RESULTS

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A. In Vivo Experiments:

I. Effect of verapamil on gastric ulceration:

1. Effect of stress (by immobilization) on control group:

Control rats injected with saline and subjected to stress by immobilization for 24 hrs. showed a mean ulcer score of (± S.E.) 1.25 ± 0.37. The incidence of ulceration was present in 75 of animals. The calculated ulcer index in this group was 93.75 (Table 7 & Fig. 7).

2. Effect of verapamil on stress ulcer:

As shown in Table (7) & Fig. (7) the small dose of verapamil (2 mg/kg) did not affect the incidence of ulceration which was similar to that in the control group (75%), but the mean ulcer score (± S.E.) was reduced to 1.112 ± 0.139. The ulcer index was 84.37, while the preventive index was 10.01%.

On the other hand, the larger dose of verapamil (10 mg/kg), decreased the mean ulcer score severity (± S.E.) to 1.0 ± 0.38 (P 0.4). The incidence of ulceration was also reduced to 67.5%. Therefore the ulcer index decreased to 67.5. The preventive index was calculated to be 28% which is higher than that after using the small dose of verapamil (2 mg/kg).

3. Effect of acetylsalicylic acid on control animals:

Control rats injected with acetylsalicylic acid and saline showed a mean ulcer score of (± S.E.) 1.5 0.42. The incidence of ulceration was present in 75% of animals. The calculated ulcer index in this group was 112.5 (Table 8 & Fig. 8).

4. Effect of verapamil on acetylsalicylic acid induced ulcer:

As shown in Table (8) and Fig. (8), verapamil (2 mg/kg) did not affect incidence of ulceration, but the ulcer severity score (± S.E.) was reduced to 1.37 ± 0.42. The ulcer index was 112.5, while the preventive index was only 8.33.

With the larger dose of verapamil (10 mg/kg), the mean ulcer severity score (± S.E.) was decreased to 1.12 ± 0.42 ($P < 0.8$). The incidence of ulceration was reduced to 67.5%. The ulcer index also decreased to 75.93. The preventive index was found to be 32.5% which is higher than that after using the small dose of verapamil (2 mg/kg).

II. Effect Of Verapamil On Gastric Contents:

1. Gastric contents of control rats:

The contents of stomach obtained from saline treated control rats showed that the mean volume (± S.E.) was 3.72 ± 0.1 ml, the mean pH (± S.E.) was 3.06 ± 0.15, while the mean acid concentration (± S.E.) was 86.25 ± 12.74 mEq/L. The mean acid output (± S.E.) per unit time was calculated to be 80.32 ± 2.5 uEq/hr and the mean pepsin concentration in the gastric contents (± S.E.) was 16.31 ± 0.28 mg/ml (Table 9 & Fig. 10).

2. Effect of verapamil on gastric contents:

Verapamil (2 mg/kg) reduced slightly the

mean volume of gastric contents to 3.16 ± 0.14 ml ($P > 0.02$). The mean pH was raised slightly to (± S.E.) 3.72 ± 0.19 ($P < 0.05$), while the mean acid concentration (± S.E.) was reduced to 66.37 ± 3.58 mEq/L ($P < 0.001$). The mean acid output (± S.E.) was reduced to 52.62 ± 4.03 uEq/hr ($P < 0.001$) and the mean pepsin concentration (± S.E.) was 13.5 ± 1.66 mg/ml ($P > 0.2$)(Table 9 & Fig. 10).

Using a larger dose of verapamil (10 mg/kg) the mean volume of gastric contents was reduced (± S.E.) to 1.22 ± 0.14 ml ($P < 0.001$). The mean pH was increased to (± S.E.) 4.25 ± 0.2 ($P < 0.005$) and the mean acid concentration (± S.E.) was reduced to 45.62 ± 3.17 ($P < 0.001$). The mean acid output (± S.E.) was also reduced to 15.5 ± 2.53 ($P < 0.001$). On the other hand, the mean pepsin concentration (± S.E.) was reduced to 12 ± 2.22 ($P < 0.05$) (Table 9 & Fig. 10).

Table (7): Effect of intraperitoneal administration of verapamil on the incidence and severity of Gastric ulcer in male albino rats induced by 24 hours immobilization. Each group consisted of 8 animals.

Dose	Stress by immobilization		
	Control	Verapamil	
		2 mg/kg	10 mg/kg
% Incidence of ulceration	75%	75%	67.5%
Mean ulcer score ± S.E.	1.25 ± 0.156	1.112 ± 0.139	1.0 ± 1.7
Ulcer index	93.75	84.37	67.5
Preventive index	-	10.005	28

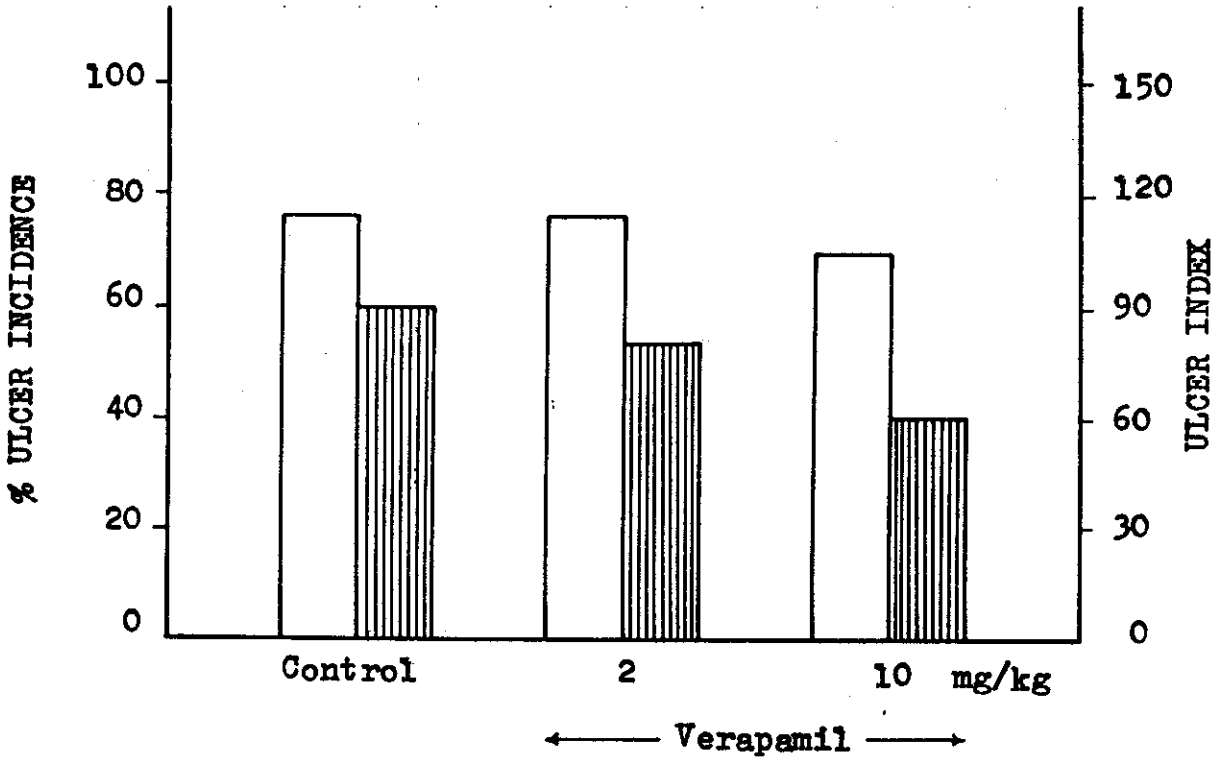

Fig. (7): Effect of intraperitoneal administration of verapamil in various doses on the incidence (□) and index (▥) of gastric ulcer in male albino rats induced by stress (24 hours immobilization).

* Each group consisted of 8 animals.

Table (8): Effect of intraperitoneal administration of verapamil on the incidence and severity of gastric ulcer in male albino rats induced by subcutaneous injection of acetylsalicylic acid. Each group consisted of 8 animals.

	Subcutaneous A.S.A. induced ulcer		
	Control	Verapamil	
Dose	-	2 mg/kg	10 mg/kg
% Incidence of ulceration	75%	75%	67.5%
Mean ulcer score ± S.E.	1.5 ± 0.187	1.37 ± 0.171	1.12 ± 1.29
Ulcer index	112.5	103.12	75.93
Preventive index	-	8.33	32.5

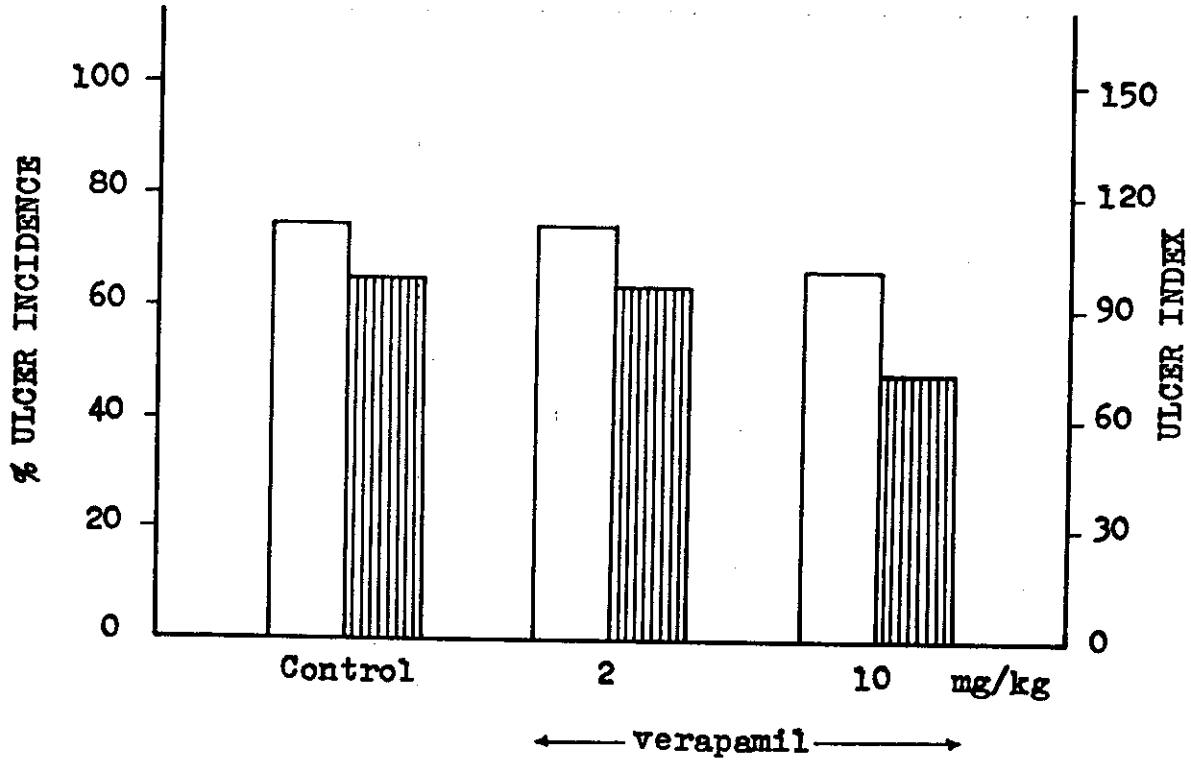

Fig. (8): Effect of intraperitoneal administration of verapamil on the incidence (□) and index (▨) of gastric ulcer in male albino rats induced by subcutaneous acetylsalicylic acid injection.

* Each group consisted of 8 animals.

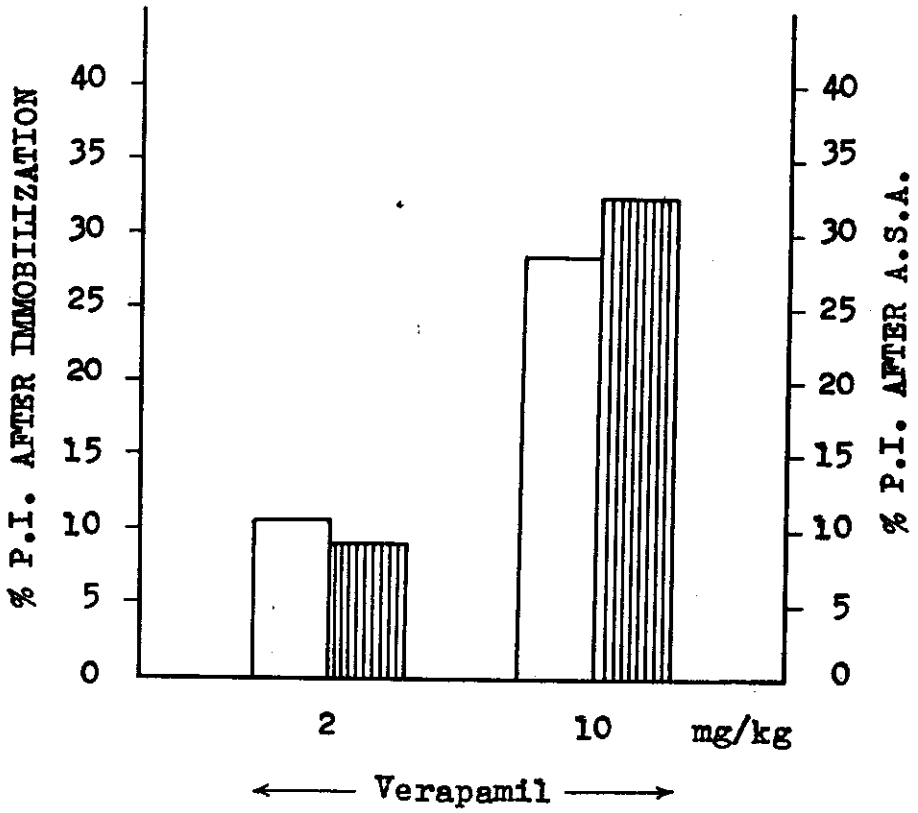

Fig. (9): The preventive index of verapamil in various doses given intraperitoneally in male albino rats on gastric ulcer induxed by immobilization (□) and ASA subcutaneous administration (▥).

P.I. = preventive index.
A.S.A. = Acetylsalicylic acid.

Table (9): Effect of various doses of verapamil given intraperitoneally on the volume, pH, acid concentration, acid output and pepsin concentration of gastric contents after 4 hours pyloric ligation (male albino rats).

	Dose mg/kg	Mean volume (ml) ± S.E.	Mean pH ± S.E.	Mean acid conc. mEq/L ± S.E.	Mean acid out put uEq/L ± S.E.	Mean pepsin conc. mg/ml ± S.E.
Control	-	3.72 ± 0.1	3.06 ± 0.15	86.25 ± 12.74	80.32 ± 2.5	16.31 ± 0.28
Verapamil	2 mg/kg	3.16 ± 0.14 (P 0.02)	3.72 ± 0.19 (P 0.05)*	66.37 ± 3.58 (P 0.001)*	52.62 ± 4.03 (P 0.001)*	13.50 ± 1.66 (P 0.2)
Verapamil	10 mg/kg	1.22 ± 0.14 (P 0.001)*	4.25 ± 0.20 (P 0.005)*	45.62 ± 3.17 (P 0.001)*	15.50 ± 2.53 (P 0.001)*	12.00 ± 2.22 (P 0.05)*

Each value represents the mean of 8 experiments ± S.E.

* significant.

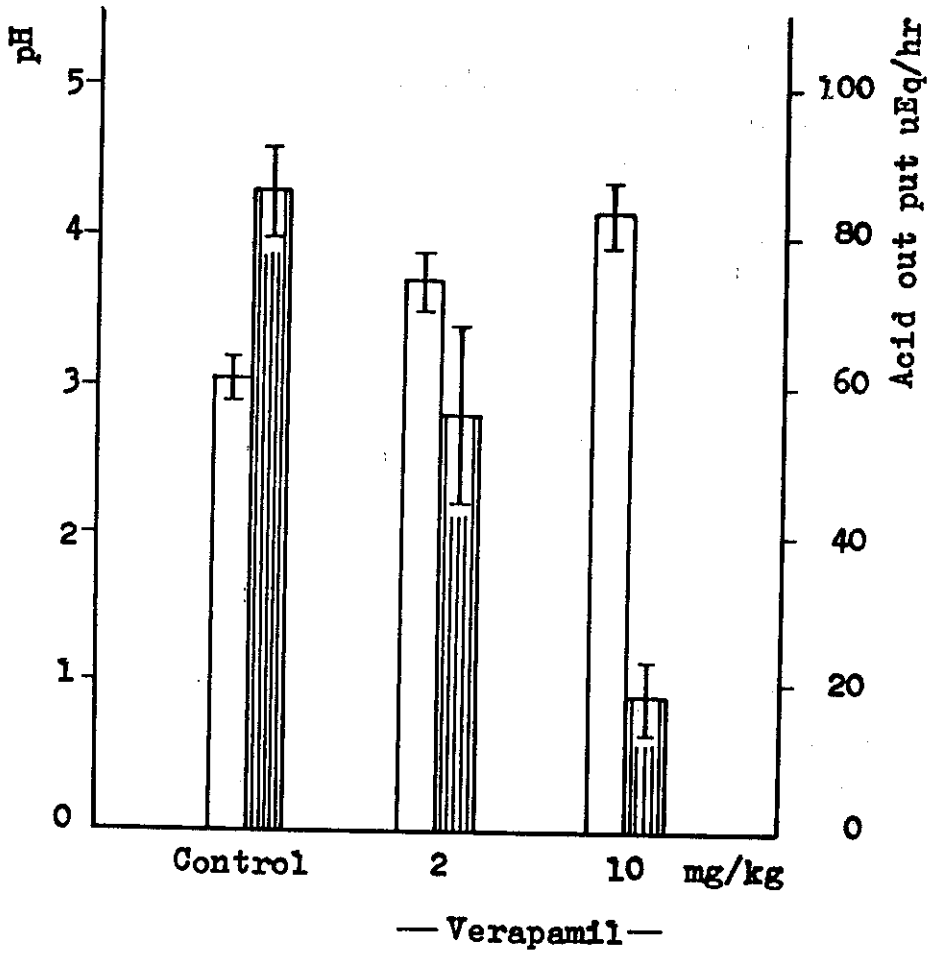

Fig. (10): Effect of various doses of verapamil on pH (□) and acid out put uEq/hr (▥) of gastric contents, 4 hours after pyloric ligation in male albino rats.

Vertical lines denote the standard deviation of mean.

B. In Vitro Experiments:

Experiments on isolated rat fundic strip:

1. Effect on potassium chloride-induced contraction:

Verapamil (in a dose of 100 ng/ml) added on top of potassium chloride-induced contraction (4 mg/ml) of the isolated rat fundic strip produced inhibition of the contraction (Fig. 11). Verapamil (in a dose of 100 ng/ml) produced decrease in the amplitude of contraction of the isolated rat fundic strip when incubated for 15 seconds (Fig. 12).

2. Effect on histamine-induced contraction:

Verapamil (in a dose of 100 ng/ml) added on top of histamine-induced contraction (300 ug/ml) of the isolated rat fundic strip produced inhibition of the contraction (Fig. 13).

Verapamil (in a dose of 100 ng/ml) produced decrease in the amplitude of contraction of the isolated rat fundic strip when incubated for 15 seconds (Fig. 14).

3. Effect on acetylcholine contraction:

Verapamil (in a dose of 100 ng/ml) added on top of acetylcholine-induced contraction (200 ng/ml) of the isolated rat fundic strip produced inhibition of the contraction (Fig. 15).

Verapamil (in a dose of 100 ng/ml) produced decrease in the amplitude of contraction of the isolated rat fundic strip when incubated for 15 second (Fig. 16).

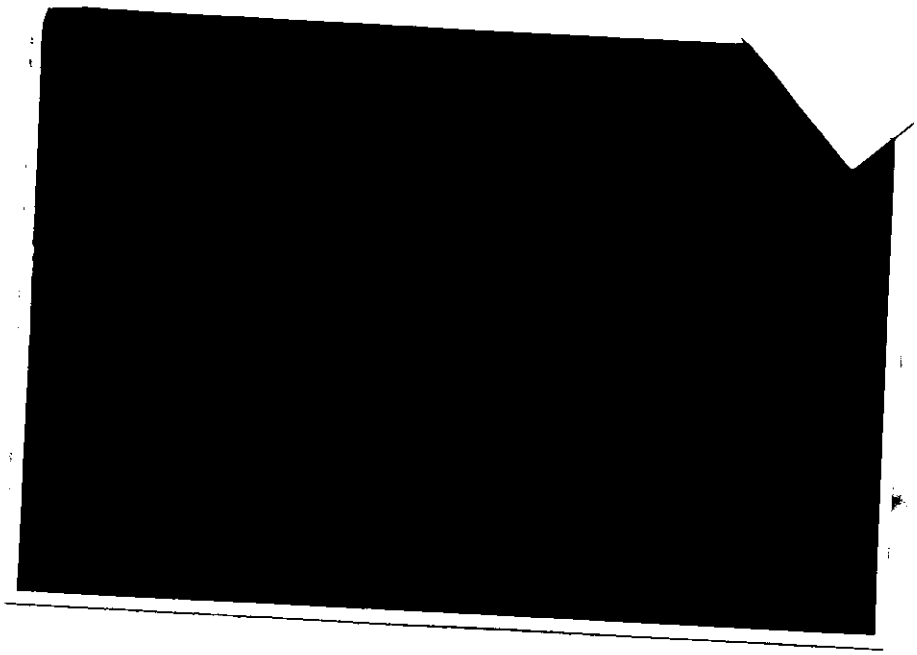

Fig. (11): A record showing the effect of verapamil in a dose of 100 nanogram/ml added on top of potassium chloride-induced contraction on the isolated rat fundic strip.

VER = verapamil.
KCl = potassium chloride.
Dose of potassium chloride is 4 mg/ml.

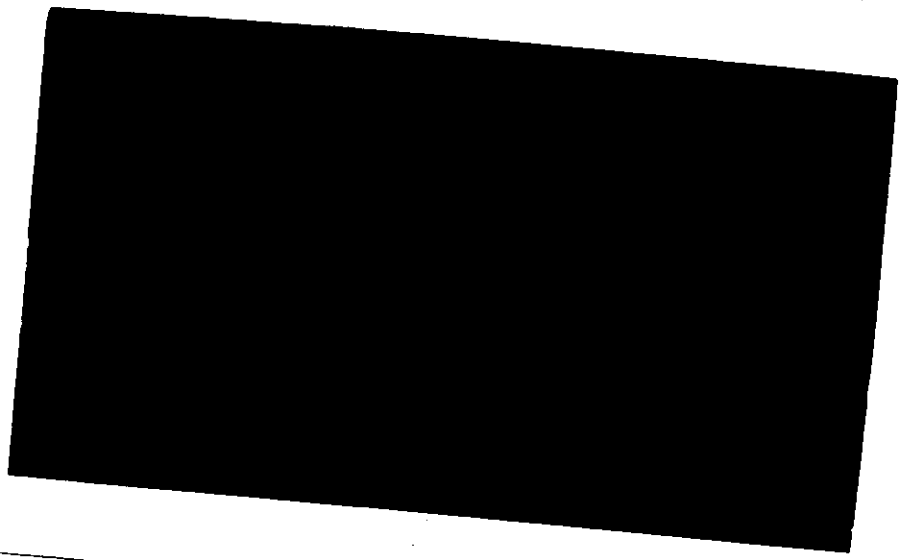

Fig. (12): A record showing the effect of incubation of verapamil in a dose of 100 nanogram/ml for 15 seconds on potassium chloride-induced contraction of the isolated rat fundic strip.

W = wash.
L = load.
VER = verapamil.
KCl = potassium chloride.
Dose of KCl is 4 mg/ml.

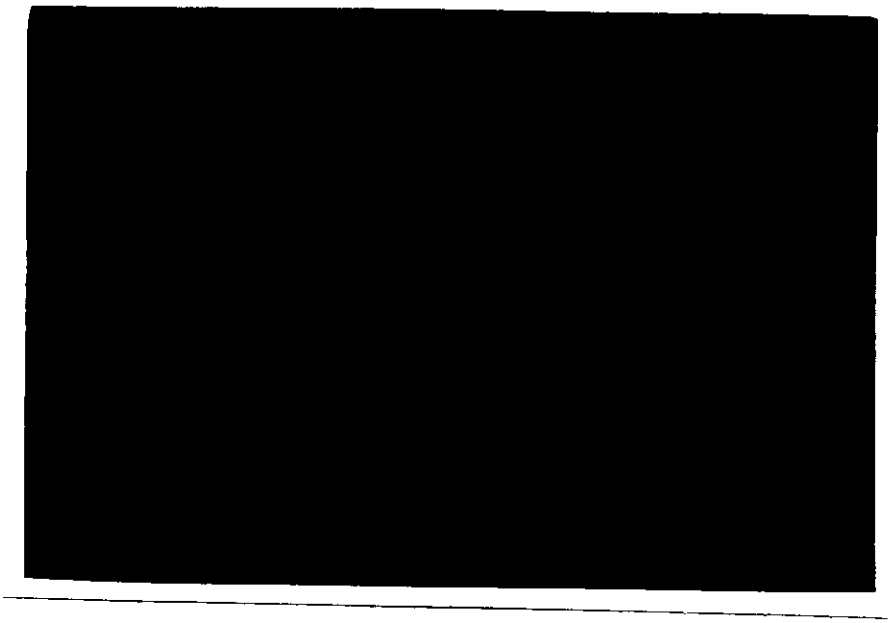

Fig. (13): A record showing the effect of verapamil in a dose of 100 nanogram/ml added on top of histamine-induced contraction of the isolated rat fundic strip.

VER = verapamil.
HIS = histamine.
Dose of histamine is 300 microgram/ml.

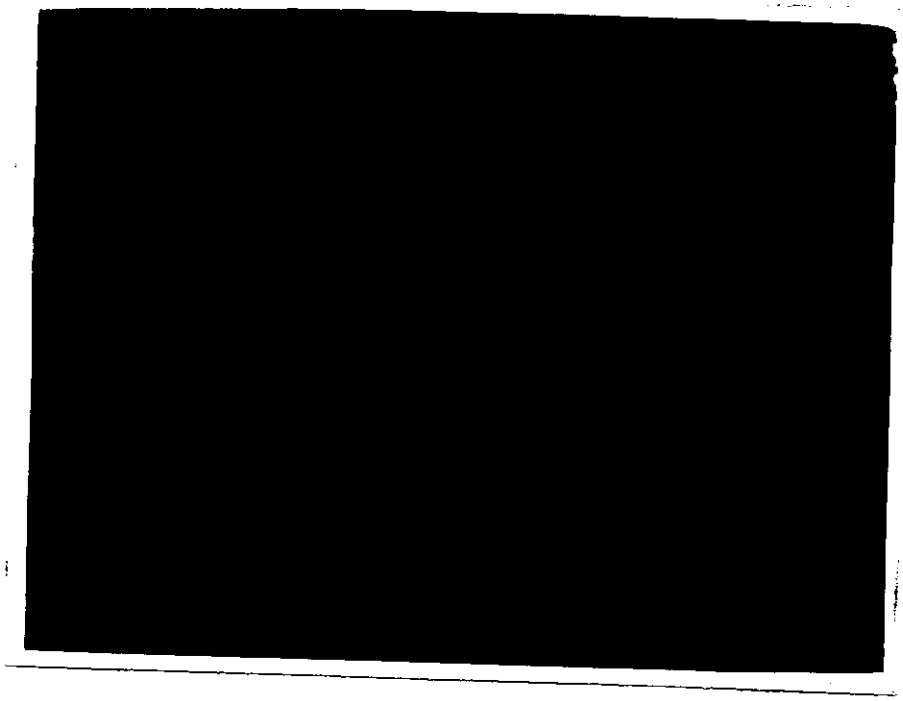

Fig. (14): A record showing the effect of incubation of verapamil in a dose of 100 nanogram/ml for 15 seconds on histamine-induced contraction of the isolated rat fundic strip.

W = wash.
L = load.
VER = verapamil.
HIS = histamine.
Dose of histamine is 300 microgram/ml.

Fig. (15): A record showing the effect of verapamil in a dose of 100 nanogram/ml added on top of acetylcholine-induced contraction of isolated rat fundic strip.

VER = verapamil.
ACh = acetylcholine.
Dose of acetylcholine is 200 nanogram/ml.

Fig. (16): A record showing the effect of incubation of verapamil in a dose of 100 nanogram/ml for 15 seconds on acetylcholine-induced contraction of the isolated rat fundic strip.

W = wash.
L = load.
VER = verapamil.
Ach = acetylcholine.
Dose of acetylcholine is 200 nanogram/ml.