Bull. Pharm. Sci., Assiut University,
Vol. 14, Parts 1&2, PP 23-34

STUDY OF THE EFFECT OF VERAPAMIL, CHLORDIAZEPOXIDE AND THEIR COMBINATION ON SPONTANEOUS LOCOMOTOR ACTIVITY IN MICE.

M.M.Abdel-Rahman

Department of Pharmacology, Faculty of Medicine, Assiut University, Assiut, Egypt

ABSTRACT

The effects of verapamil, chlordiazepoxide (CDX) separately or and in combination on spontaneous locomotor activity (SLMA) of mice were investigated using an activity cage apparatus. Results of the present study revealed that the i.p. injection of verapamil in three dose levels (0.3, 0.6 and 1.3 mg/kg) elicited a dose dependent decrease, both in intensity and duration, of SLMA of mice. The i.p. administration of CDX in doses of 5 and 10 mg/kg brought about a significant dose-related diminution of SLMA of mice. Verapamil, in its three levels, administered concurrently with CDX, in its two dose levels, resulted in a significant potentiation of CDX-induced inhibition of SLMA. However, This potentiation caused by verapamil was much more evident with the smaller dose level of CDX (5 mg/kg), than with the higher dose level (10 mg/kg).

Available reports are in agreement with our results. These reports indicate that verapamil might have the ability to suppress SLMA of mice and to potentiate the CDX-induced inhibition of SLMA via different modes of action.

INTRODUCTION

Verapamil, a calcium channel antagonist, is widely used for the treatment of supraventricular arrhythmias and ischaemic heart disease[1,2]. The drug has been reported to have some sort of efficacy against mania[3]. This calcium entry blocker can antagonise 5-hydroxytryptamine (5-HT) at its receptor sites in the human blood platelets[3] as well as in the rabbit's aorta[4].

It has been reported by many investigators[5,6,7] that 5-HT plays an important role in controlling spontaneous locomotor activity (SLMA). Accordingly, any drug having the ability to alter serotonergic activity in the brain can possibly exert an action on SLMA. Since verapamil was reported to antagonise 5-HT it might affect the spontaneous locomotor activity of mice.

Chlordiazepoxide (CDX) which is well known for its anti-anxiety properties[8] has been also reported by many authors to reduce 5-HT transmission, release or turnover in the brain[8,9,10,11,12,13].

Several interactions between CDX and other drugs in terms of its effect on locomotor activity and behaviour have been reported, these include interactions with morphine[14,15] naloxone[16], pentobarbital[17], reserpine[18], haloperidol[19] amitryptylline, imipramine[20] MAO inhibitors[21], anticholinergic drugs[22]; amphetamine[23,24] and cocaine[25].

To our knowledge there is no record concerning the possible interaction of CDX and verapamil on spontaneous locomotor activity. Therefore, the objective of the present work is to investigate possible effect of verapamil, if any, on SLMA and its modifying role on the effect of CDX on SLMA.

MATERIALS AND METHODS

Chemicals:

Verapamil hydrochloride and chlordiazepoxide were obtained from Sigma Company.

Animals:

Male albino mice weighing 18-22 gm were used in this study. Animals were allowed free access to food and water ad libitum. Measurement of the spontaneous locomotor activity of mice throughout the whole work was carried out at 9.00 AM to 1:00 PM.

Apparatus:

An activity cage apparatus (Cat. No. 7400 UGO Basile, Biological research apparatus, 21025 Camerio-Varese, Italy) was employed to record SLMA. The cage floor of this apparatus is made up of 30 evently-spaced stainless steel bars. Odd bars are earthed whilst even bars are active. Besides, the bridges that the animal makes or breaks with its paws link or disconnect on one or more of the active bars with the earth, and thus producing random configurations which change as the animal moves. The resulting changes in configuration are converted into pulses are recorded by a print-out counter at the present intervals.

Animals were placed singly in the activity cage and their SLMA was recorded for 5 min before drug administration (control value) and at 5 min intervals following the i.p. injection of drugs. Drugs were allowed to exert their action over a period of 30 min. A control non-treated group of mice was included in the first set of experiments in an attempt to study the influence of experimental conditions on the SLMA of mice. In addition, the mean percentage change in the total score of SLMA performed by different groups of animals was calculated in order to determine the pattern of change in the total score over the whole period of the investigation.

EXPERIMENTS

1-Study of the effect of experimental conditions on SLMA of mice.

In this set of experiments the SLMA of mice was studied using two groups of animals (each consisting of 8 mice). The first group was injected with saline solution whereas the second group was not treated with any agent. Recording of SLMA was taken for 5 min before saline injection and at 5 min intervals during a peroid of 30 min after saline administration. The percentage change in the total score recorded during the entire 30-min period was computed for both groups.

2-Influence of verapamil on SLMA of mice :

The influence of verapamil, given i.p., in three dose levels (0.3, 0.6 and 1.3 mg/kg) on the SLMA of mice was investigated in groups of animals (each consisting of at least 8 mice). Readings of SLMA were taken at the same time intervals as in experiment number 1. The methods for calculating the changes in the score of SLMA were similar to those of experiment number 1. For comparison, control saline-treated mice were dealt with in the same way as those treated with verapamil.

3-Effect of chlordiazepoxide (CDX) on SLMA of mice:

In this part of our investigation the effect of i.p. injection of two dose levels of CDX (5 mg/kg,) on the SLMA of mice was studied in groups of animals consisting of 8 mice. The time intervals for recording SLMA and its method of calculation were similar to those in the previous experiments. SLMA of control mice that were injected with saline was also recorded at the same time intervals as those used with CDX-treated animals.

4-Effect of verapamil on CDX-induced change in SLMA of mice:

In these experiments, the influence of the i.p. administration of the 3 dose levels of verapamil (0.3, 0.6 and 1.3 mg/kg) on the CDX-induced alteration in SLMA of mice was studied. Chlordiazepoxide was used in dose levels (5 and 10 mg/kg) and groups of at least 8 mice were utilized. The time periods for reading SLMA and the methods of SLMA calculations were identical to those employed in the foregoing experiments. Besides, control groups of saline-injected mice were also included in this set of experiments.

Statistical analysis:

Results were calculated statistically using the Student's t-test[26].

RESULTS AND DISCUSSION

The data shown in Figure (1) concerning the SLMA of saline treated mice (recorded at 5 min intervals over a period of 30 min) revealed that SLMA was diminished significantly $P < 0.05$) at all selected periods of time.

Similarly, nontreated mice which were handled in the same way as saline-treated ones were found to show a progressive decrease in SLMA with time. In addition, the mean percentage fall in SLMA at various time intervals of both saline-treated and non-treated animals was found to be more or less the same.

Thus, studying the effect of experimental conditions on SLMA of mice indicated that both saline-treated and non-treated mice showed a decrease in SLMA. This effect is presumably attributed to acclimatization of the animals due to their presence in the activity cage. Accordingly, one can conclude that saline has no significant effect on SLMA of mice and this is in agreement with the observations of Shian et al[27].

In the second set of experiments a significant reduction of SLMA of mice was observed following the i.p. administration of the three dose levels (0.3, 0.6 and 1.3 mg/kg) of verapamil (Table 1). This depressant effect of the drug on SLMA proved to be dose-related. The administration of this calcium channel blocker in a dose of 0.3 mg/kg manifested a lowering of SLMA only in the first 5 min following its administration, whereas the dose of 0.6 mg/kg of the drug resulted in depression of SLMA, an action that lasted for 15 min after drug injection. Moreover the highest dose of the verapamil (1.3 mg/kg) produced a longer-lasting decrease in SLMA (for 25 min).

It is noteworthy that the i.p. injection of each of the three dose levels of verapamil led to a significant diminution of the mean percentage change in the total score of mice recorded during the whole 30 min period of the investigation.

In this part of the study, verapamil was found to possess a dose-related depressant effect on SLMA of mice as it is seen in Table (1). The most probable explanation of this verapamil's inhibitory effect on SLMA is its ability to antagonize 5-HT at its receptor sites[3,4]. In agreement with this suggestion is that 5-HT antagonist was able to inhibit the hyperactivity induced by dopamine and amphetamine in rats[28].

A second possible interpretation of verapamil-induced inhibition of SLMA comes from a finding which relates this effect to its calcium channel blocking activity[29].

A third cause of the inhibitory effect of verapamil on SLMA is prob-

ably due to its ability to enhance, dopaminergic activity in the brain[30,31].

In the third set of experiments, the intraperitoneal injection of two dose levels (5 and 10 mg/kg) of chlordiazepoxide (CDX) into the mice gave rise to a significant ($P < 0.05$) depression of SLMA (Table 2). The CDX-induced inhibition of SLMA was found to be dose-dependent.

Chlordiazepoxide (5 mg/kg) showed a depressant effect on SLMA of mice. This effect required a period of 15 min to appear, after that time, the action of CDX was persistent to the end of the period of the study. On the other hand, the larger dose (10 mg/kg) of chlordiazepoxide elicited a decrease in the recorded SLMA which lasted from the first 5 min to the end of the 30-min period. Besides, the degree of CDX-induced fall in SLMA of mice was positively related to the administered dose of the drug.

With respect to the total score of SLMA of mice, the two dose levels (5 and 10 mg/kg) of chlordiazepoxide demonstrated a significant drop in the mean percentage change of this score (Figure. 3).

The present data showed that CDX caused a significant decrease in SLMA of mice, the duration and intensity of which were dose-dependent. This effect might be explained in a number of ways: (1) a reduction of 5-HT transmission in the brain[9]. (2) modulation of the serotonergic transmission in the brain through an action on GABA[8,32] (3) a reduction of dopaminergic activity in the brain[33] and (4) inhibition of calcium entry into nerve terminals[29,34].

Results of the fourth set of experiments (Tables 3 and 4) indicated that verapamil in its three dose levels potentiated the depressant effects of CDX (used in doses of 5 mg/kg and 10 mg/kg) on SLMA of mice.

As it is evident from Table (3) that the concurrent administration of CDX (5 mg/kg) and verapamil (0.3 mg/kg) resulted in a significant reduction

of SLMA 5 min following administration of two drugs ($P < 0.05$). With the same dose level of chlordiazepoxide and a higher dose of verapamil (0.6 mg/kg), a 10-min inhibition of SLMA was obtained. In addition, a combination of CDX (5 mg/kg) and verapamil (1.3 mg/kg) resulted in a significant ($P < 0.05$) lowering of the SLMA over a period of 15 min. It is noteworthy that the intensity of SLMA inhibition caused by the combination was dependent on verapamil dose. It has been found that 0.3, 0.6 and 1.3 mg/kg of verapamil given simultaneously with CDX in a dose of 5 mg/kg led to a decrease in the order of 45.61, 60.78 and 61.95% of SLMA respectively at 5 min following administration of the combination.

It was also found that the concomitant administration of CDX (5 mg/kg) and verapamil in its three dose levels resulted in a significant inhibition of the total score of SLMA (Figure. 4).

As it is shown in Table (4), the administration of verapamil in a dose of 0.3 mg/kg togther with CDX in a dose of 10 mg/kg did not potentiate SLMA inhibition caused by CDX alone. However, when the higher dose level of verapamil (0.6 mg/kg) was taken concurrently with CDX (10 mg/kg), it was able to significantly potentiate the CDX-induced depression of SLMA only 10 min following administration of the combination. Besides, the simultaneous administration of the highest dose of verapamil (1.3 mg/kg) and CDX (10 mg/kg)

brought about a diminution of SLMA at 5, 10, 23 and 30 min following administration of this combination of drugs.

Figure (5) shows the percentage change in the total score of SLMA of mice. In this figure it is obvious that the administration of 10 mg/kg of CDX together with the higher doses of verapamil (0.6 and 1.3 mg/kg) was capable of manifesting a significant reduction of the mean percentage change in the total score of SLMA.

Compared with CDX alone, the combinations of verapamil (0.3, 0.6 and 1.3 mg/kg) and CDX (5 mg/kg) were able to depress significantly SLMA of mice at times when CDX alone did not elicit any significant change. The combination of verapamil and CDX (0.3 : 5 mg/kg) lowered SLMA significantly 5 min. following its administration. At this time, CDX alone was not able to reduce SLMA. The other two combinations of verapamil and CDX (0.6 : 5 mg/kg and 1.3 :5 mg/kg) led to significant reductions of SLMA at 5 and 10 min. for the first combination and at 5, 10 and 15 min. for the second one. Furthermore, the total score of SLMA registered during the 30-min. period was found to be significantly reduced after the administration of CDX in a dose of 5 mg/kg with each of the three dose levels of verapamil (0.3, 0 6 and 1.3 mg/kg).

With the use of the higher dose level of CDX (10 mg/kg), the potentiating effect of verapamil on CDX-induced suppression of SLMA was not as evident as that observed with the use of the lower dose of CDX (5 mg/kg). In other words, the lowest dose level of verapamil (0.3 mg/kg) did not potentiate at all the effects of CDX on SLMA. The higher dose of verapamil (0.6 mg/kg) brought about a significant potentiation only at 10 min. following administration of the combination. Besides, the highest dose level of verapamil (1.3 mg/kg) increased the depressant effect of CDX on SLMA immediately after i.p. injection of the drug combination (at 5 and 10 minutes) and at the end of the investigation period (25 and 30 min).

The limited ability of verapamil in its three dose levels to exhibit considerable potentiation of the depressant effect of the larger dose of CDX (10 mg/kg) on SLMA can be easily explained on the basis that SLMA of mice is already profoundly depressed by the higher dose of CDX to such an extent that the potentiating effect of verapamil is less likely to appear at time intervals when SLMA was adequately inhibited. A combination of verapamil and CDX (1.3 : 10 mg/kg) resulted in a complete inhibition (100% $\pm$ 0.00) of SLMA in all animals 30 min following administration of this combination. In addition, a significant potentiation of CDX-inhibition was noticed 25 min following administration of this combination.

The ability of verapamil to increase the CDX-induced reduction of SLMA is not unexpected because the two drugs have some pharmacological properties in common. Verapamil is well known as a calcium channel blocker. Therefore, its combined administration with CDX may lead to a greater diminution of SLMA since CDX was also reported to possess some sort of calcium channel blockade[29]. Besides, both drugs were reported to modulate serotonergic activity in the brain with subsequent reduction of SLMA. In this respect verapamil was reported to act as an antagonist of 5-HT at its receptor sites[3,4]. Moreover, CDX was shown to reduce 5-HT transmission in the brain by inhibiting directly 5-HT turnover[10]. Concerning its effect on dopaminergic activity in the brain, verapamil

was demonstrated to affect its dopamine content[28]. Besides, CDX was shown to inhibit the dopaminergic neurons in the brain by potentiating the inhibitory effect of GABA[33,35]. All these reports suggest that it is possible that verapamil can potentiate the effect of CDX on SLMA through different modes of action.

Table 1 : Influence of Verapamil on the Spontaneous Locomotor Activity (SLMA) of Mice.

Tim (min)	5	10	15	20	25	30	Total score of SLMA recorded during the whole 30 min period.
Saline-treated control (n = 8)	14.25 ± 1.84	22.98 ± 1.47	39.40 ± 4.84	49.88 ± 4.60	64.81 ± 5.14	80.95 ± 4.56	828 ± 63
Verapamil 0.3 mg/kg (n = 8)	26.58* ± 3.36	32.10 ± 1.99	39.06 ± 2.20	62.73 ± 4.33	66.76 ± 4.11	85.43 ± 5.35	787 ± 43
Verapamil (0.6 mg/kg) (n = 8)	29.60* ± 3.57	39.33* ± 2.84	55.34* ± 3.40	62.25 ± 3.97	78.62 ± 3.49	85.68 ± 3.10	898 ± 20
Verapamil (1.3 mg/kg) (n = 10)	28.31* ± 3.48	52.12* ± 4.29	64.29* ± 5.49	73.19* ± 6.48	83.01* ± 4.81	85.16 ± 4.54	648 ± 64

Data represent the mean percentage decrease in SLMA. Values are the mean of (n) experiments ± S.E.
(*) Statistically significant from control values ($P < 0.05$).

Table 2 : Influence of Chlordiazepoxide on the Spontaneous Locomotor Activity (SLMA) of Mice.

Time (min)	5	10	15	20	25	30	Total score of SLMA recorded during the whole 30 min period.
Saline-treated mice (control)	11.93 ± 2.51	27.38 ± 4.66	40.10 ± 3.47	46.57 ± 5.12	67.04 ± 2.63	75.64 ± 3.29	999 ± 125
Chlordiazepoxide (5 mg/kg)	17.68 ± 4.57	39.60 ± 8.93	74.10* ± 4.53	87.75* ± 1.64	95.81* ± 0.60	96.23* ± 0.34	507 ± 20
Chlordiazepoxide (10 mg/kg)	39.20* ± 1.60	78.12* ± 1.97	91.25* ± 2.07	96.51* ± 1.02	95.08* ± 0.75	97.06* ± 0.49	347 ± 22

Data represent the mean percentage decrease in SLMA. Each is the mean of (8)experiments ± S.E.
(*) Statistically different from control values ($P < 0.05$).

Table 3 : Effect of the Combined Administration of Chlordiazepoxide (5 mg/kg) and Verapamil (0.325, 0.625 and 1.25 mg/kg) on the Spontaneous Locomotor Activity (SLMA) of Mice.

Time (min)	5	10	15	20	25	30	Total score of SLMA recorded during the whole 30 min period.
Control (n = 8)	18.29 ± 2.41	28.55 ± 2.88	45.90 ± 2.64	59.53 ± 6.44	72.17 ± 4.12	72.69 ± 3.42	998 ± 101
Chlordiazepoxide (5 mg/kg) (n = 9)	16.03 ± 8.57	40.27 ± 13.4	78.76^{+} ± 4.76	88.44^{+} ± 3.17	95.80^{+} ± 0.93	95.40^{+} ± 1.44	533 ± 99
Chlordiazepoxide (5mg/kg)+verapamil (0.3 mg/kg) (n = 10)	45.61* ± 6.99	65.37 ± 6.69	83.81 ± 4.37	89.40 ± 4.78	95.75 ± 1.31	92.69 ± 3.21	351 ± 83
Chlordiazepoxide (5mg/kg)+verapamil (0.6 mg/kg) (n = 8)	60.78* ± 4.04	83.22* ± 3.27	85.13 ± 4.69	94.63 ± 1.60	95.20 ± 2.13	98.76 ± 1.09	334 ± 52
Chlordiazepoxide (5mg/kg)+verapamil (1.3 mg/kg) (n = 8)	61.95* ± 4.26	85.77* ± 3.83	92.40* ± 3.59	92.06 ± 3.17	96.00 ± 1.82	98.55 ± 0.58	205 ± 81

Data represent the mean percentage decrease in SLMA.
Values are the mean of (n) experiments ± S.E.
(+) Statistically different from saline-injected animals ($P < 0.05$).
(*) Statistically different from chlordizepoxid-injected mice ($P < 0.05$).

Table 4 : Effect of the Concurrent Administration of Chlordiazepoxide (10 mg/kg) and Verapamil (0.3, 0.6 and 1.3 mg/kg) on the Spontaneous Locomotor Activity (SLMA of Mice).

Time (min)	5	10	15	20	25	30	Total score of SLMA recorded during the whole 30 min period
Control (n = 8)	13.98 ± 2.37	22.30 ± 4.53	39.57 ± 3.57	41.78 ± 2.10	72.45 ± 1.28	81.83 ± 3.08	914 ± 69
Chlordiazepoxide (10 mg/kg) (n = 9)	45.65^{+} ± 4.60	83.56^{+} ± 4.18	94.23^{+} ± 2.71	95.92^{+} ± 2.72	96.93^{+} ± 0.87	96.00^{+} ± 1.78	265 ± 37
Chlordiazepoxide (10mg/kg)+verapamil (n = 7)	49.50 ± 5.03	90.10 ± 4.40	94.94 ± 3.10	98.11 ± 0.22	99.93 ± 0.57	99.34 ± 1.42	178 ± 41
Chlordiazepoxide (10mg/kg)+verapamil (n = 9)	54.88 ± 4.09	95.64* ± 1.59	95.02 ± 1.70	98.07 ± 0.94	98.52 ± 1.82	99.92 ± 1.88	184 ± 29
Chlordiazepoxide (10mg/kg)+verapamil (n = 8)	74.36* ± 3.67	97.51* ± 0.95	98.43 ± 0.82	98.04 ± 1.23	99.85* ± 0.11	100.0* ± 0.00	187 $^{+}$ 31

Data pressent the mean percentage decrease in SLMA. Values are the mean of (n) experiments ± S.E.
(+) Statistically different from saline-injected animals ($P < 0.05$).
(*) Statistically different from chlordiazepoxide-injected mice ($P < 0.05$).

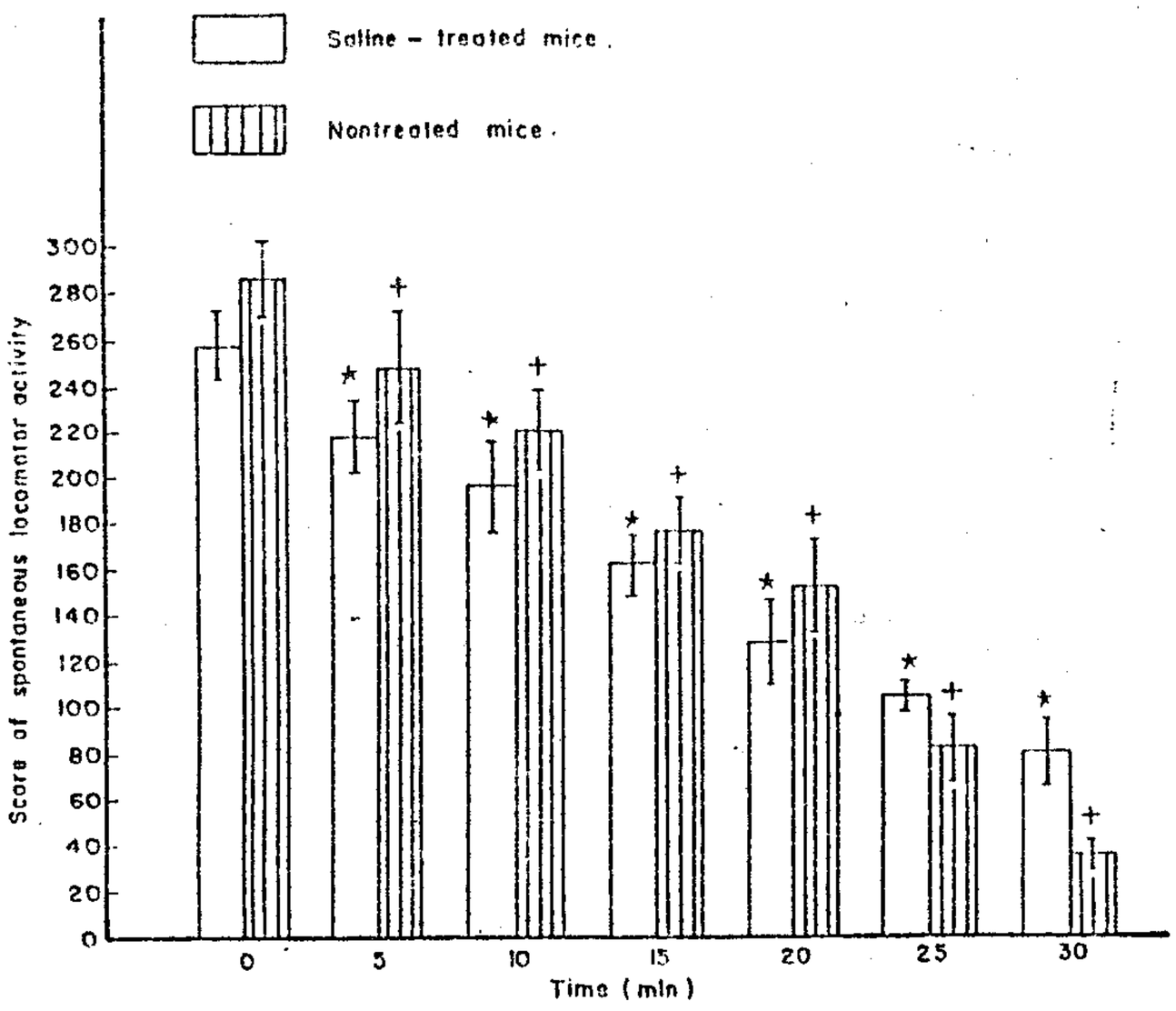

Fig.(1): Changes in SLMA of saline-treated and non-treated mice. Values are the mean ± S.E. (n = 8).
* Saline treated + control.
(* or +) means significant at $P < 0.05$

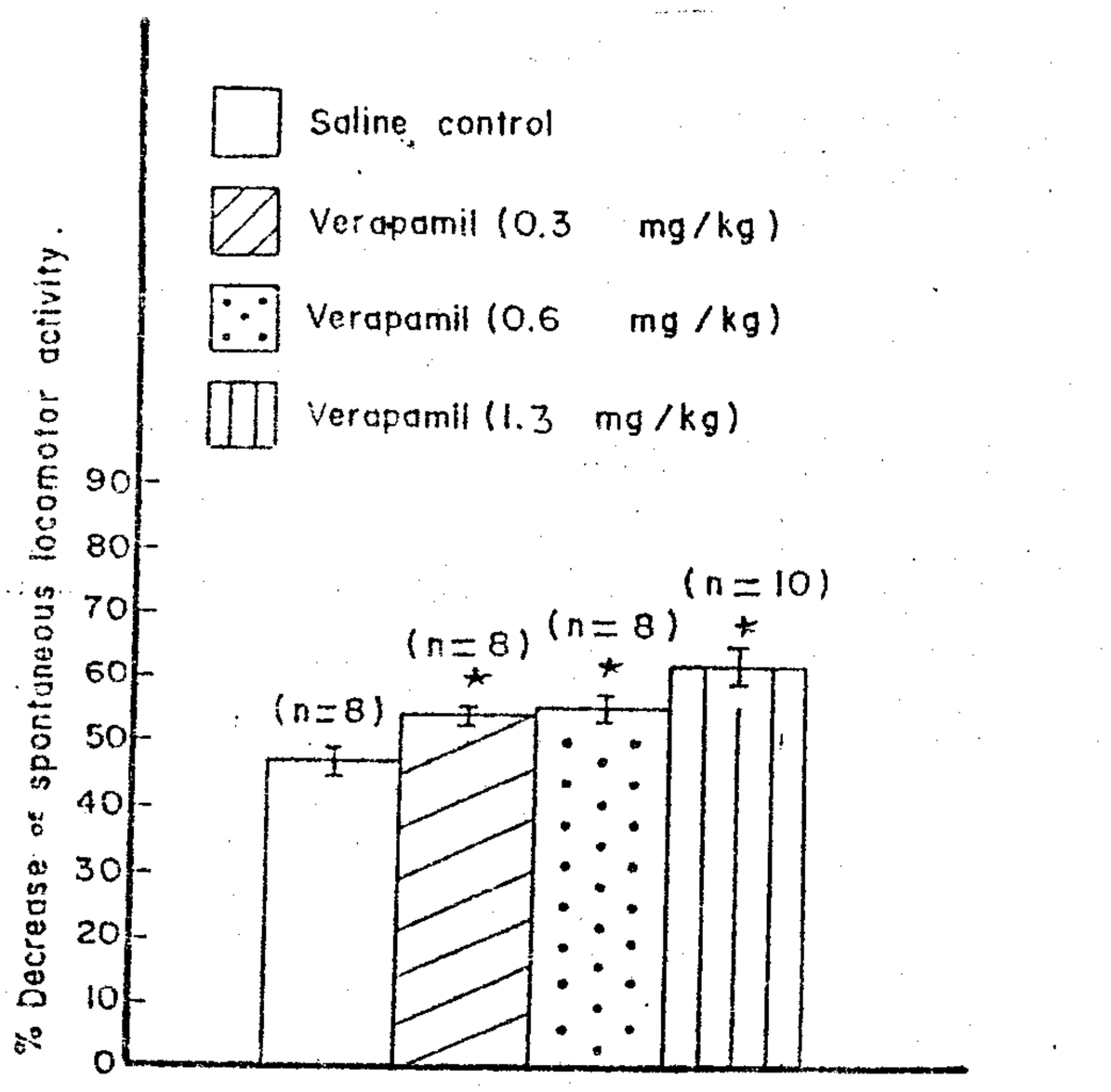

Fig. (2): Percentage decrease of the total score of spontaneous locomotor activity of mice 30 minutes following I.P. injection of verapamil. Values are mean ± S.E.
(*) $P < 0.05$.

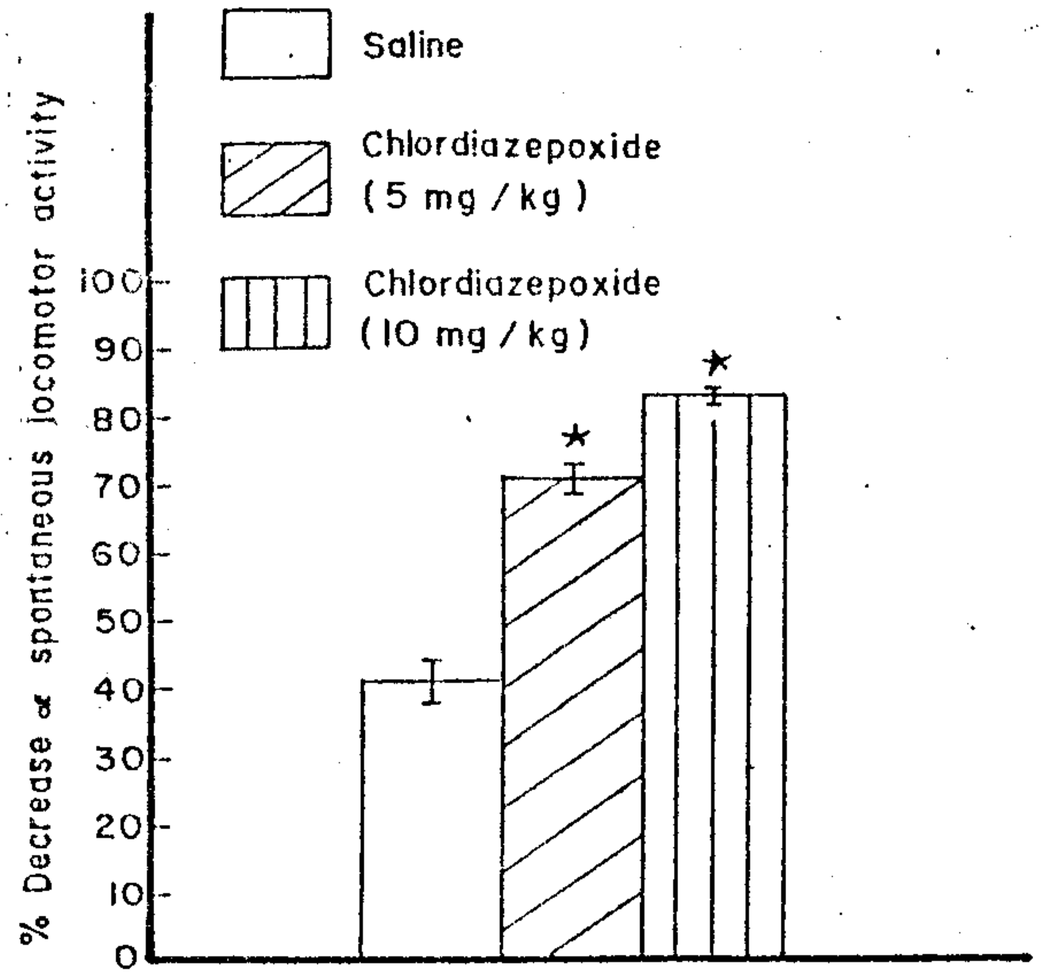

Fig. (3): Percentage decrease of the total score of spontaneous locomotor activity of mice following I.P. injection of chlordiazepoxide. Values are mean ± S.E. (n = 8).
(*)P < 0.05.

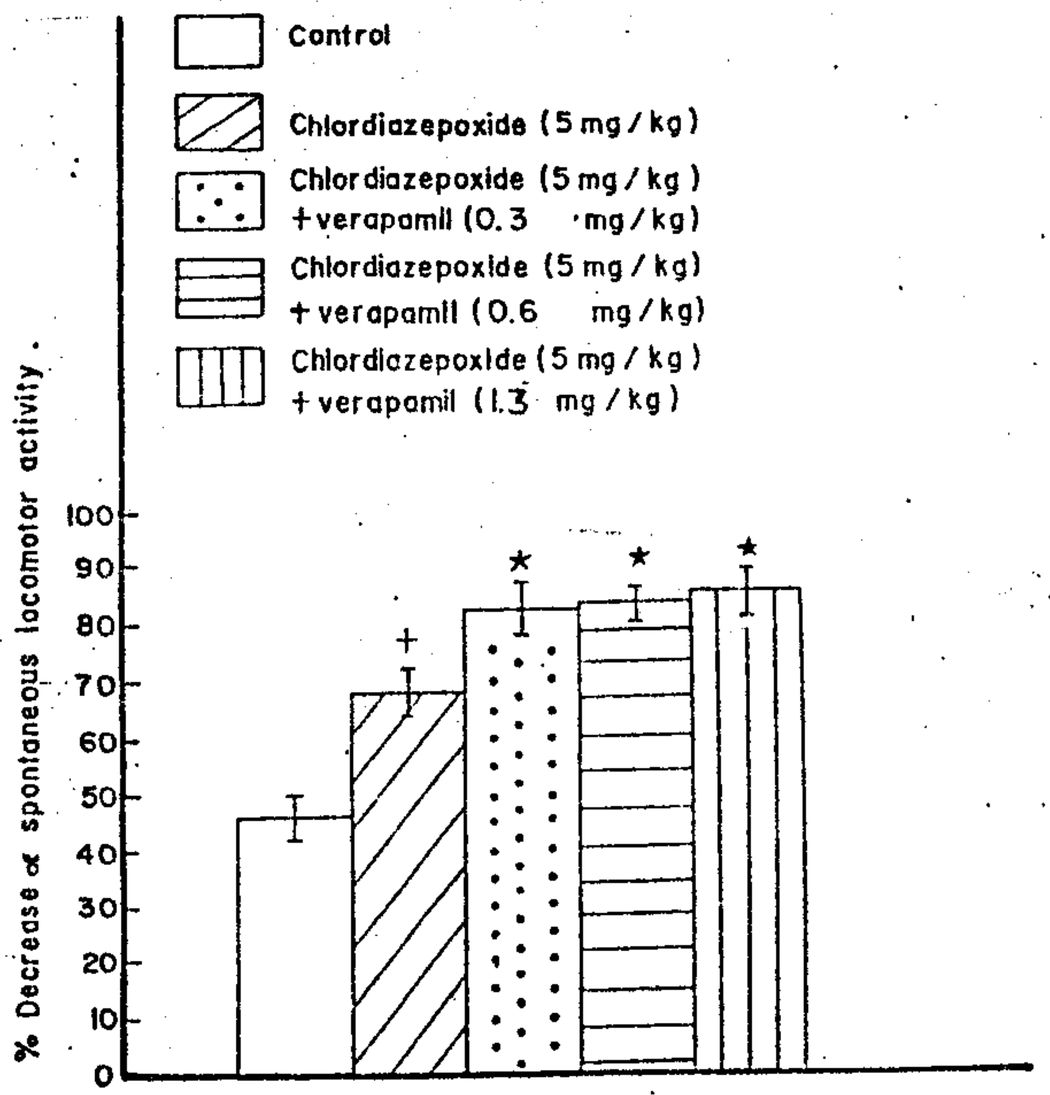

Fig. (4): Percentage decrease of the total score of spontaneous locomotor activity of mice 30 minutes following I.P. administration of chlordiazepoxide (5 mg/kg) alone and in combination with verapamil. Values are mean ± S.E. (n = 8).
(*)P < 0.05.

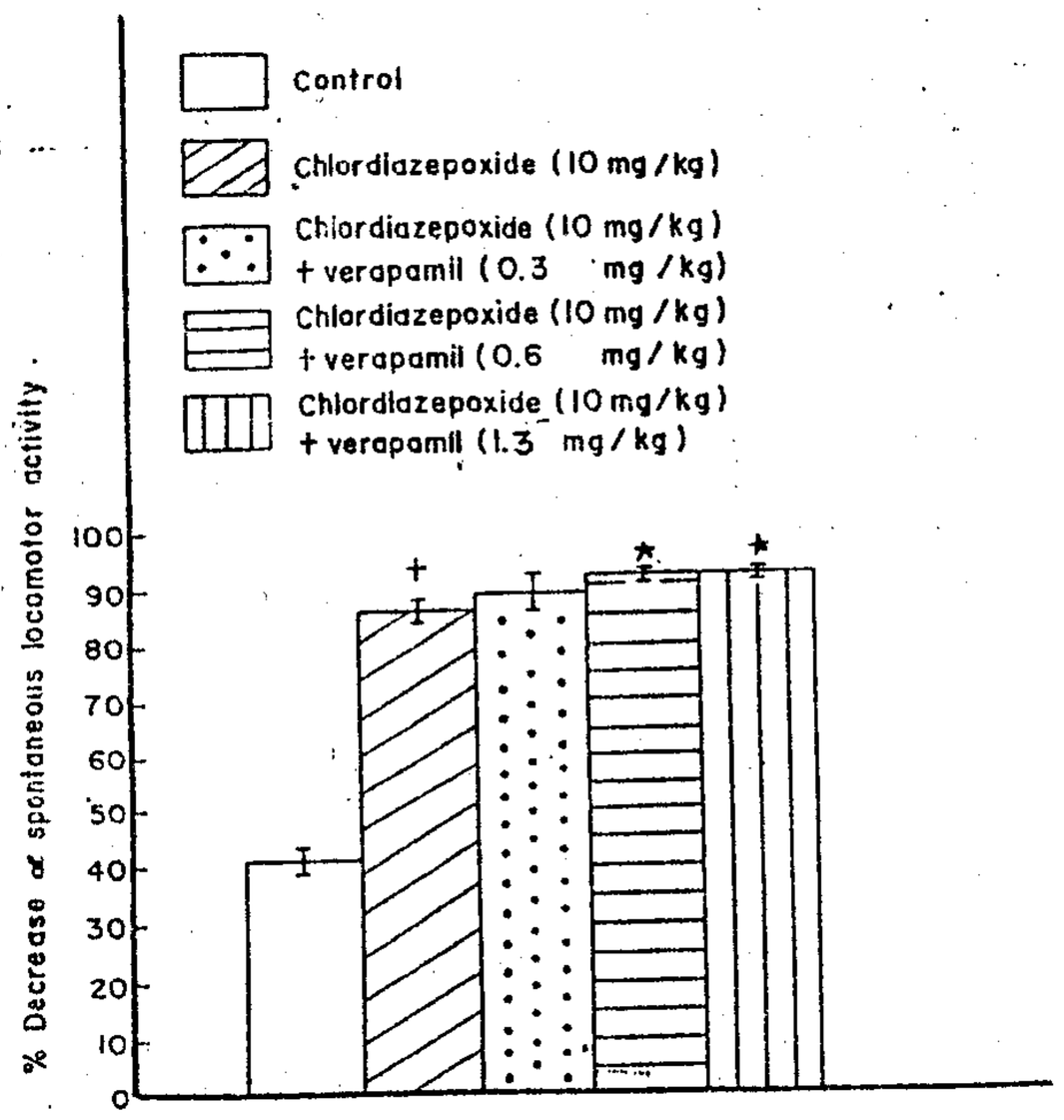

Fig. (5): Percentage decrease of the total score of spontaneous locomotor activity of mice of chlordiazepoxide (10 mg/kg) alone and in combination with verapamil. Values are mean ± S.E. (n = 8).
(*)P < 0.05.

REFERENCES

1-J.G.Reves, I.Kissin, W.A.Lell, and S.Tosone,: Anesthesiol., 57, 504 (1982).

2-R.Paoletti, and S.Govoni,: Pharmac. Rev. Commun., 19, 196 (1987).

3-H.Affolter, W.B.Burkard and A.Pletscher: Eur. J.Pharmacol., 22, 157 (1982).

4-M.Ohashi, R.Kanai, and I.Takayanagi: J. Pharmacol. Exp. Ther., 233, 830 (1985).

5-B.Costall, R.J.Naylor, C.D.Marsden and C.J.Pycock: J. Pharm., Pharmacol., 523 (1976).

6-C.J.Pycock, R.W.Horton, and C.J.Carter: Adv. Biochem. Psychopharmacol., 14, 323 (1978).

7-D.L.Jones, G.J.Mogenson, and M. Wu: Neuropharmacology 20, 29 (1981).

8-P.Soubrie, C.Plas, A.Ferron and J.Gloviniski: J. Pharmacol. Exp. Ther., 226, 526 (1983).

9-L.Stein, J.D.Belluzi and C.D.Eise: Psychiatry. 174, 665 (1977).

10-A.Sanner, A.Pletscher: Eur. J. Pharmacol., 55, 315 (1979).

11-W.Hunkeler, H.Monler, L.Pieri, P.Polc, E.P.Bonetti, R.Cumin, R.Schaffner and W.Haefely: Nature (London) 290, 514 (1981).

12-H.W.M.Steinbusch, Neuro Sci., 6, 618 (1981).

13-J.Collinge and C.J.Pycock: Eur.Pharmacol., 85, 9(1982).

14-V.Cuomo, I.Cortese and G.Racagni: Neuropharmacology 20 (3), 301 (1981).

15-M.Sansone, and A.Oliverio,: Arch. Int. Pharmacodyn. Ther., 247, 71 (1980).

16-M.L.Billingsley, and R.K.Kubena: Life Sci., 22 (10), 897 (1978).

17-D.E.McMillan, J. Pharm. Exp. Ther. 207, 515 (1978).

18-M.Sansone: Pharmacol. Res. Commun., 10 (5), 479 (1978 b).

19-T.Fukuda and T.Tsumagari: Jpn. J Pharmacol., 34 (2), 131 (1984).

20-M.Sansone (1978 a) Psychopharmacology., 59, 151 (1978 a).

21-M.Sansone: Pharmacol. Res. Commun., 19 (8), 724 (1977).

22-M.Sansone, J. Hano: Psychopharmacol., (Berlin). 64, 181 (1979).

23-J.E.Barrett: Pharmacol. Biochem. Bheav., 5, 285 (1976).

24-M.Sansone, and J.Ventulani,: Pol. J. Pharmacol., 32, 125 (1980).

25-G.Mcllo: Br. J. Pharmacol., 54, 141 (1977).

26-G.W.Snedecor and W.C.Cochran: Statistical methods 6th ed., Iowa state University Press. Iowa, USA. (1967).

27-L.R.Shian, M.H.Wu, M.T.Lin and L.T. Go,: Pharmacology 30, 259 (1985).

28-B.Costall, A.M.Bomeney, R.J.Naylor, and M.B.Tyers: Br. J. Pharmacol., 92, 881 (1987).

29-S.W.Leslie, M.B.Friedman and R.R.Coleman: Biochem Pharmacol., 29,2439 (1980).

30-G.Gianutoss and J.L.Palmeri: Psychopharmacology 79, 329 (1983).

31-P.Protais, J.J.Bonnet, J. Costentin and J.C.Schwartz: Naunyn Schmiedeberg, 5 Arch. Pharmacol., 325, 93 (1984).

32-M.F.Chesslet, A.Cheramy, R.Romo, M.Desban and J.Glowinski, J. Exp. Brain Res., 258, 229 (1983).

33-P.G.Dorey, and G.N.Woodruff: Br.J. Pharmacol.,91, 301 (1987).

34-H.Fujiwara,N.Kato, H.Shuntoh and C.Tanaka,: Br. J. Pharmacol., 91, 287 (1987).

35-H.M.Geller, B.J.Hoffer and A.B.Taylor: Naunyn Schmiedeberg's Arch. Pharmacol., 304, 81 (1978).

دراسة تأثير عقار الفيرابااميل وعقارالكلورديازيبوكسيد ومخلوطات مختلفة منهما على النشاط الحركى الذاتى المحدود فى الفئران

محمود محمد عبد الرحمن

قسم الفارماكولوجى - كلية الطب - جامعة اسيوط

اجريت هذه الدراسة لفحص تأثير عقارى الفيرابامبل والكلورديازيبوكسيد ومخلوطات من هذين العقارين بنسب متفاوته على النشاط الحركى للفئران ولقد اظهرت نتائج هذه الدراسة ان حقن عقار الفيرابااميل داخل التجويف البريتونى للفئران فى جرعات مقدارها ٣ر٠، ٦ر٠، ٣ر١ محم / كجم يؤدى الى تقليل النشاط الحركى الذاتى لهذه الحيوانات ، وان هذا الانخفاض فى نشاط الفئران يعتمد على الجرعة المعطاه من مادة الفيرابااميل ، ولقد لوحظ ان هذا التقليل فى حركية الفئران يزداد فى شدته وطول مدته مع زيادة جرعة الفيرابااميل .

ولقد ادى حقن مادة الكلوردياازيبوكسيد داخل التجويف البريتونى للفئران فى جرعتين مقدارهما ٥ ، ١٠ محم / كجم ، الى تثبيط الحركية الذاتية للفئران بدرجة تعتمد على الجرعة المعطاه من مادة الكلورديازيبوكسيد.

ولقد دلت نتائج هذه الدراسة من خلال اعطاء الفيرابااميل (فى الجرعات الثلاث المذكورة سابقا) فى نفس الوقت مع عقار الكلورديازيبوكسيد (فى جرعتين مقدارهما ٥ ، ١٠ محم / كجم) على ان عقار الفيرابااميل فى استطاعته ان يزيد من قدرة دواء الكلورديازيبوكسيد من تثبيط النشاطى الحركى الذاتى للفئران ، الا ان قدرة مادة الفيرابااميل على احداث مثل هذا التأثير المقوى لدواء الكلورد يازيبوكسيد كانت اكثر وضوحا عن استخدام عقار الفيرابااميل مع الجرعة الاصغر من الكلورديازيبوكسيد (٥ مجم / كجم) .

received in 3/3/1991 - accepted in 5/11/1991