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## **Comparative evaluation of locomotor activity of pregabalin and lamotrigine alone and in combination with sodium valproate in albino mice**

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### **ABSTRACT**

The present study was designed to evaluate the effect of Pregabalin and Lamotrigine alone and in combination with Sodium valproate on locomotor activity in Albino Mice by using actophotometer. Drugs which modulate neurotransmitters in the brain will affect Locomotor activity, which is the index of mental alertness. For this study 36 healthy albino mice were randomly selected and divided into 6 equal groups. Locomotor activity score by actophotometer was observed for 5mins before and after intragastric administration of distilled water 0.5ml, Sodium valproate 100mg/kg, Lamotrigine 10mg/kg, pregabalin 100mg/kg, combination of Pregabalin (100mg/kg) plus sodium Valproate (100mg/kg) and combination of Lamotrigine (10mg/kg) plus sodium Valproate (100mg/kg) to mice of group 1 to 6 respectively. The results were analyzed statistically. There was no significant difference in the basal locomotor activity score between the control, standard and test groups. Sodium Valproate alone treated animals, combination of Pregabalin plus Sodium Valproate and combination of Lamotrigine plus Sodium Valproate treated mice significantly affect mental alertness in comparison to placebo.

**Key WORDS:** Anticonvulsant, Mental alertness, Actophotometer



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### **INTRODUCTION**

Most of the central nervous system acting drugs influence the locomotor activities in man and animals. Locomotor activity score is the index of mental alertness. The CNS depressant drugs such as barbiturates and alcohol reduce the motor activity while the stimulants such as caffeine and amphetamines increases the activity can be an index of wakefulness (alertness) of mental activity [1]. Sodium valproate, Pregabalin and Lamotrigine are novel anticonvulsant drugs used for the treatment of epilepsy as well as for other non-epileptic conditions and it mainly acts through central nervous system [2]. In many situations co-administration of Sodium valproate, Pregabalin and Lamotrigine are unavoidable. Nevertheless, the combined effect of these drugs on locomotor activity have not been carefully studied. Hence this study was designed to evaluate the locomotor activity of Pregabalin and Lamotrigine alone and in combination with Sodium valproate in Albino Mice.

### **METHODOLOGY**

For this study 36 healthy Wister albino mice weighing 20 to 30 gm., were procured from the Central animal house of Sri Muthukumaran Medical College & RI, Chennai, and were kept in the Pharmacology experimental laboratory for about 10 days. Mice were divided into 6 groups of 6 in each. They were maintained at room temperature (25±2°C) under standard 12:12 hr. Light Dark cycle, fed on germinating grams and water ad libitum. Locomotor activity by Actophotometer was conducted to mice of group 1 to 6 after administration of Standard and test drugs. The study protocol was approved by the Institutional animal ethics committee. Mice of group 1 received distilled water and served as negative control (Placebo). Group 2, 3 and 4 received Sodium valproate 100mg/kg, Lamotrigine 10mg/kg and pregabalin 100mg/kg respectively. Mice of group 5 were treated with combination of Pregabalin (100mg/kg) plus sodium Valproate (100mg/kg). Group 6 received combination of Lamotrigine (10mg/kg) plus sodium Valproate

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(100mg/kg). All the drugs were administered via intragastric route

**Locomotor activity by Actophotometer:** To assess the locomotor activity, the mice were placed individually in the activity cage for 5 minutes. When the beam of light falling on the photocell is cut off by the animal, a count is recorded. The basal activity score for all the animals were noted for 5 minutes. The locomotor activity score for each animal was observed again 30 mins after administration of standard, test and control drugs [3].

**Statistical Analysis:** The results were analyzed statistically by One-way ANOVA followed by LSD post hoc test using SPSS16.0 software. The data were expressed as mean  $\pm$  standard error mean (SEM) and  $P < 0.05$  was considered significant.

## RESULTS

There was no significant difference in the locomotor activity score before treatment between the control, standard and test groups. There was significant reduction in the locomotor activity in the Sodium Valproate alone treated group, combination of Pregabalin plus Sodium Valproate treated group and combination of Lamotrigine plus Sodium Valproate treated group in comparison to control group. Whereas Lamotrigine alone and Pregabalin alone treated group did produce significant reduction in the mental alertness when compared to Placebo. When compared to Valproate alone treated group, Lamotrigine plus Sodium Valproate combination treated groups produced significant reduction in the locomotor activity whereas combination Pregabalin plus Sodium Valproate treated group failed to produce significant change in the locomotor activity (Table 1).

## DISCUSSION

Central nervous system is complex, regulating/controlling various body functions through the balance of variety of stimulating and inhibitory neurotransmitters. Any drug that alters the action of any of the neurotransmitters may affect various neurobehavioral and neuroendocrine functions [4]. Sodium valproate acts by prolonging the recovery of voltage-activated  $\text{Na}^+$  channels

from inactivation, inhibiting the low-threshold (T)  $\text{Ca}^{2+}$  current and by increasing GABA levels [5]. Pregabalin, a novel anticonvulsant drug acts by increasing neuronal GABA level and by decreasing the release of glutamate [2]. Lamotrigine acts by delaying the recovery from inactivation of recombinant  $\text{Na}^+$  channels and inhibiting synaptic release of glutamate [6]. Sodium valproate, Pregabalin and Lamotrigine acts by altering the neurotransmitters in the Central nervous system. Hence, the present study was undertaken to assess the effect of these drugs on mental alertness by using Actophotometer in wistar albino mice. In this study, there is no significant change in the basal locomotor activity score between the control, standard and test group. Sodium Valproate alone treated group, combination of Pregabalin plus Sodium Valproate treated group and combination of Lamotrigine plus Sodium Valproate treated group significantly ( $P < 0.05$ ) affect the mental alertness in comparison to placebo group. When compared to standard drug (Valproate) alone treated group, Lamotrigine plus Sodium Valproate combination treated groups produced significant ( $P < 0.05$ ) reduction in the locomotor activity. Combination of Pregabalin plus Sodium Valproate treated group failed to produce significant effect on mental alertness when compared to sodium valproate alone treated group.

## CONCLUSION

To conclude, Sodium Valproate alone treated animals more significantly affect mental alertness than pregabalin and lamotrigine alone treated mice in comparison to placebo. Combination of Pregabalin plus Sodium Valproate treated mice showed less significant effect on mental alertness than Lamotrigine plus Sodium Valproate combination treated animals in comparison to standard drug. Further research with stronger study design in larger samples for longer duration of time is recommended to substantiate and add vital information to the result of this study.

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**Table 1: Effect of drugs on locomotor activity using Actophotometer in Albino Mice**

Group	Drug	Dose	Locomotor Activity Score	
			Before Treatment	After Treatment
1	Distilled Water (Placebo)	0.5ml	681.33 ± 20.03	667.50 ± 21.71
2	Sodium Valproate (Standard)	100mg/kg	678.00 ± 18.63	547.50 ± 26.08*
3	Lamotrigine	10mg/kg	637.17 ± 20.46	645.50 ± 22.83
4	Pregabalin	100mg/kg	662.00 ± 27.26	653.83 ± 28.08
5	Pregabalin + Sodium Valproate	100mg/kg + 100mg/kg	628.67 ± 23.48	517.50 ± 15.71*
6	Lamotrigine + Sodium Valproate	10mg/kg + 100mg/kg	616.83 ± 38.37	462.17 ± 28.18 *#

One-way ANOVA followed by LSD post hoc test

\*compared to Placebo  $P < 0.05$ ,

# Compared to Standard  $P < 0.05$

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