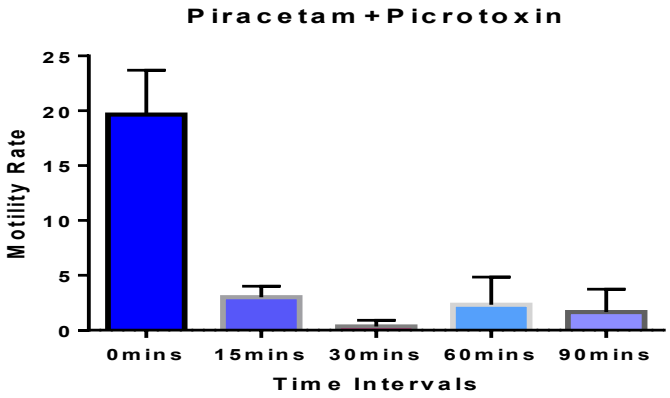
Graph No. 20

5.24.1 NOOTROPIC EFFECT OF PIRACETAM ON ACTOPHOTOMETER TEST IN MICE



Graph No. 21

5.24.3. NOOTROPIC EFFECT OF PIRACETAM WITH ANTAGONIST PICROTOXIN ON ACTOPHOTOMETER TEST IN MICE



OPEN FIELD:
Test Drug: Test drug (50mg/kg i.p) group, atropine (10mg/kg i.p.) group, picrotoxin (0.8mg/kg i.p.) group treated animal showed significant CNS depressant activity when compared with before treatment (0mins), The horizontal, vertical, grooming and lifting of limbs movement was decreased with the significant statistical analyzed value as seen in table no. 1-4 and graph no. 1-2.

Baclofen: Baclofen (1.25mg/kg oral) group, atropine (10mg/kg i.p.) group & picrotoxin (0.8mg/kg i.p.) group treated animal showed significant decreased in anxiolytic activity when compared with before treatment (0mins), The horizontal, vertical, grooming & lifting of limbs movement was decreased with the significant statistical analyzed value as seen in table no. 5-8 & graph no. 3-4.

Zolpidem: Zolpidem (1.5mg/kg oral) group, atropine (10mg/kg i.p.) group & picrotoxin (0.8mg/kg i.p.) group treatment animal showed significant CNS depressant activity when compared with before treatment (0mins), The horizontal, vertical, grooming & lifting of limbs movement was decreased with the significant statistical analyzed value as seen in table no. 9-12 & graph no. 5-6.

Pregabalin: Pregabalin (3mg/kg oral) group, atropine (10mg/kg i.p.) group and picrotoxin (0.8mg/kg i.p.) group treatment animal showed significant CNS depressant activity when compared with before treatment (0mins), The horizontal, vertical, grooming & lifting of limbs movement was decreased with the significant statistical analyzed value as seen in table no. 13-16 & graph no. 7-8.

Piracetam: Piracetam (200mg/kg i.p.) group, atropine (10mg/kg i.p.) group & picrotoxin (0.8mg/kg i.p.) group treatment animal showed significant decreased in anxiolytic activity when compared with before treatment (0min), The horizontzal, vertical, grooming & lifting of limbs movement was decreased with significant statistical analyzed value as seen in table no. 17-20 & graph no. 9-10.

ACTOPHOTOMETER TEST:
Test Drug: The effect on the actophotometer test of test drug (50mg/kg i.p.) along with atropine (10mg/kg i.p.) was similar to the reaction of test drug administered alone. Thus, no significant antagonism is seen. Its statistical significance is noted to be ($p<0.01$) as seen in table no. 21 and graph no. 11. After treatment with GABA antagonist picrotoxin doesn't showed any significance antagonism with statistical analyzed significant value ($p<0.01$) as seen in table no.21 and graph no. 12.

Baclofen (1.25mg/kg oral) treated animal showed CNS depressant & muscle relaxant as seen in table no.22 and graph no. 13 with statistical analyzed significant value ($p<0.01$). After treatment with Anti-muscarinic drug Atropine showed significant statistical analyzed value ($p<0.01$) with little increased activity at 60mins, as shown in table no. 22 and graph no. 14. After treatment with GABA antagonist PICROTOXIN doesn't show any blocking significant effect with statistical analyzed value ($p<0.01$) when compared with only baclofen activity as shown in table no. 22 and graph no. 15.

Zolpidem (1.5mg/kg oral) treated animal showed decrease anxiolytic activity as seen in table no. 23 and graph no. 16 with statistical analyzed value

($p<0.05$) . After treatment with anti-muscarinic drug ATROPINE doesn't showed significant effect to activity of test drug as seen in table no. 23. After treatment with GABA agonist Picrotoxin showed increased activity at 90mins, with a significant statistical analyzed value ($p>0.05$) as seen in table no. 23 and graph no. 17.

Pregabalin (3mg/kg oral) treated animalshowed CNS depressant with significant significant value ($p<0.01$) as seen in table no. 24 and graph no. 18. The effect on the actophotometer test of anti-muscarinic atropine showed little increased activity at 90mins with a significant statistical analyzed value ($p<0.05$) as seen in table no. 24. After treatment with GABA agonist Picrotoxin (0.8mg/kg i.p.) as it also showed little increased reaction activity at 60 mins with a significant statistical analyzed value ($p<0.05$) as seen in table no. 24 and graph no. 19.

Piracetam: Effect on actophotometer test of Piracetam (200mg/kg i.p.) along with anti-muscarinic drug Atropine was similar to the reaction of piracetam administered alone.Thus, there is no significant antagonism seen. Its stataistical significant value ($P<0.01,0.001$) as seen in Table no. 25: Graph no. 20. After the treatment of GABA antagonigst Picrotoxin doesnot show any significant antagonism with statistical anlaysed value ($P>0.05$) as seen in Table no. 25 : Graph no.21.

ACKNOWLWDGEMENT:

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