Results

RESULTS

I. IN-VITRO EXPERIMENTS:

•Effect and site of action of risperidone on isolated rabbit's heart:

It was observed that risperidone in doses of 2, 4, and 8μg/mL produced a statistically non-significant decrease of the amplitude of contraction of the isolated rabbit's heart. While addition of risperidone in a dose of 16μg/mL produced a statistically significant ($P<0.05$) decrease of the amplitude of contraction. Moreover, it was observed that a dose of 32μg/mL produced also a statistically highly significant ($P<0.01$) decrease of the amplitude of contraction (Fig. 7, 10) (Tab. 1).

The percentages of this reduction in the amplitude of contraction were 12.24%, 18.37%, 24.49%, 42.86%, and 63.27% for the doses of 2, 4, 8, 16, and 32μg/mL respectively.

It was found that addition of atropine in a dose of 4μg/mL to the isolated rabbit's heart preparation did not abolish the negative inotropic effect of risperidone (in a dose of 32μg/mL) (Fig. 11).

It was also observed that nicotine large dose (NLD) in a dose of 0.1μg/mL did not also abolish the effect of risperidone (in a dose of 32μg/mL) on the isolated rabbit's heart (Fig.12).

•Effect of methanol on the isolated rabbit's heart:

Addition of methanol in different equivalent concentration levels of 0.2, 0.4, 0.8, 1.6, and 3.2mL of methanol 0.08% produced no change of the amplitude of contraction of the isolated rabbit's heart (Fig. 8).

•Effect and site of action of haloperidol on isolated rabbit's heart:

It was observed that addition of haloperidol in a dose of 2μg/mL produced a statistically significant ($p<0.05$) reduction of the amplitude of contraction of the isolated rabbit's heart, while the drug in doses of 4 &8μg/mL produced a statistically highly significant ($p<0.01$) reduction of contraction. Doses of 16 and 32μg/mL produced a statistically very highly significant ($P<0.001$) decrease of the amplitude of contraction of the isolated rabbit's heart (Fig. 7, 13) (Tab.1).

The percentages of that reduction were 51.85%, 68.52%, 75.93%, 94.44% and 98.15% for the doses of 2, 4, 8, 16 and 32μg/mL respectively.

It was found that addition of haloperidol in a dose of 32μg/mL produced a reduction of the contractility of the isolated heart, which was not affected by the addition of atropine in a dose of 4μg/mL (Fig.14).

The Negative inotropic effect of haloperidol in the dose of 32μg/mL was not also affected by addition of nicotine large dose (NLD) in a dose of 0.1μg/mL (Fig. 15).

•Effect of lactic acid on isolated rabbit's heart:

It was observed that addition of lactic acid in different equivalent concentration levels of 0.2, 0.4, 0.8, 1.6, and 3.2mL of lactic acid 0.009% produced no effect on the isolated heart preparation (Fig. 9).

Table (1): Effects of risperidone and haloperidol on mean ± SE of amplitude of contraction {cm} of isolated rabbit's heart.

Drug \ Dose	control	2 µg	4 µg	8 µg	16 µg	32 µg
Risperidone	4.9±0.52	4.3±0.41 p1>0.05	4±0.35 p1>0.05	3.7±0.44 p1>0.05	*2.8±0.47 p1<0.05	**1.8±0.3 p1<0.01
Haloperidol	5.4±0.73	*2.6±0.72 p2<0.05	**1.7±0.81 p2<0.01	**1.3±0.82 p2<0.01	***0.3±0.71 p2<0.001	***0.1±0. p2<0.001

P1 Compares mean ± SE of amplitude of ventricular contractility {cm} after addition of risperidone with that of control.

P2 Compares mean ± SE of amplitude of ventricular contractility {cm} after addition of haloperidol with that of the control.

N. B.
Control: normal contractions of isolated heart.
* Significant ($p<0.05$).
** Highly significant ($p<0.01$).
*** Very highly significant ($p<0.001$).

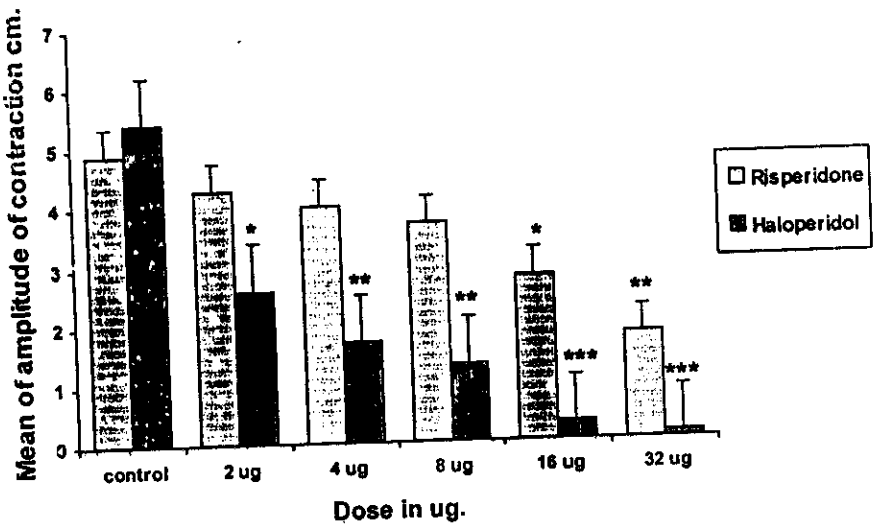


Fig. (7): A histogram showing the effects of risperidone and haloperidol on isolated rabbit's heart.

N.B. **control:** normal contractions of the isolated heart.

* Significant ($p<0.05$) compared to control.

** Highly Significant ($p<0.01$) compared to control.

*** Very highly Significant ($p<0.001$) compared to control.

Vertical lines represent SE of mean.

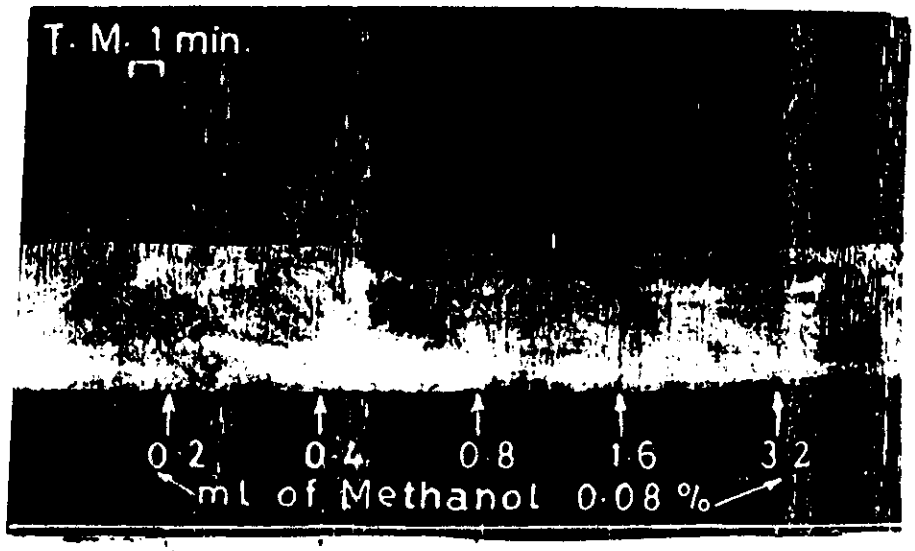


Fig. (8): A record showing the effect of methanol on isolated rabbit's heart.

Addition of methanol 0.08% in different equivalent concentration levels of 0.2, 0.4, 0.8, 1.6, and 3.2mL produced no effect on the isolated rabbit's heart.

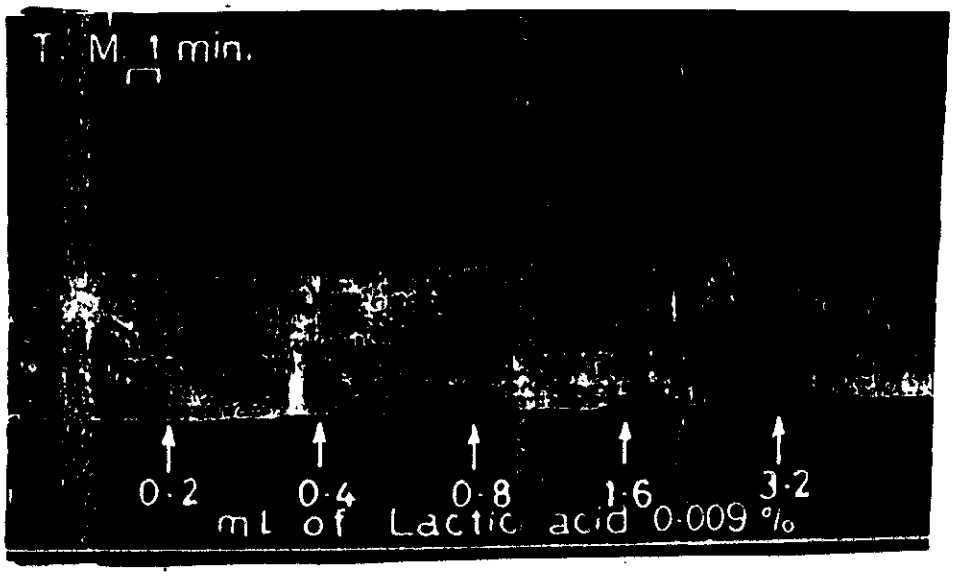


Fig. (9): A record showing the effect of lactic acid on the isolated rabbit's heart.

Addition of lactic acid 0.009% in different equivalent concentration levels of 0.2, 0.4, 0.8, 1.6, and 3.2mL produced no effect on the isolated rabbit's heart.

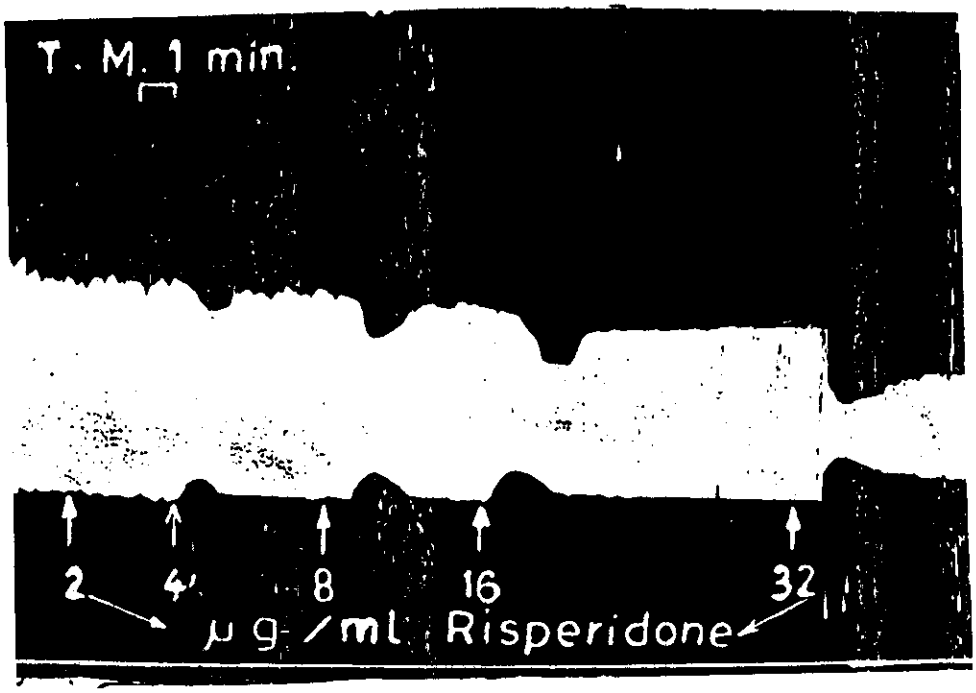


Fig. (10): A record showing the effect of different doses of risperidone on the amplitude of contraction of the isolated rabbit's heart.

Addition of risperidone in gradually increasing doses (2, 4, 8, 16, and 32 μg/mL) to isolated rabbit's heart produced a statistically non-significant decrease of amplitude of contraction in doses of 2, 4, and 8μg/mL, a statistically significant ($p<0.05$) decrease in a dose of 16μg/mL, and a statistically highly significant ($p<0.01$) decrease in a dose of 32μg/mL.

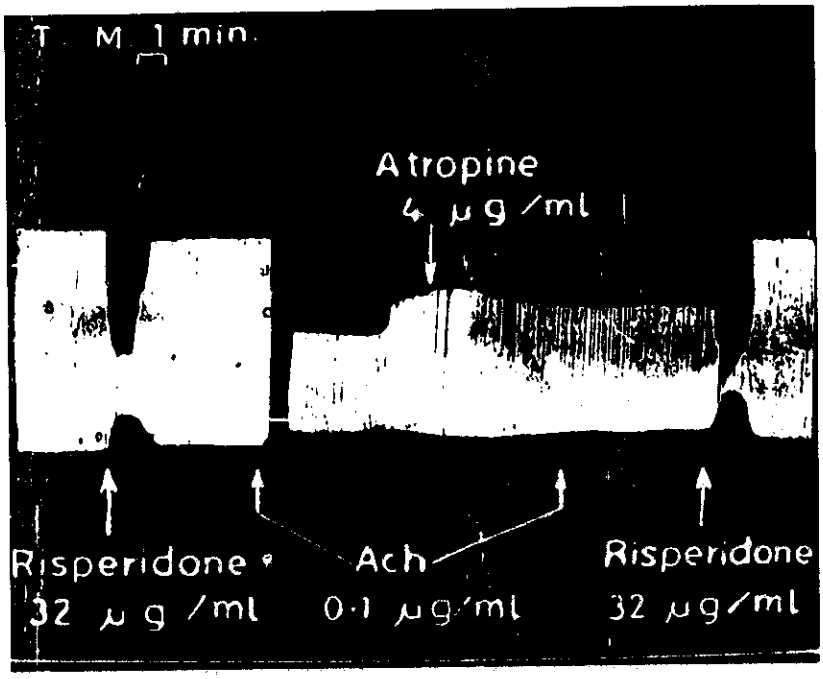


Fig. (11): A record showing the interaction of risperidone and atropine in the isolated rabbit's heart.

Addition of atropine in a dose of 4µg/mL to isolated rabbit's heart did not affect risperidone-induced reduction of amplitude of contraction.

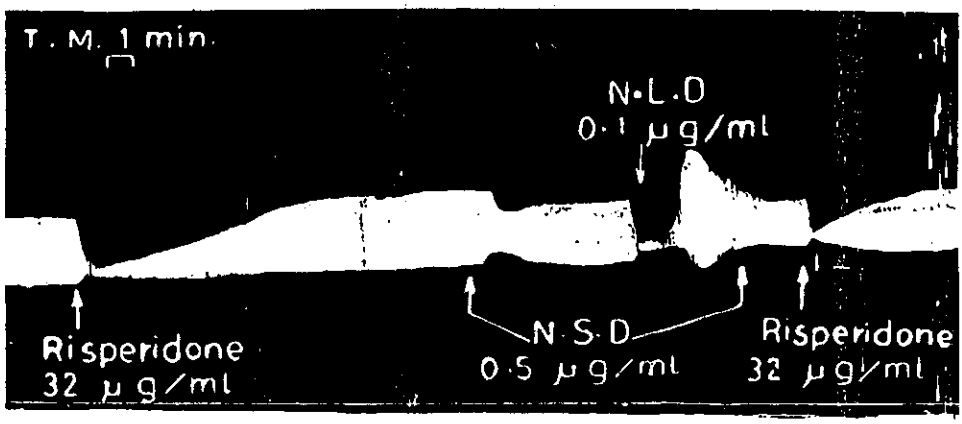


Fig. (12): A record showing the interaction of risperidone and NLD in isolated rabbit's heart.

Addition of NLD in a dose of 0.1µg/mL to isolated rabbit's heart did not affect risperidone-induced reduction of amplitude of contraction.

N.B. NLD: nicotine large dose.

Fig.(13) : A record showing the effect of different doses of haloperidol on amplitude of contraction of isolated rabbit's heart.

Addition of haloperidol in gradually increasing doses (2, 4, 8, 16, and 32μg/mL) to isolated rabbit's heart produced a statistically significant ($p<0.05$) reduction of amplitude of contraction in a dose of 2μg/mL, a statistically highly significant ($p<0.01$) reduction in doses of 4 & 8μg/mL, and a statistically very highly significant ($p<0.001$) reduction in doses of 16 &32μg/mL.

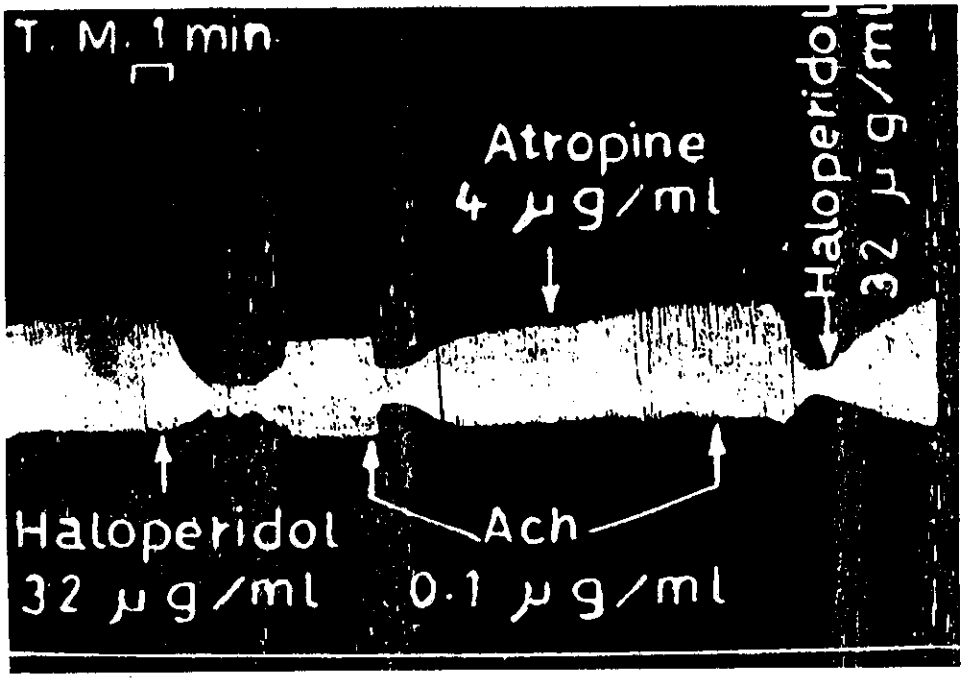


Fig. (14): A record showing the interaction between haloperidol and atropine in the isolated rabbit heart.

Addition of atropine in a dose of 4µg/mL to isolated rabbit's heart did not block haloperidol-induced reduction of amplitude of contraction.

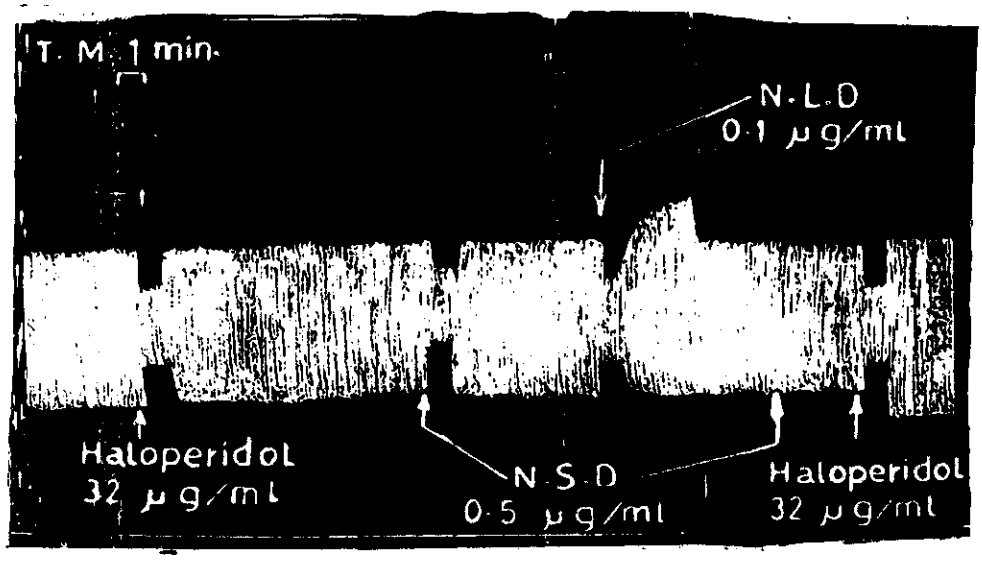


Fig. (15): A record showing the interaction between haloperidol and NLD in the isolated rabbit's heart.

Addition of NLD in a dose of 0.1µg/mL to isolated rabbit's heart did not block haloperidol-induced reduction of amplitude of contraction.

N.B. NLD: nicotine large dose.

•Effect and site of action of risperidone on the isolated rabbit's aortic strip:

It was observed that preincubation of risperidone in doses of (2 & 4μg/mL) for 5 minutes before addition of norepinephrine in a dose of 5μg/mL produced a statistically non-significant reduction of the norepinphrine-induced contractile response of the rabbit' aortic strip. The percentages of this reduction were 24.44% and 26.67% for the doses of 2 and 4μg/mL respectively (Fig. 16, 19) (Tab. 2).

It was also found that preincubation of the drug in doses of 8 &16μg/mL produced a statistically significant ($p<0.05$) decrease of norepinephrine-induced contractile response of the isolated aorta (Fig. 16, 19) (Tab. 2).The percentages of this reduction were 55.56% and 66.67% respectively.

Preincubation of risperidone in a dose of 32μg/mL also produced a statistically highly significant ($p<0.01$) reduction of norepinephrine-induced contractile response of the isolated aorta (Fig. 16, 19) (Tab. 2), and the percentage of this reduction was 80%.

Preincubation of risperidone in gradually increasing doses of 2, 4, 8, 16, and 32μg/mL for 2 minutes before addition of serotonin in a dose of 3μg/mL produced also a reduction of serotonin-induced contractile response of the isolated rabbit's aortic strip (Fig. 20).

It was found that the preincubation of risperidone in gradually increasing doses of 2, 4, 8, 16, and 32μg/mL for 2 minutes before the addition of angiotensin in a dose of 2μg/mL did not produce any change of

the angiotensin-induced contractile response of the isolated aortic strip (Fig. 21).

•Effect of methanol on isolated rabbit's aortic strip:

Preincubation of methanol 0.08% for 2 minutes in different equivalent concentration levels of 0.2, 0.4, 0.8, 1.6, and 3.2mL, was detected to produce no change in the norepinephrine-induced contractile response of isolated rabbit's aortic strip (Fig. 17).

•Effect and site of action of haloperidol on isolated rabbit's aortic strip:

It was found that preincubation of gradually increasing doses of haloperidol (2,4,8,16μg/mL) for 5 minutes before the addition of norepinephrine in a dose of 5μg/mL produced a statistically non-significant decrease of norepinephrine-induced contractile response of the isolated rabbit aortic strip (Fig. 16, 22) (Tab. 2).

The percentages of this decrease were 6.98%, 9.3%, 30.24%, and 41.86% for the doses of 2, 4, 8 and 16μg/mL respectively.

While the preincubation of haloperidol in a dose of 32μg/mL for 5 minutes before the addition of norepinephrine in a dose of 5μg/mL produced a statistically significant ($p<0.05$) reduction of the norepinephrine-induced contractile response of the isolated aorta (Fig. 16, 22) (Tab. 2), and the percentage of this reduction was 53.49%.

It was also observed that preincubation of gradually increasing doses of haloperidol (2, 4, 8, 16, and 32μg/mL) for 2 minutes before addition of

serotonin in a dose of 3μg/mL produced a reduction of serotonin-induced contractile response of the isolated aortic preparation (Fig. 23).

On the other hand, it was oserved that preincubation of gradually increasing doses of haloperidol (2, 4, 8, 16, and 32μg/mL) for 2 minutes before the addition of angiotensin in a dose of 2μg/mL did not affect the angiotensin-induced contractile response of the isolated aortic strip (Fig. 24).

•Effect of lactic acid on isolated rabbit's aortic strip:

It was observed that preincubation of lactic acid 0.009% in different equivalent concentration levels of 0.2, 0.4, 0.8, 1.6, and 3.2mL produced no change in the norepinephrine-induced contractile response of the isolated rabbit's aortic strip (Fig. 18).

Table (2): Effects of risperidone and haloperidol on mean ± SE of of amplitude of contraction {cm} of isolated rabbit's aortic strip.

Dose / Drug	Control	2µg	4µg	8µg	16µg	32µg
Risperidone	4.5±0.61	3.4±0.61 p1>0.05	3.3±0.54 p1>0.05	*2±0.63 p1<0.05	*1.5±0.52 p1<0.05	**0.9±0.64 p1<0.01
Haloperidol	4.3±0.41	4±0.32 p2>0.05	3.9±0.53 p2>0.05	3±0.22 p2>0.05	2.5±0.33 p2>0.05	*2±0.43 p2>0.05

P1: Compares the amplitude of contraction of isolated aorta after addition of risperidone with that of control.

P2: Compares the amplitude of contraction of isolated aorta after addition of haloperidol with that of control.

N. B. Control: norepinephrine-induced contraction.

* Significant ($p<0.05$).

** Highly significant ($p<0.01$).

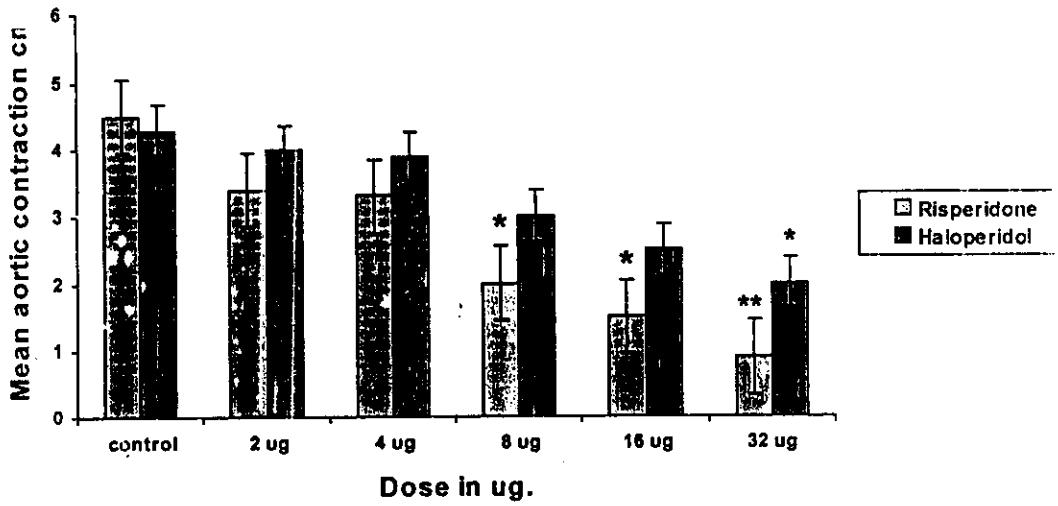


Fig. (16): A histogram showing the effects of risperidone and haloperidol on norepinephrine-induced aortic strip contraction.

N.B. **Control:** norepinephrine-induced contraction.

* Significant ($p<0.05$) compared to control value.

** Highly significant ($p<0.01$) compared to control value.

Vertical lines represent SE of mean.

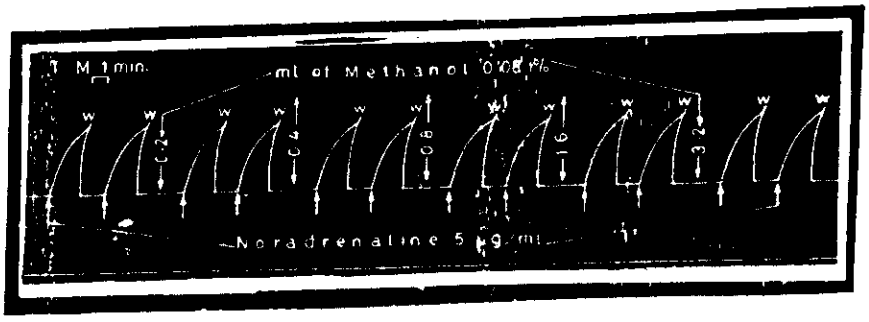


Fig. (17): A record showing the effect of methanol on NE-induced contraction of isolated rabbit's aortic strip.

Preincubation of methanol 0.08% for 2 min. in different equivalent concentration levels of 0.2, 0.4, 0.8, 1.6, and 3.2mL produced no change in NE-induced contractile response of isolated aorta.

N. B. NE: Norepinephrine.

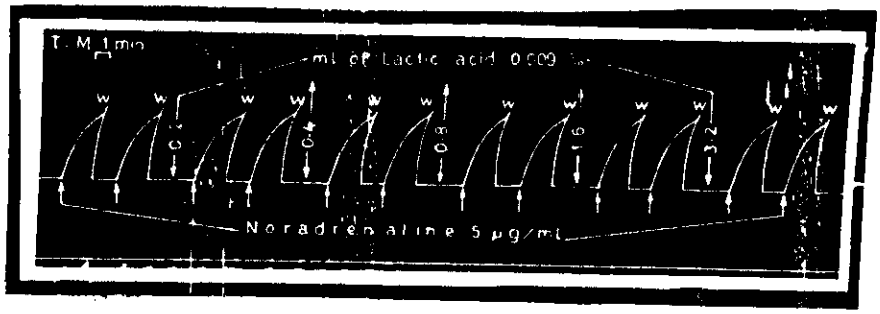


Fig. (18): A record showing the effect of lactic acid on NE-induced contraction of isolated rabbit's aortic strip.

Preincubation of lactic acid 0.009% in different equivalent concentration levels of 0.2, 0.4, 0.8, 1.6, and 3.2mL produced no change in NE-induced contractile response isolated aorta.

N.B. NE: norepinephrine.

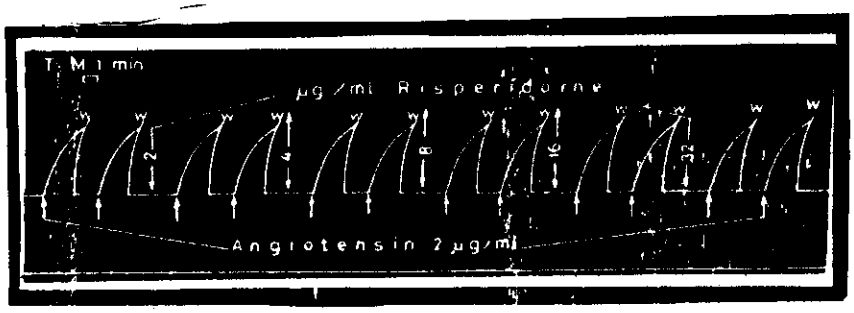


Fig. (21): A record showing the effect of risperidone on angiotensin-induced contractile response of isolated rabbit's aortic strip.

Preincubation of risperidone in gradually increasing doses of (2, 4, 8, 16, and 32μg/mL) for 2 min. before addition of angiotensin in a dose of 2μg/mL did not produced any change of angiotensin-induced contractile response of isolated aorta.

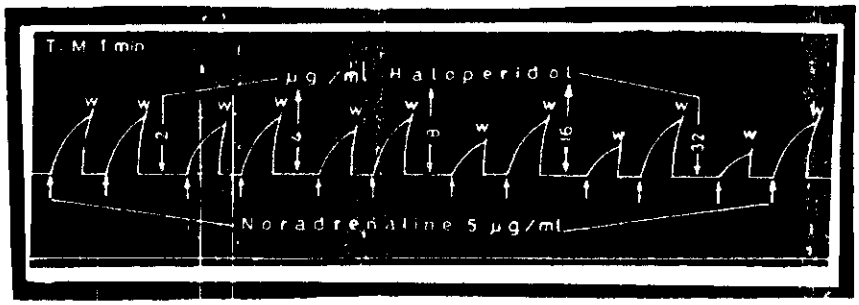


Fig. (22): A record showing the effect of haloperidol on NE-induced contractile response of isolated rabbit's aortic strip.

Preincubation of gradually increasing doses of haloperidol (2, 4, 8, and 16µg/mL) for 5 min. before addition of NE in a dose of 5µg/mL produced a statistically non-significant reduction of NE-induced contractile response of isolated aorta, and preincubation of haloperidol in a dose of 32µg/mL produced a statistically significant ($p<0.05$) reduction of NE-induced contractile response of isolated aorta.

N.B. NE: norepinephrine.

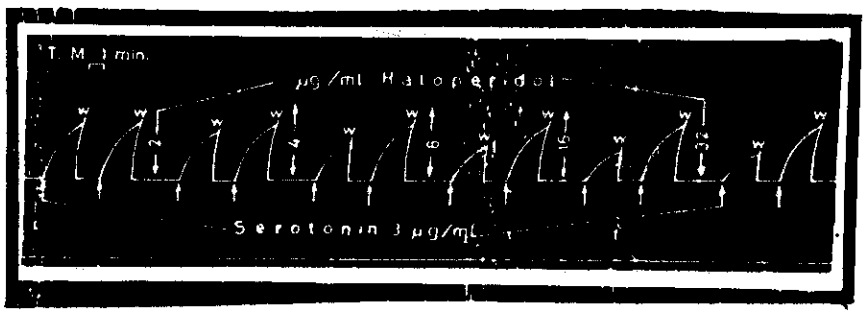


Fig. (23): A record showing the effect of haloperidol on the 5HT-induced contractile response of isolated rabbit's aortic strip.

Preincubation of gradually increasing doses of haloperidol (2, 4, 8, 16, and 32µ/mL) for 2 min. before addition of serotonin in a dose of 3µg/mL produced a reduction of serotonin-induced contractile response of isolated aorta.

N.B. 5-HT: serotonin.

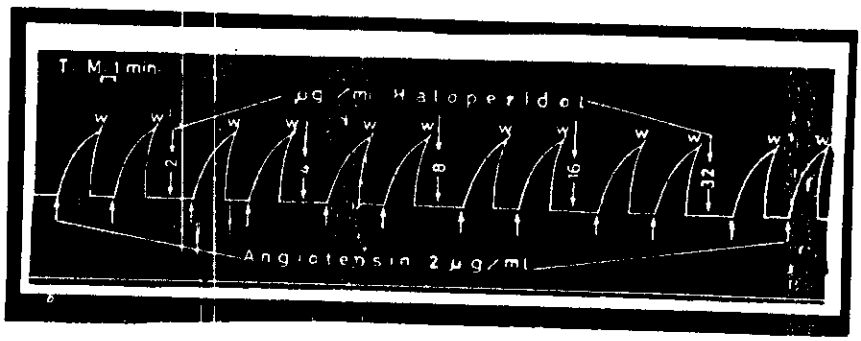


Fig. (24): A record showing the effect of haloperidol on angiotensin-induced contractile response of isolated rabbit's aortic strip.

Preincubation of gradually increasing doses of haloperidol (2, 4, 8, 16, and 32µg/mL) for 2 min. before addition of angiotensin in a dose of 2µg/mL did not affect angiotensin-induced contractile response of isolated aorta.

•Effect and site of action of risperidone on isolated rabbit's jejunum:

Addition of risperidone to isolated rabbit's jejunum preparation in a dose of 2μg/mL produced a statistically significant ($p<0.05$) increase of the amplitude of contractions of the isolated rabbit jejunum (Fig. 25, 28) Tab. 3).The percentage of that increase was 14.29%.

It was also observed that risperidone in a dose of 4μg/mL produced a statistically highly significant ($p<0.01$) increase of the amplitude of contractions of the isolated jejunum and the percentage of this increase was 28.57% (Fig. 25, 28) (Tab. 3).

The drug in doses of 8 and 16μg/mL produced a statistically very highly significant ($p<0.001$) increase of the amplitude of contractions.The percentages of this increase were 42.86% and 57.14% for the doses of 8 and 16μg/mL respectively (Fig.25, 28) (Tab. 3).

It was also observed that addition of risperidone in a dose of 8μg/mL produced an increase of the amplitude of contractions of the isolated rabbit jejunum, which was not abolished by the addition of atropine in a dose of 4μg/mL (Fig. 29). Meanwhile, the addition of nicotine large dose (NLD) in a dose of 1μg/mL did not also abolish the effect of risperidone (Fig. 30).

The effect of risperidone on the amplitude of contraction of the isolated jejunum was not also affected by the addition of phenramine in a dose of 10μg/mL (Fig. 31).

While the addition of cyproheptadine in a dose of 5μg/mL abolished the effect of risperidone on the isolated jejunum when added in a dose of 8μg/mL (Fig. 32).

•Effect of methanol on the isolated rabbit's jejunum:

It was observed that addition of methanol in different equivalent concentration levels of 0.2, 0.4, 0.8, 1.6 and 3.2mL of 0.08% of methanol produced no change in the amplitude of contractions of the isolated jejunum preparation (Fig. 26).

•Effect and site of action of haloperidol on isolated rabbit's jejunum:

Haloperidol was added in different concentration levels of 2, 4, 8 and 16 and 32μg/mL to the isolated jejunum preparation. It was observed that the drug in doses of 2 and 4μg/mL produced a statistically non-significant increase of the amplitude of contractions of the isolated jejunum (Fig. 25, 33) (Tab. 3). The percentages of this increase are 13.15% and 27.57% for the doses of 2 and 4μg respectively.

Addition of the drug in a dose of 8μg/mL produced a statistically significant ($p<0.05$) increase of the amplitude of contractions of the isolated jejunum (Fig. 25, 33) (Tab. 3), and the percentage of this increase was 39.39%.

When haloperidol added in a dose of 16μg/mL, it produced a statistically significant ($p<0.01$) increase of the amplitude of contractions of

the isolated jejunum which was by percentage of 48.5% (Fig. 25, 33) (Tab. 3).

Addition of haloperidol in a dose of 8µg/mL produced an increase of the amplitude of contractions of the isolated jejunum which was not abolished by the addition of atropine in a dose of 4µg/mL nor by nicotine large dose (NLD) in a dose of 1µg/mL (Fig. 34, 35).

The addition of phenramine in a dose of 10µg/mL also did not affect the contractile response of the isolated jejunum (Fig. 36). While the addition of cyproheptadine in a dose of 5µg/mL abolished the effect of naloperidol on the isolated jejunum preparation (Fig. 37).

•Effect of lactic acid on the isolated rabbit's jejunum:

Addition of lactic acid in different equivalent concentration levels of 0.2, 0.4, 0.8, 1.6 and3.2mL of 0.009% lactic acid produced no change in the amplitude of contractions of the isolated rabbit jejunum (Fig. 27)

Table (3): Effects of risperidone and haloperidol on mean ± SE of amplitude of contraction {cm} of isolated rabbit's jejunum.

Dose / Drug	Control	2µg	4µg	8µg	16µg
Risperidone	3.5±0.31	*4±0.43 p1<0.05	**4.5±0.33 p1<0.01	***5±0.51 p1<0.001	***5.5±0.51 p1<0.001
Haloperidol	3.3±0.02	3.8±0.21 p2>0.05	4.2±0.24 p2>0.05	*4.6±0.32 p2<0.05	**4.9±0.25 p2<0.01

P1 Compares mean ± SE of amplitude of contraction of isolated jejunum after addition of risperidone with that of control.

P2 Compares mean ± SE of amplitude of contraction of isolated jejunum after addition of haloperidol with that of control.

N. B. Control: amplitude of normal contractions.
* Significant ($p<0.05$).
** Highly significant ($p<0.01$).
*** Very highly significant ($p<0.001$).

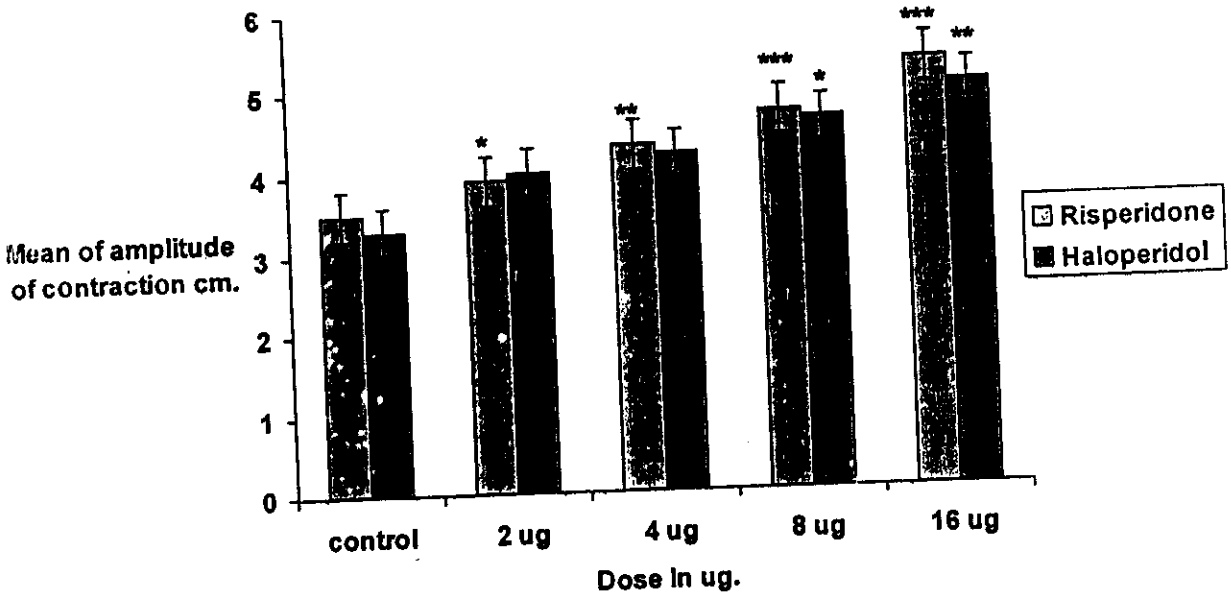


Fig.(25): A histogram showing effects of risperidone and haloperidol on the mean of the amplitude of contraction of isolated rabbit's jejunum.

N.B. **control**: amplitude of normal contraction.

* Significant ($p<0.05$) compared to control.
** Highly Significant ($p<0.01$) compared to control.
*** Very highly Significant ($p<0.001$) compared to control.
Vertical lines represent standard error of mean.

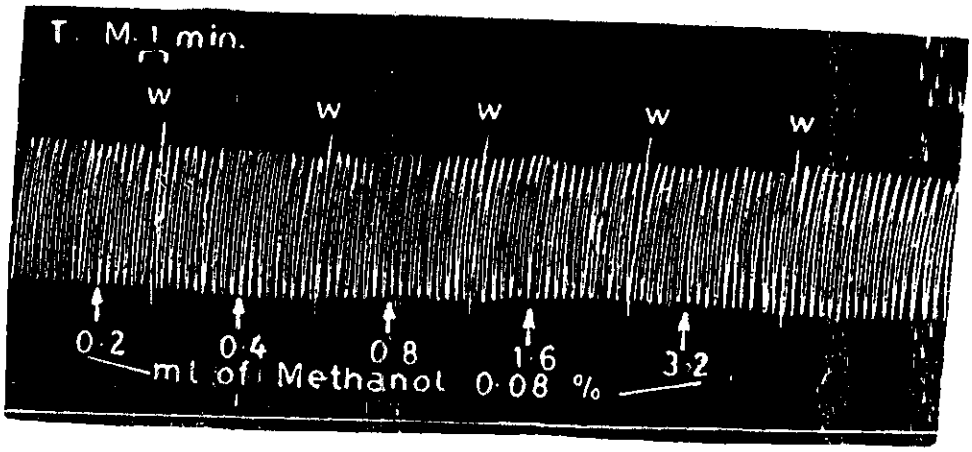


Fig. (26): A record showing the effect of methanol on isolated rabbit's jejunum.

Addition of methanol 0.08% in different equivalent concentration levels of (0.2, 0.4, 0.8, 1.6, and 3.2mL/mL) produced no change in amplitude of contraction of isolated rabbit's jejunum.

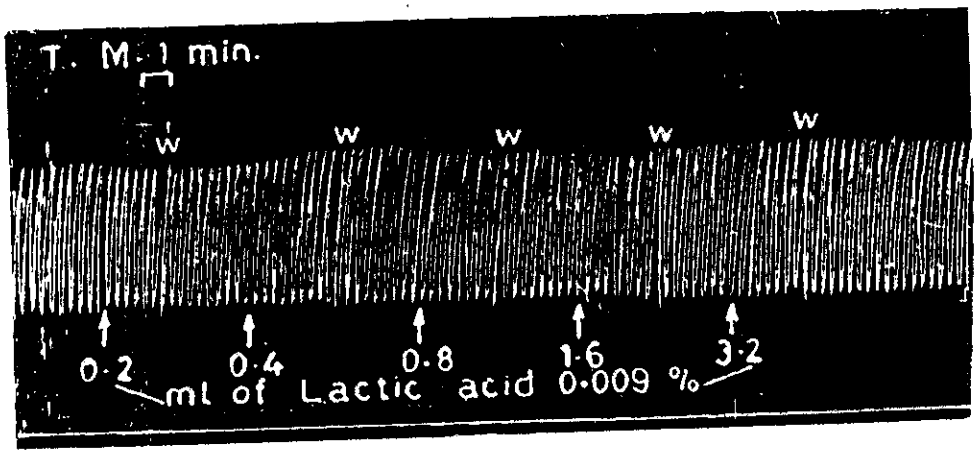


Fig. (27): A record showing the effect of lactic acid on isolated rabbit's jejunum.

Addition of lactic acid 0.009% in different equivalent concentration levels of (0.2, 0.4, 0.8, 1.6, and 3.2mL) produced no change in the amplitude of contraction of isolated rabbit's jejunum.

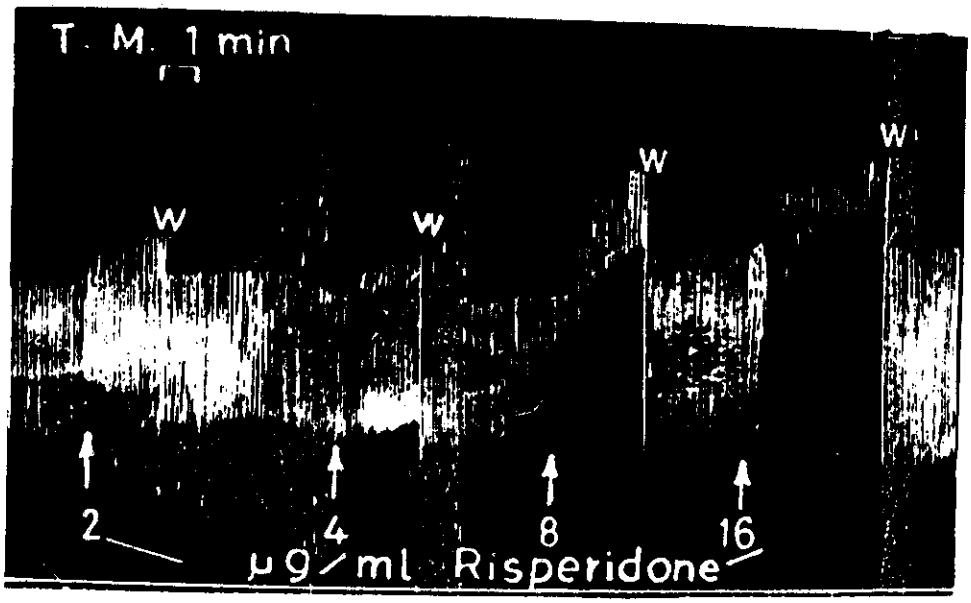


Fig. (28): **A record showing the effect of different doses of risperidone on the amplitude of contraction of isolated rabbit's jejunum.**

Addition of risperidone in a dose of 2µg/mL produced a statistically significant ($p<0.05$) increase of amplitude of contraction of isolated rabbit's jejunum, risperidone in a dose of 4µg/mL produced a statistically highly significant ($p<0.01$) increase of amplitude of contraction, the drug in doses of 8 & 16µg/mL produced a statistically very highly significant ($p<0.001$) increase of amplitude of contraction.

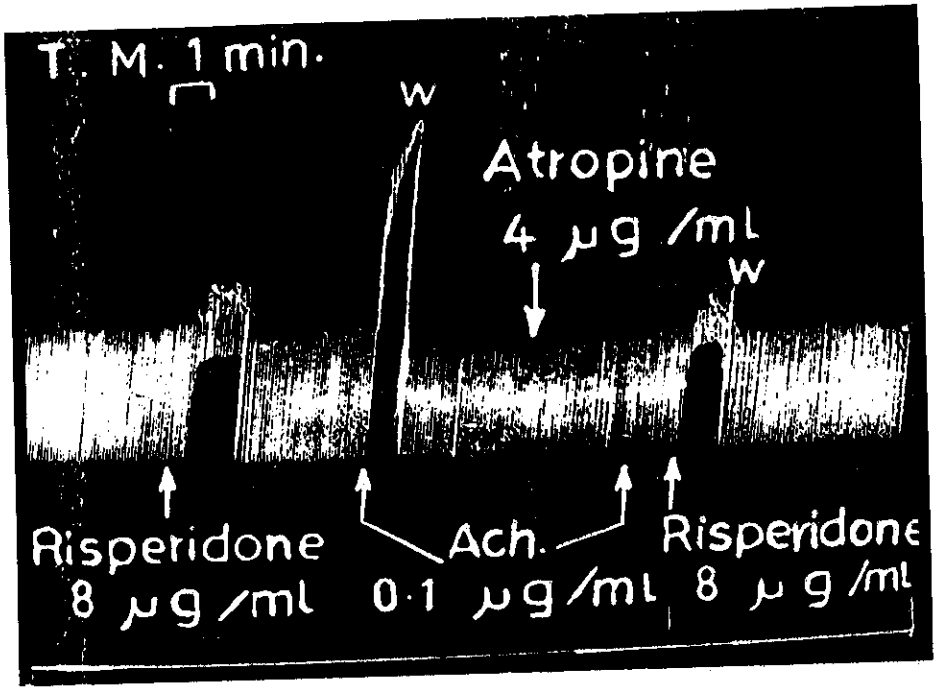


Fig. (29): A record showing the interaction between risperidone and atropine in the isolated rabbit's jejunum.

Addition of atropine in a dose of 4µg/mL did not abolish risperidone-induced increase of amplitude of contraction of isolated rabbit's jejunum.

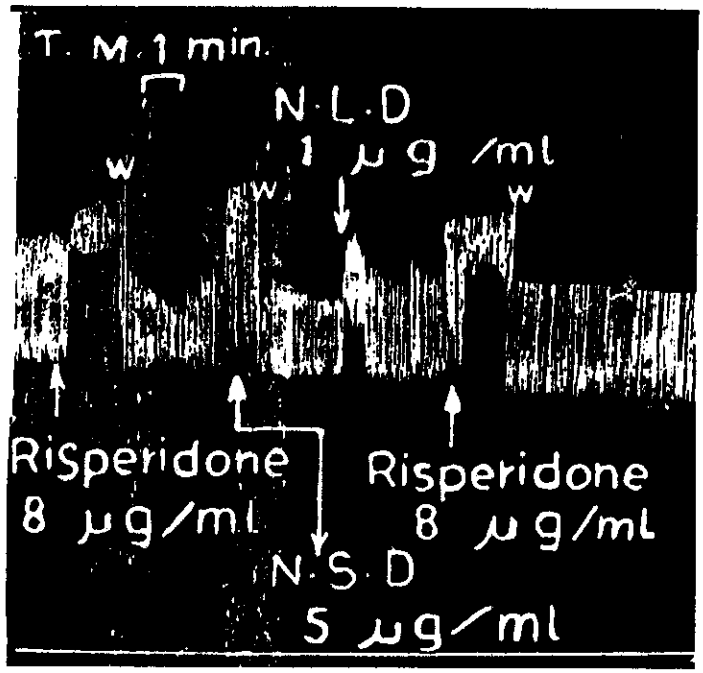


Fig. (30): A record showing the interaction between risperidone and NLD in the isolated rabbit's jejunum.

Addition of NLD in a dose of 1µg/mL did not abolish risperidone-induced increase of amplitude of contraction of isolated rabbit's jejunum.

N.B. NLD: nicotine large dose.

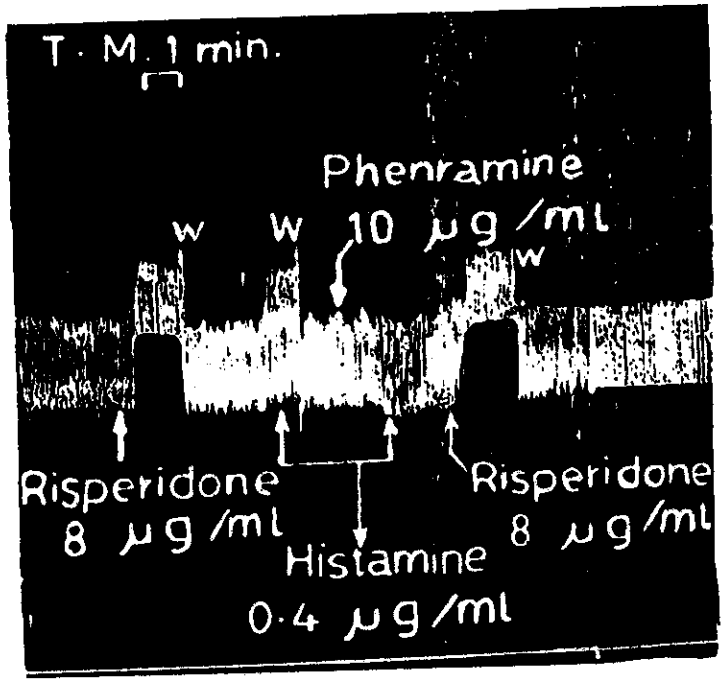


Fig. (31): A record showing the interaction between risperidone and phenramine in the isolated rabbit's jejunum.

Addition of phenramine in a dose of 10µg/mL did not affect risperidone-induced increase of amplitude of contraction of isolated rabbit's jejunum.

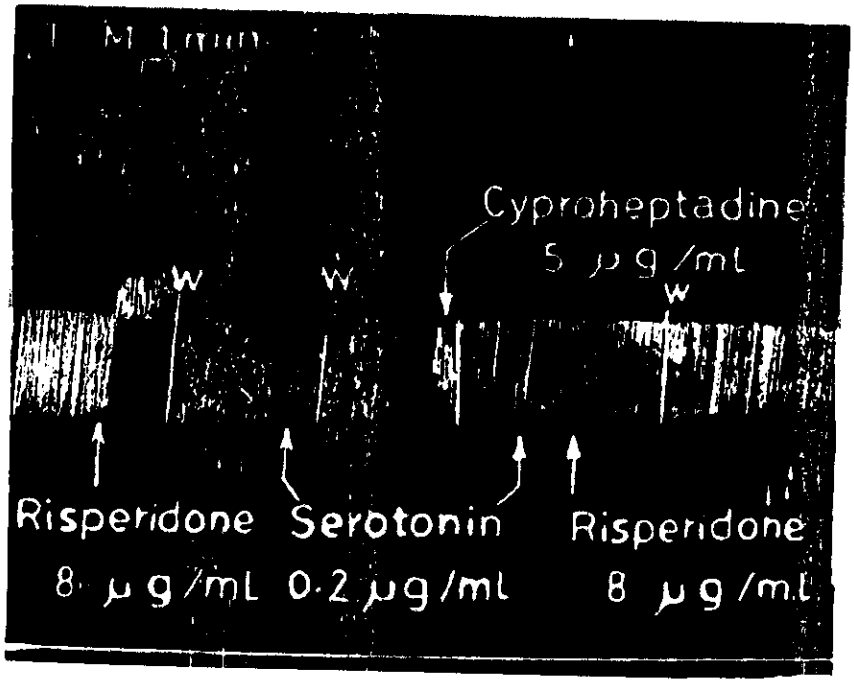


Fig. (32): A record showing the interaction between risperidone and cyproheptadine in the isolated rabbit's jejunum.

Addition of cyproheptadine in a dose of 5µg/mL abolished the risperidone-induced increase of amplitude of contraction of isolated rabbit's jejunum.

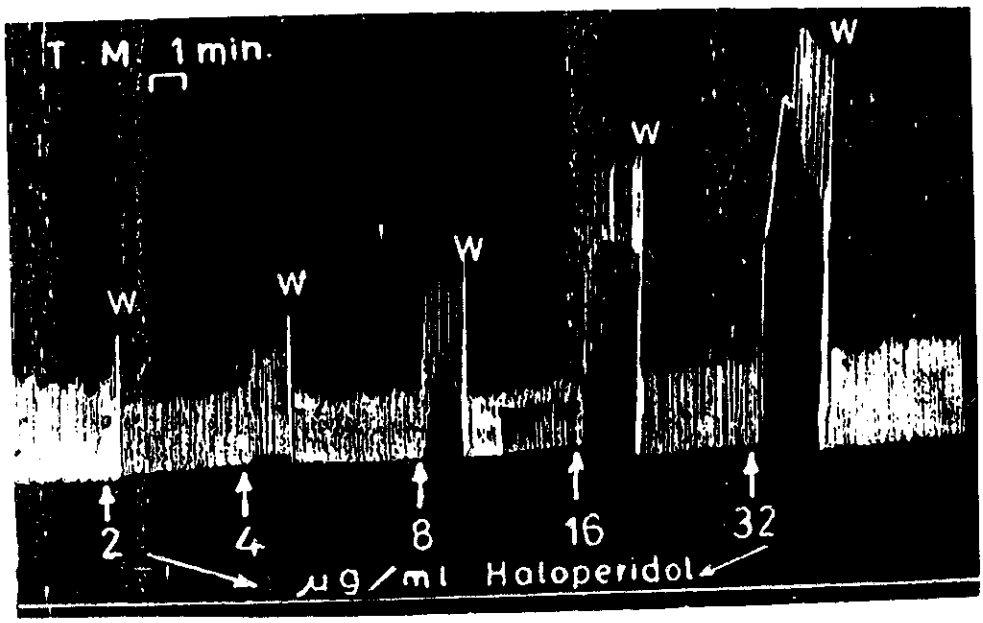


Fig. (33): A record showing the effect of different doses of haloperidol on the amplitude of contraction of isolated rabbit's jejunum.

Addition of haloperidol in doses of 2 &4µg/mL produced a statistically non-significant increase of amplitude of contraction of isolated jejunum, haloperidol in dose of 8µg/mL produced a statistically significant ($p<0.05$) increase of amplitude of contraction, and the drug in doses of 16 & 32µg/mL produced a statistically highly significant ($p<0.01$) increase of amplitude of contraction..

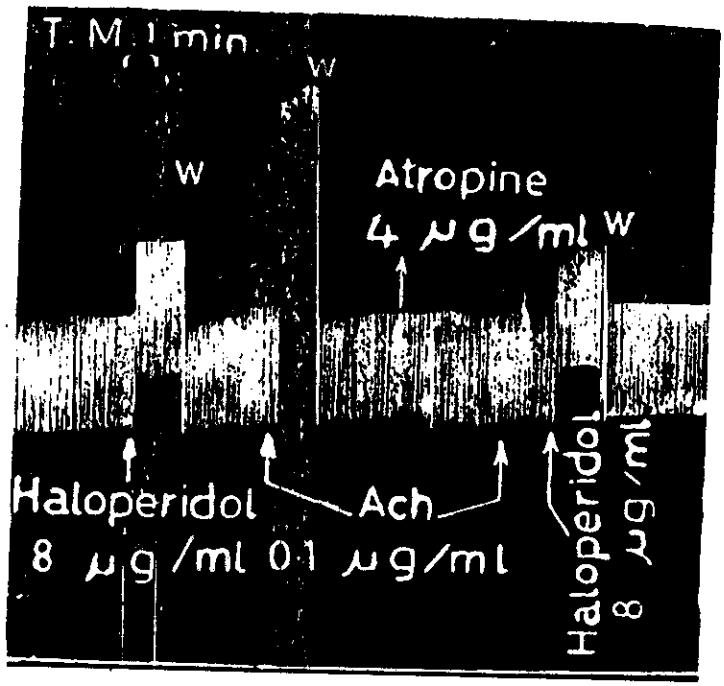


Fig. (34): A record showing the interaction between haloperidol and atropine in the isolated rabbit's jejunum.

Addition of atropine in a dose of 4µg/mL did not abolish haloperidol-induced increase in amplitude of contraction of isolated rabbit's jejunum.

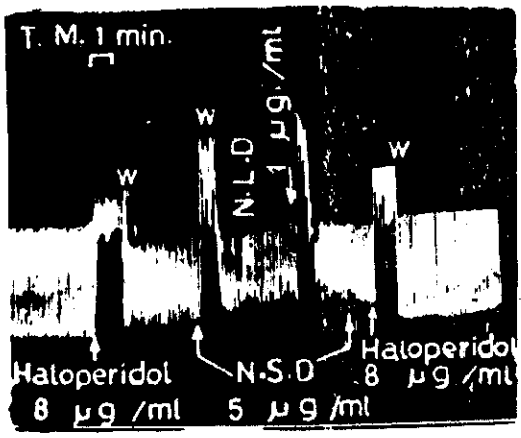


Fig. (35): A record showing the interaction between haloperidol and NLD in the isolated rabbit's jejunum.

Addition of NLD in a dose of 1µg/mL did not affect haloperidol-induced increase of amplitude of contraction of isolated rabbit's jejunum.

N.B. NLD: nicotine large dose.

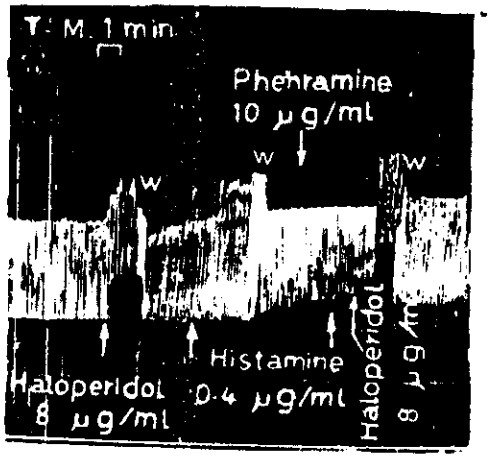


Fig. (36): A record showing the interaction between haloperidol and phenramine in the isolated rabbit's jejunum.

Addition of phenramine in a dose of 10µg/mL did not abolish haloperidol-induced increase of amplitude of contraction of isolated rabbit's jejunum.

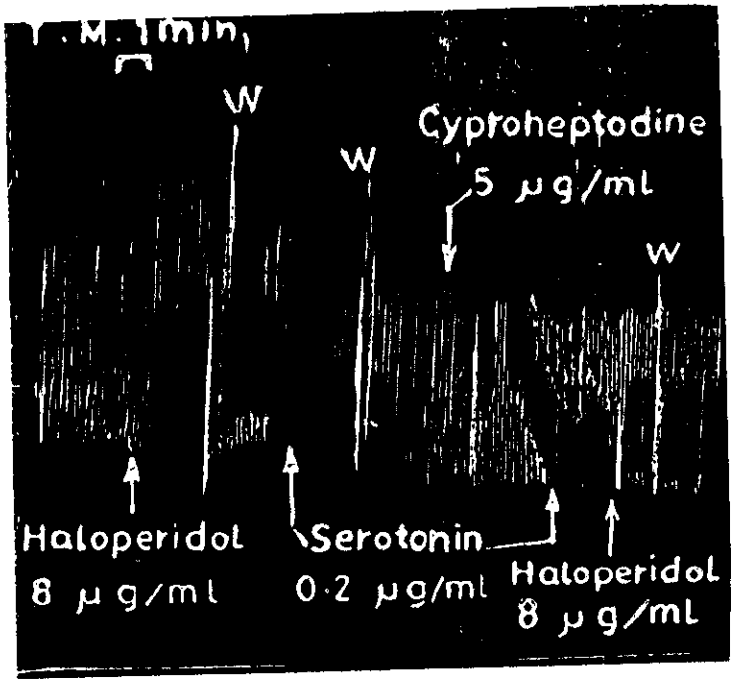


Fig. (37): A record showing the interaction between haloperidol and cyproheptadine in the isolated rabbit's jejunum.

Addition of cyproheptadine in a dose of 5µg/mL abolished haloperidol-induced increase of amplitude of contraction of isolated rabbit's jejunum.

II. IN VIVO EXPERIMENTS:

II.1. Effect of risperidone on systolic blood pressure of rats:

At the beginning of the experiment, the recorded mean basal systolic blood pressure was 103.33±10.46mmHg (Fig.38, 39) (Tab. 4). Risperidone was injected intraperitonially (IP) in rats in a dose of 0.3mg/Kg.

The recorded systolic blood pressure 30 and 60 minutes after the injection of the drug, detected a statistically very highly significant ($p<0.001$) decrease of mean of systolic blood pressure to 81±9.52 and 79±10.2mmHg respectively (Fig. 38, 39) (Tab.4).

the recorded systolic blood pressure after 90 minutes detected a statistically highly significant ($p<0.01$) reduction of mean of systolic blood pressure to 90±11.47mmHg, and the reduction in mean of systolic blood pressure after 120 minutes to 97.5±13.2mmHg was statistically non-significant (Fig.38, 39) (Tab. 4).

Intraperitonial injection (IP) of methanol in equivalent volume and concentration produced a statistically non-significant change of mean of systolic blood pressure of rats.

II.2.Effect of haloperidol on the systolic blood pressure of rats:

Concerning the effect of haloperidol on systolic blood pressure, the recorded mean basal systolic blood pressure at the start of the experiment was 93.33±8.43mmHg (Fig.38, 40) (Tab. 4). Haloperidol was injected intraperitonially (IP) in a dose of 0.5mg/Kg.

The recorded mean of systolic blood pressure after 30 minutes was decreased to 72.17±8.91mmHg and this reduction was statistically highly significant ($p<0.01$),after 60 minutes the recorded mean of systolic blood pressure decreased to 65.6±9.65mmHg and this reduction was statistically very highly significant ($p<0.001$) (Fig.38, 40) (Tab. 4).The recorded mean systolic blood pressure returned to the basal value after 90 minutes (Fig. 38, 40) (Tab. 4).

Intraperitonial injection of lactic acid in equivalent concentration and volume produced a statistically non-significant change of mean of systolic blood pressure in rats.

Table (4): Effects of risperidone and haloperidol on mean systolic blood pressure {mmHg} ± SE after IP injection (in doses of 0.3 and 0.5 mg/Kg respectively) in rats.

Time / Drug	0-time	30min.	60min.	90min.	120min.
Risperidone	103.33±10.46	***81±9.52 p1<0.001	***79±10.2 p1<0.001	**90±11.47 p1<0.01	97.5±13.2 p1>0.05
Haloperidol	93.33±8.43	**72.17±8.91 p2<0.01	***65.6±9.65 p2<0.001	93.33±9.27 p2>0.05	93.33±9.27 p2>0.05

P1 Compares mean ± SE {mmHg} of systolic blood pressure after IP injection of risperidone with that at 0-time.

P2 Compares mean ± SE {mmHg} of systolic blood pressure after IP injection of haloperidol with that at 0-time.

N.B.
** Highly significant ($p<0.01$).
*** Very highly significant ($p<0.001$).
0-time: control systolic blood pressure: before IP injection of the drug.
IP: Intraperitonial.

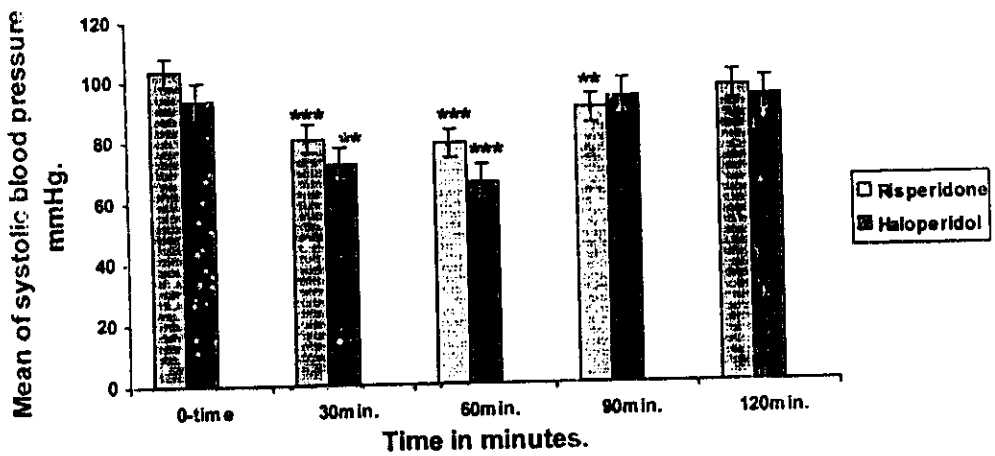
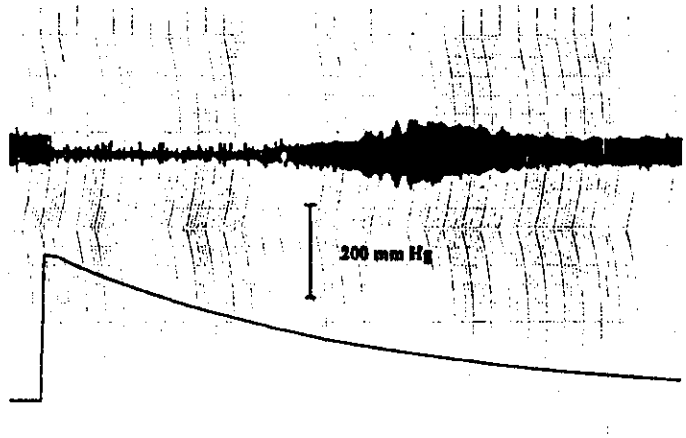


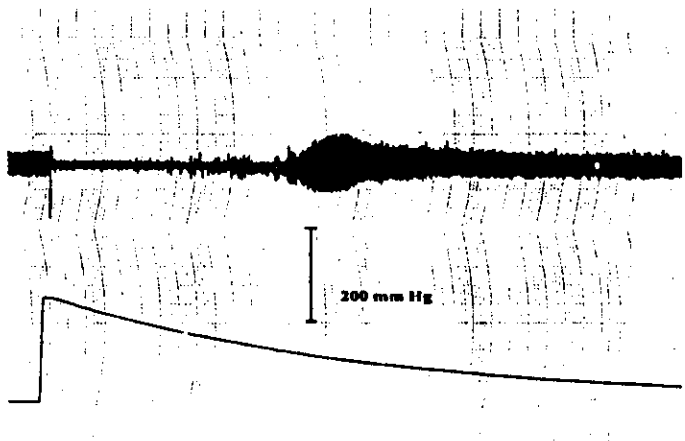
Fig.(38): A histogram showing the effects of risperidone and haloperidol on mean of systolic blood pressure of rats.

N.B. 0-time: control systolic blood pressure: before IP injection of the the drugs (0.3 mg/Kg risperidone, 0.5 mg/Kg haloperidol).

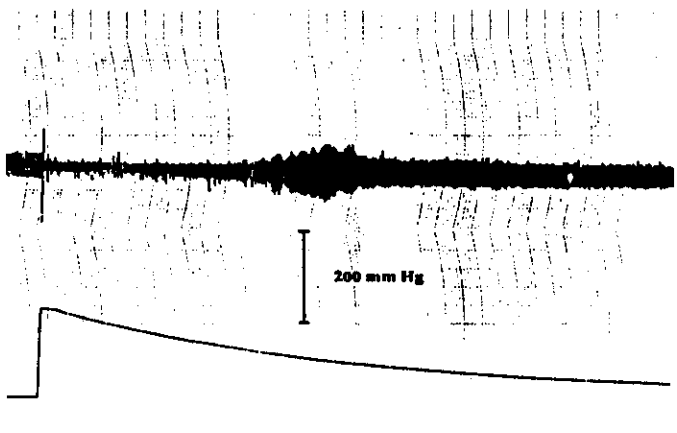
** Highly significant ($p<0.01$).
*** Very highly significant ($p<0.001$).
Vertical lines represent SE of mean.



a)



b)



c)

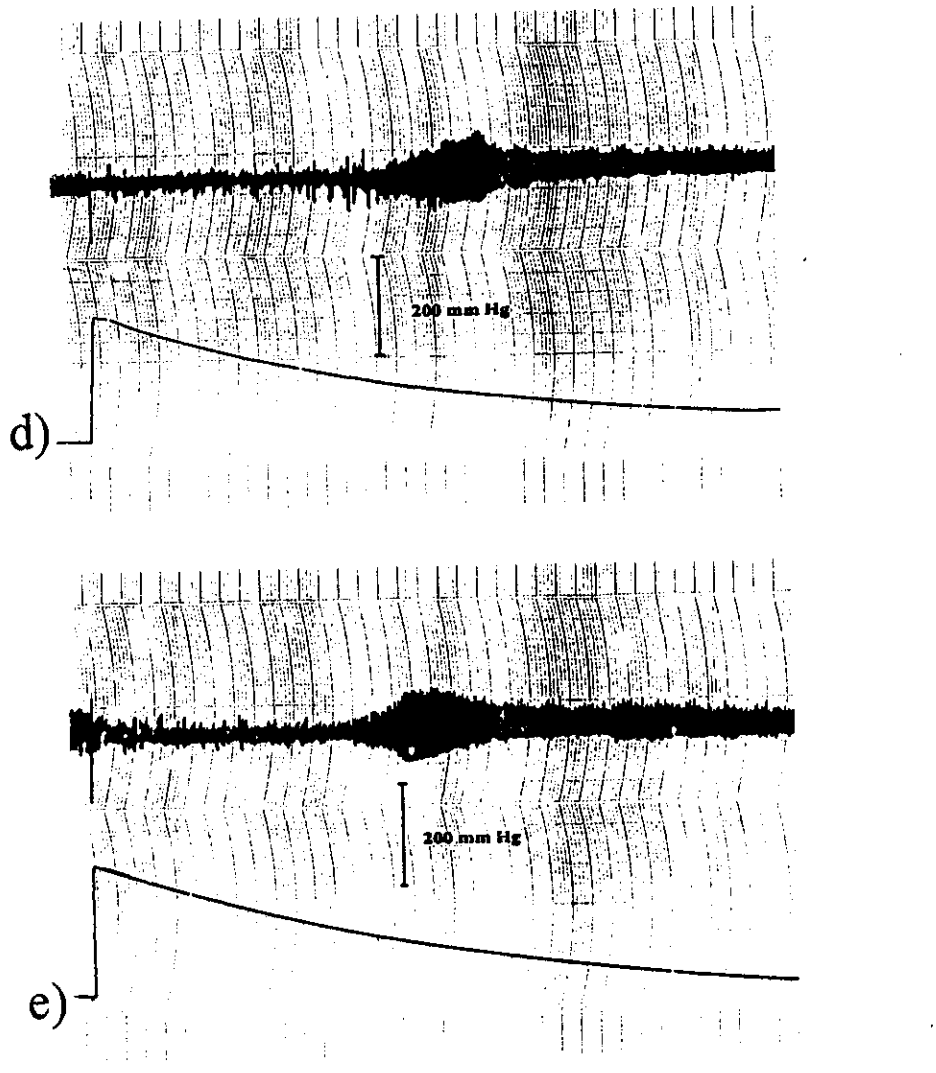
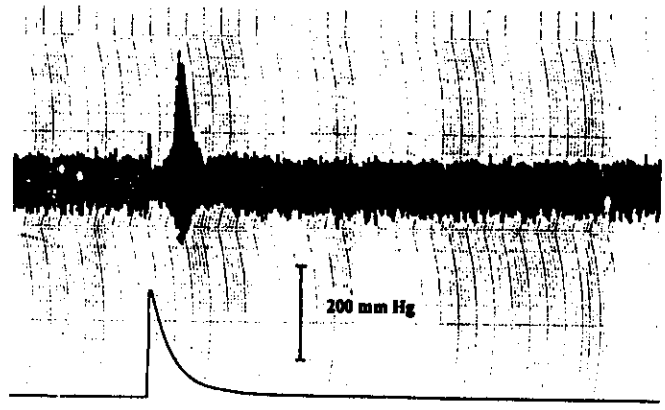


Fig. (39) : Effect of risperidone on systolic blood pressure after acute intraperitoneal administration of 0.3 mg/kg of risperidone in rats:

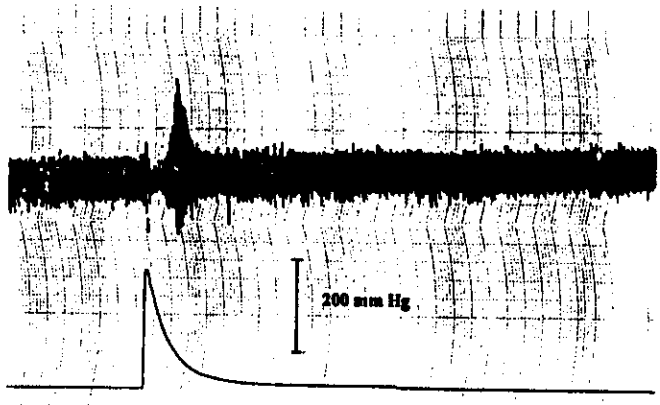
a) SBP at 0 –time before injection of risperidone.
b) SBP at 30 min. after injection of risperidone.
c) SBP at 60 min. after injection of risperidone.
d) SBP at 90 min. after injection of risperidone.
e) SBP at 120 min. after injection of risperidone.

N.B.

- **Upper trace represents pulse blood flow.**
- **Lower trace represents cuff pressure.**
- **The systolic blood pressure measured at the start of pulsation and referenced to the pressure curve.**
- **SBP : Systolic blood pressure.**



a)



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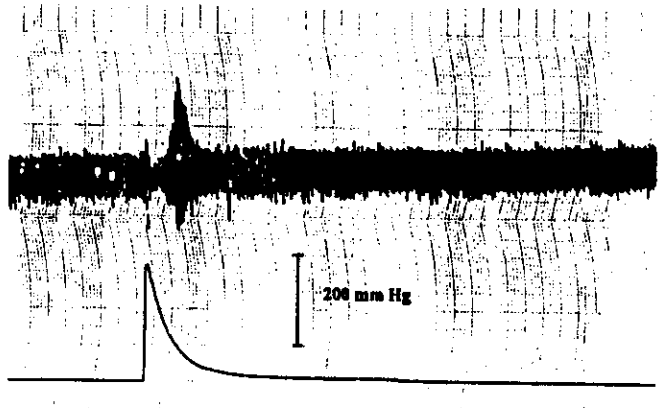

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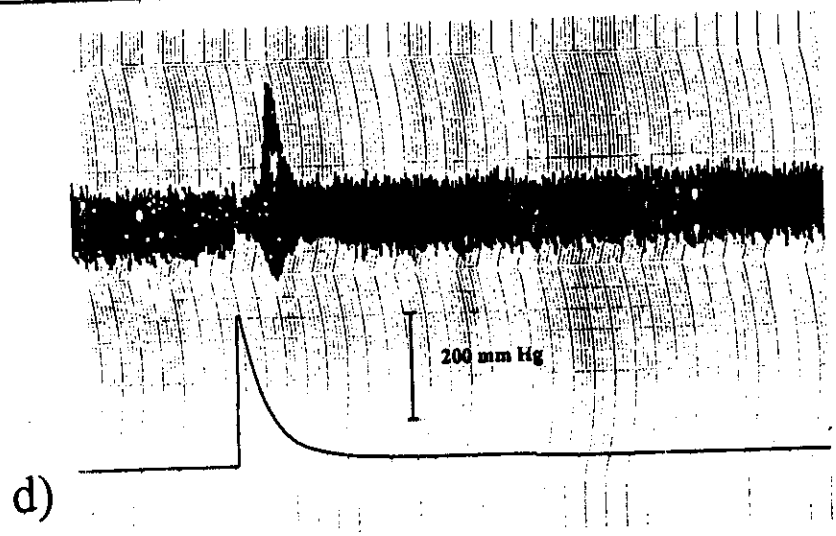


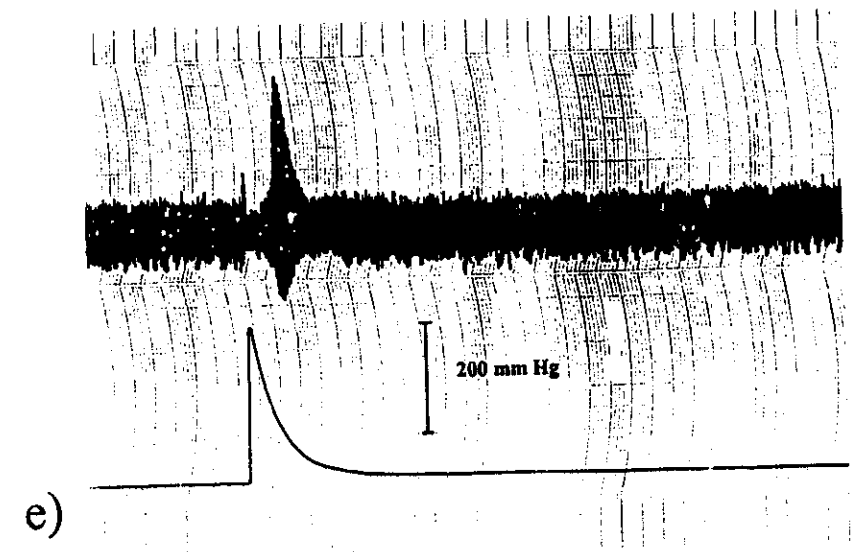


Fig. (40) : Effect of haloperidol on systolic blood pressure after acute intraperitoneal administration of 0.5 mg/kg of haloperidol in rats:

a) SBP at 0 –time before injection of haloperidol.
b) SBP at 30 min. after injection of haloperidol.
c) SBP at 60 min. after injection of haloperidol.
d) SBP at 90 min. after injection of haloperidol.
e) SBP at 120 min. after injection of haloperidol.

N.B.

- Upper trace represents pulse blood flow.
- Lower trace represents cuff pressure.
- The systolic blood pressure measured at the start of pulsation and referenced to the pressure curve.
- SBP : Systolic blood pressure.

II.3. Effect of risperidone on ECG tracing of rats:

Effect on heart rate (HR):

At the start of the experiment,the recorded mean HR was 325±20.3 beats/m (Fig. 41, 42) (Tab.5). Risperidone was injected intraperitonially (IP) in a dose of 0.3mg/Kg which produced a statistically non-significant decrease of mean HR after 30,60,90 and 120 minutes to the values of 290.8±38.13 ,290.8±38.13,2 and 277.5±34, and 278.33±27.6 beats/m. respectively (Fig. 41, 42) (Tab. 5).

Intraperitonial (IP) injection of methanol in equivalent concentration and volume produced a statistically non-significant change of mean HR in rats.

II.4. Effect of haloperidol on ECG tracing of rats:

Effect on heart rate (HR):

Regarding the effect of haloperidol on HR, the recorded basal mean HR was 325±11.18 beats/m. (Fig. 41, 43) (Tab. 5).

Haloperidol was injected in a dose of 0.5mg/Kg intraperitonially (IP) and it was observed that it produced a statistically significant ($p<0.001$) decrease of mean HR after 30,60,90 and 120 minutes to the values of 230.33±16.11, 220±18.47, 220±18.47 and 203±18.23 beats/m. respectively (Fig. 41, 42) (Tab. 5).

Intraperitonial injection of lactic acid in equivalent concentration and volume produced a statistically non-significant change of mean HR in rats.

Table(5): Effects of risperidone and haloperidol on HR {beats/minutes} ± SE after IP injection (in doses of 0.3 and 0.5 mg/Kg respectively) in urethane-anaesthetized rats.

Time / Drug	0-time	30min.	60min.	90min.	120min.
Risperidone	325±20.3	290.8±38.13 p1>0.05	290.8±38.13 p1>0.05	277.5±34 p1>0.05	278.33±27.6 p1>0.05
Haloperidol	325±11.18	***230.33±16.11 p2<0.001	***220±18.47 p2<0.001	***220±18.47 p2<0.001	***203±18.23 p2<0.001

P1 Compares HR {beats/min.} ± SE after IP of risperidone injection with that at 0-time.

P2 Compares HR {beats/min.} ± SE after IP injection of haloperidol with that at 0-time.

N.B. ***Very highly Significant ($p<0.001$).
0-time: control HR: before drug injection.
HR: heart rate.
IP: intraperitonial.

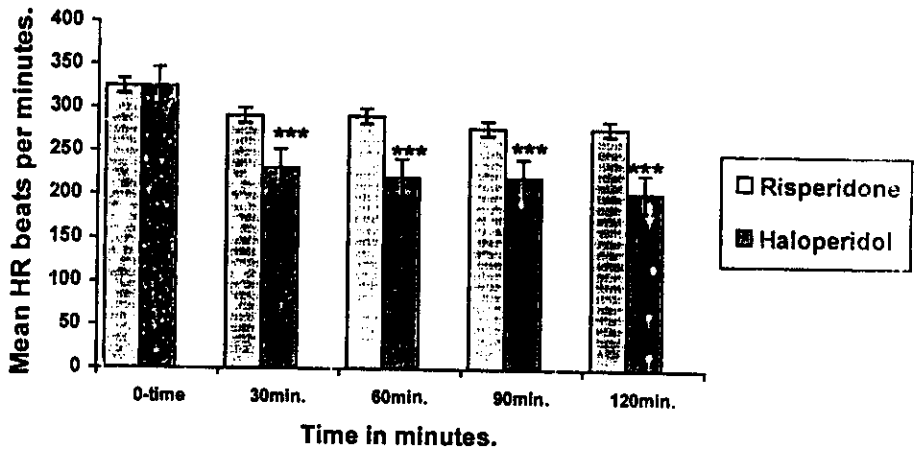
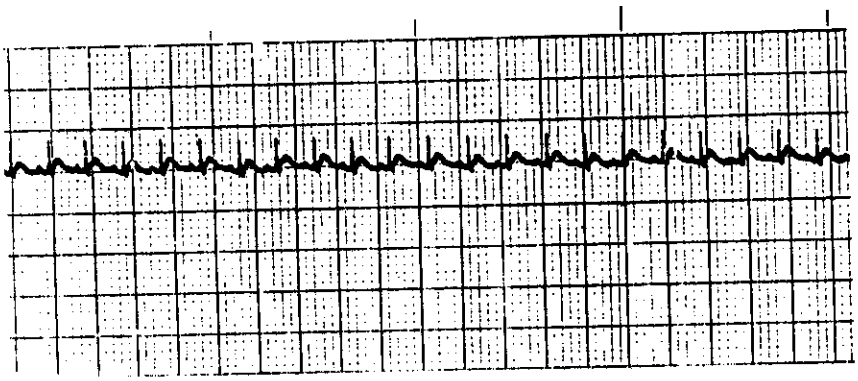


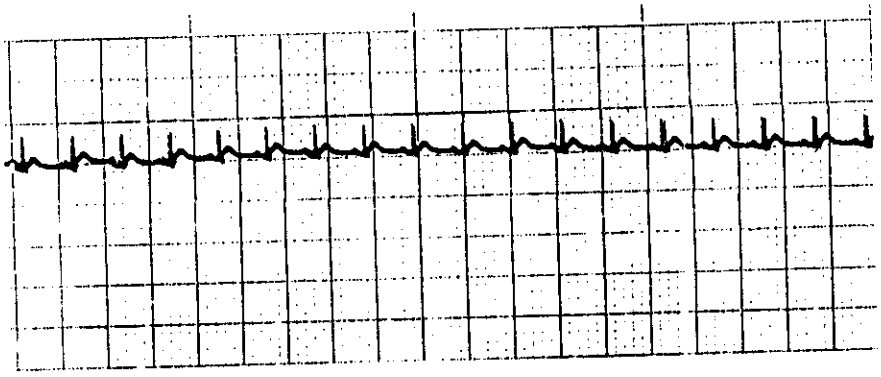
Fig.(41): A histogram showing the effects of risperidone and haloperidol on mean HR of rats.

N.B. **0-time**: control HR before IP injection of the drugs (0.3 mg/Kg of risperidone, 0.5 mg/Kg of haloperidol).
HR: heart rate.
***Very highly Significant ($p<0.001$).
Vertical lines represent SE of mean.

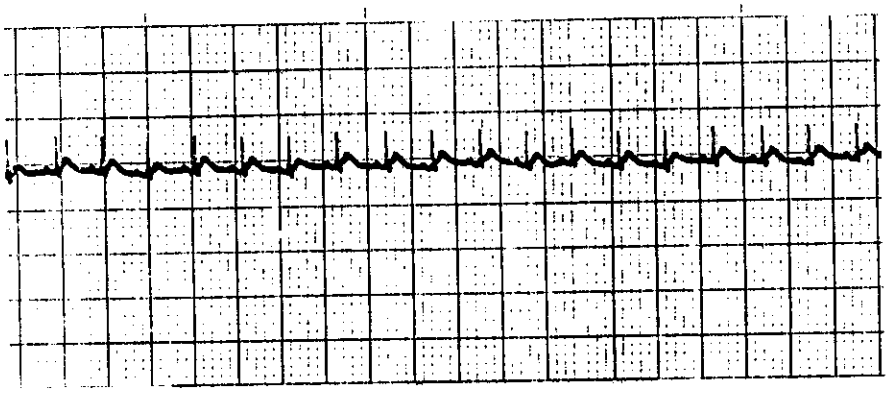
a)



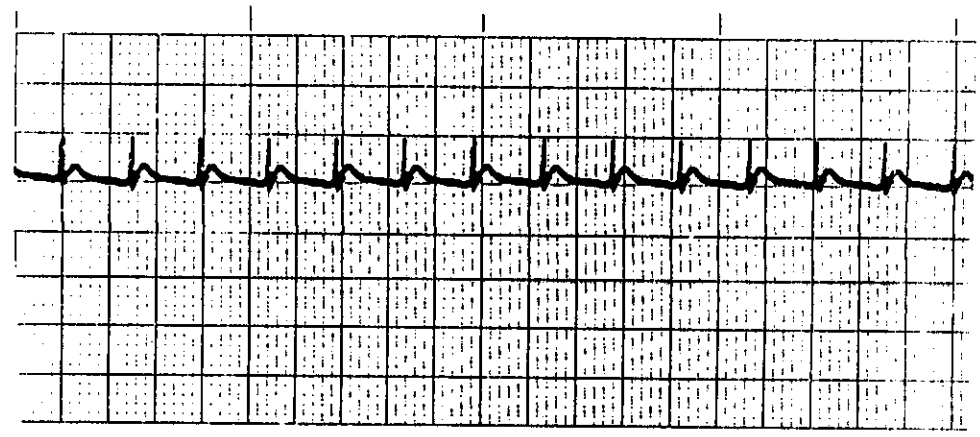
b)



c)



d)



e)

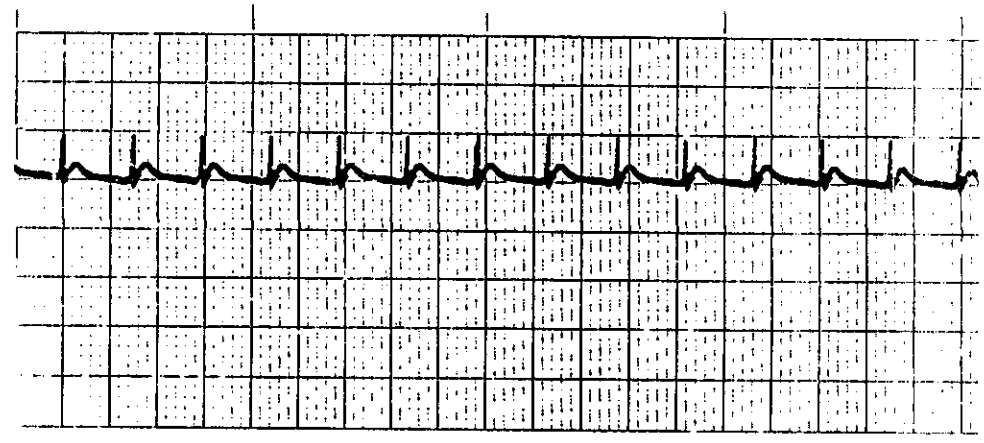


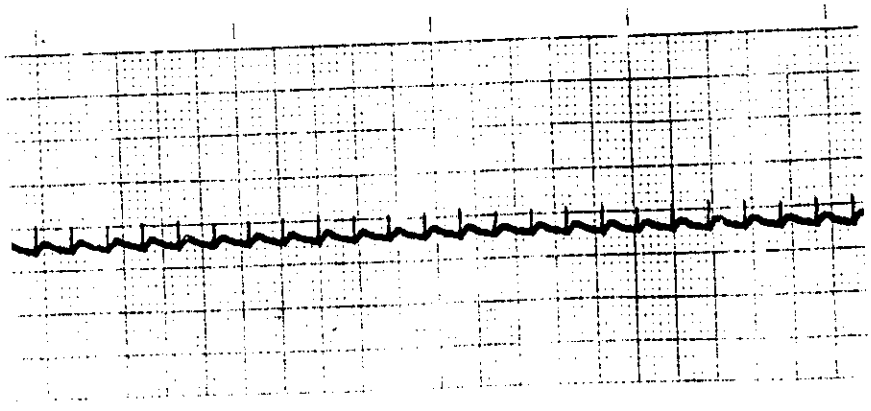
Fig. (42) : Effect of risperidone on ECG traces after acute intraperitoneal administration of 0.3 mg/kg of risperidone in urethane-anaesthetized rats :

a) HR at 0 –time before injection of risperidone.
b) HR at 30 min. after injection of risperidone.
c) HR at 60 min. after injection of risperidone.
d) HR at 90 min. after injection of risperidone.
e) HR at 120 min. after injection of risperidone.

N.B.

HR: Heart rate.

a)



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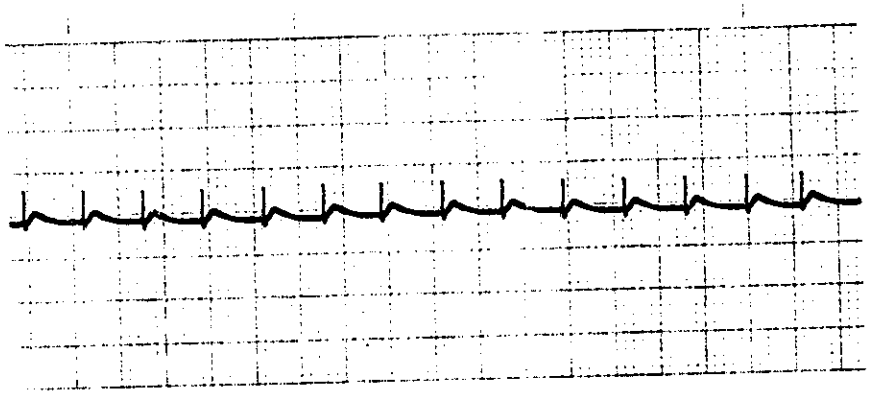

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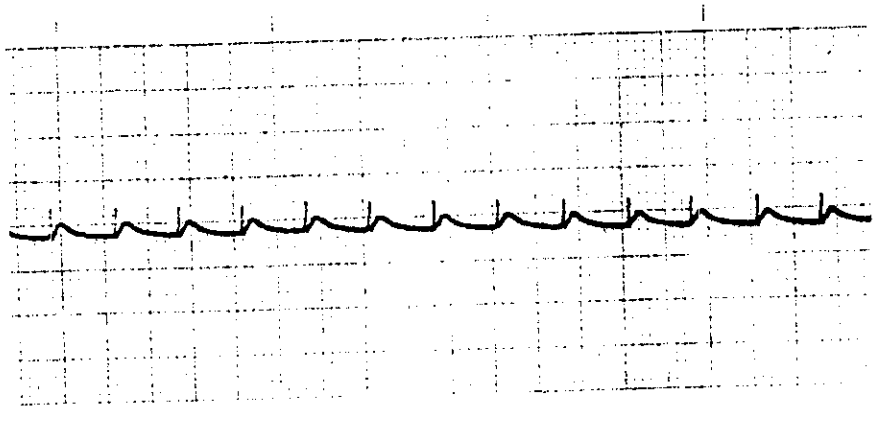

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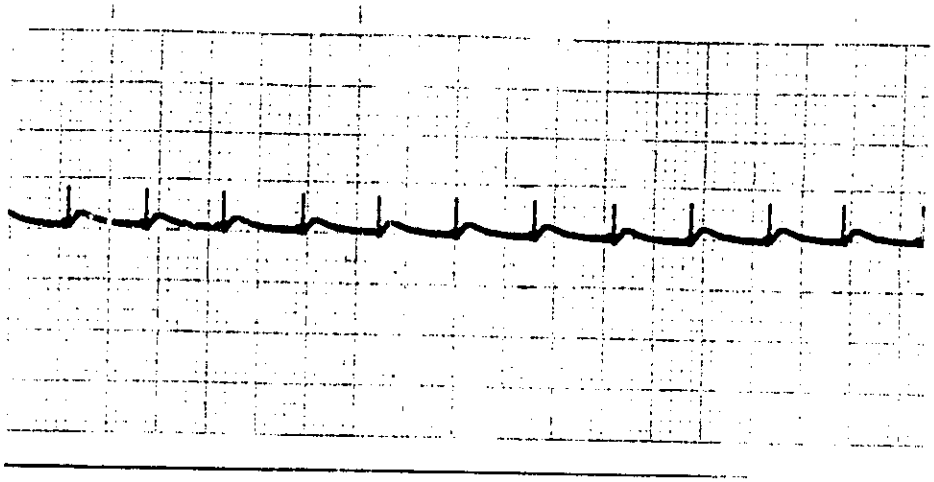

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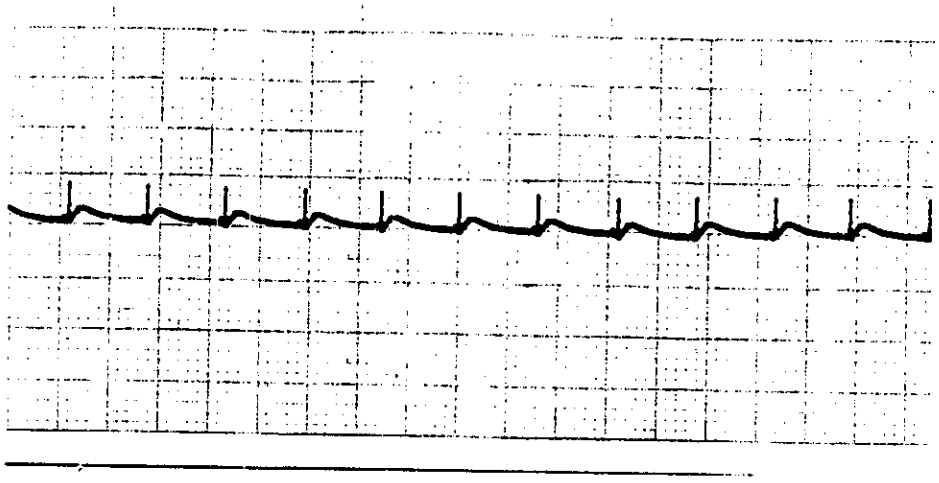

Fig. (43) : Effect of haloperidol on ECG traces after acute intraperitoneal administration of 0.5 mg/kg of haloperidol in urethane-anaesthetized rats:

a) HR at 0 –time before injection of haloperidol.
b) HR at 30 min. after injection of haloperidol.
c) HR at 60 min. after injection of haloperidol.
d) HR at 90 min. after injection of haloperidol.
e) HR at 120 min. after injection of haloperidol.

N.B.
HR : Heart Rate

II.5. Effects of risperidone and haloperidol on the holeboard Learning task in rats:

Subacute ketamine injection in a dose of 25mg/Kg in male albino rats led to an impairment in the holeboard learning compared to the controls.

Holeboard learning was tested 24 hours after discontinuing the last ketamine injection because learning deficits became apparent only 24 hours after the last ketamine injection.

The means of percents of correct responses in the risperidone study were 87.5 ± 5.2%, 85.7 ± 8%, 42.85 ± 10% and 83.33 ± 10% for the control, risperidone, ketamine and ketamine/ risperidone groups respectively (Fig.44, 46) (Tab. 6).

On the other hand, the means of percents of correct responses in the haloperidol study were 66 ± 9.8%, 80 ± 8%, 44.44 ± 9.5% and 50 ± 8.5% for the control, haloperidol, ketamine and ketamine/ haloperidol groups respectively (Fig. 45, 46) (Tab. 6).

It was observed that the combined application of ketamine intraperitonially (IP) in a dose of 25mg/ Kg and risperidone intraperitonially IP in a dose of 0.1mg/Kg over 5 days significantly ($p<0.05$) reduced the ketamine-induced deficit in the short term memory (Fig.44, 46) (Tab. 6).

Methanol injection intraperitonially produced a statistically non-significant change in means of percents of correct responses in rats.

The combined application of ketamine and haloperidol « intraperitonially in a dose of 0.5mg/Kg » showed a statistically non-significant tendency to antagonize the ketamine-induced deficits (Fig. 45) (Tab. 6).

While lactic acid injection IP produced a statistically non-significant change in means of percents of correct responses in rats.

Table (6): Effects of risperidone (0.1mg/Kg IP) and haloperidol (0.5mg/Kg IP) on mean ± SE of the percentage of the correct responses of rats in the holeboard learning task 24 hours after the last ketamine injection.

Risperidone study		Haloperidol study	
Control group	87.5±5.2	Control group	66±9.8
Risperidone group	85.7±8	Haloperidol group	80±8
Ketamine group	42.85±10 *P1<0. 05	Ketamine group	44.44±9.5 *P2<0.05
Ketamine/Risperidone group	83.33±10 #P1<0.05	Ketamine/Haloperidol group	50±8.5 #P2>0.05

*P1 compares mean ± SE of the percent of correct responses of ketamine group to the control group.

#P1 compares mean ± SE of correct responses of ketamine/risperidone group to ketamine group.

*P2 compares mean ± SE of percent of correct responses of ketamine group to control group.

#P2 compares mean ± SE of percent of correct responses of ketamine/haloperidol group to ketamine group.

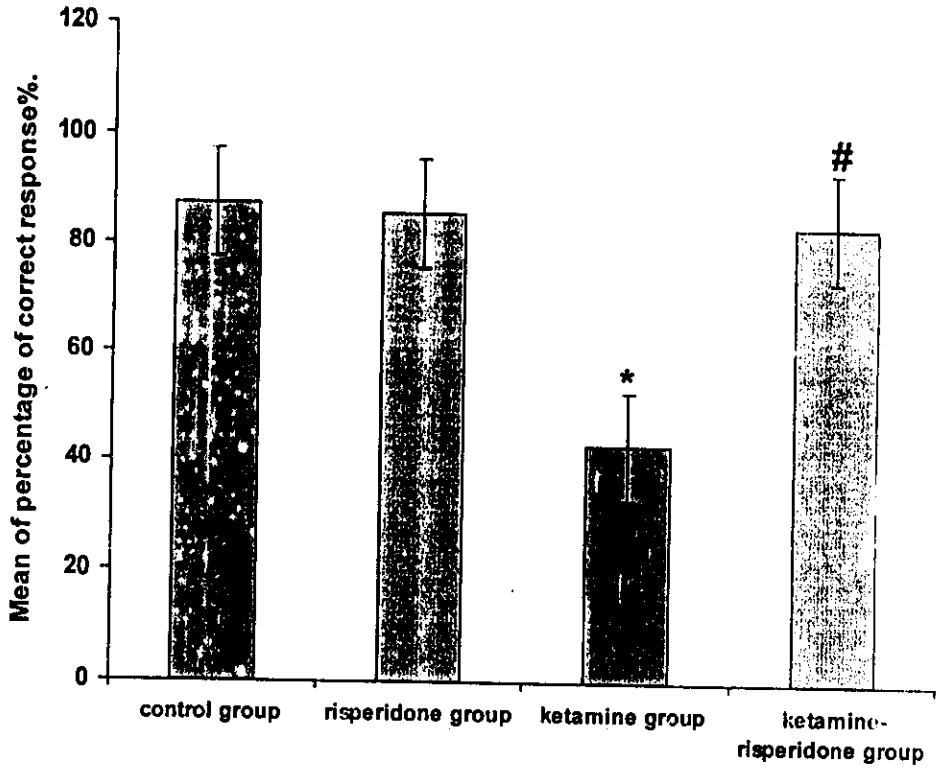

Fig. (44): Histogram showing the effect of risperidone on the holeboard learning task in rats.

N.B. * Significant (P<0.05) compared to the control group.

Significant (P<0.05) compared to the ketamine group.

Vertical lines represent SE of mean.

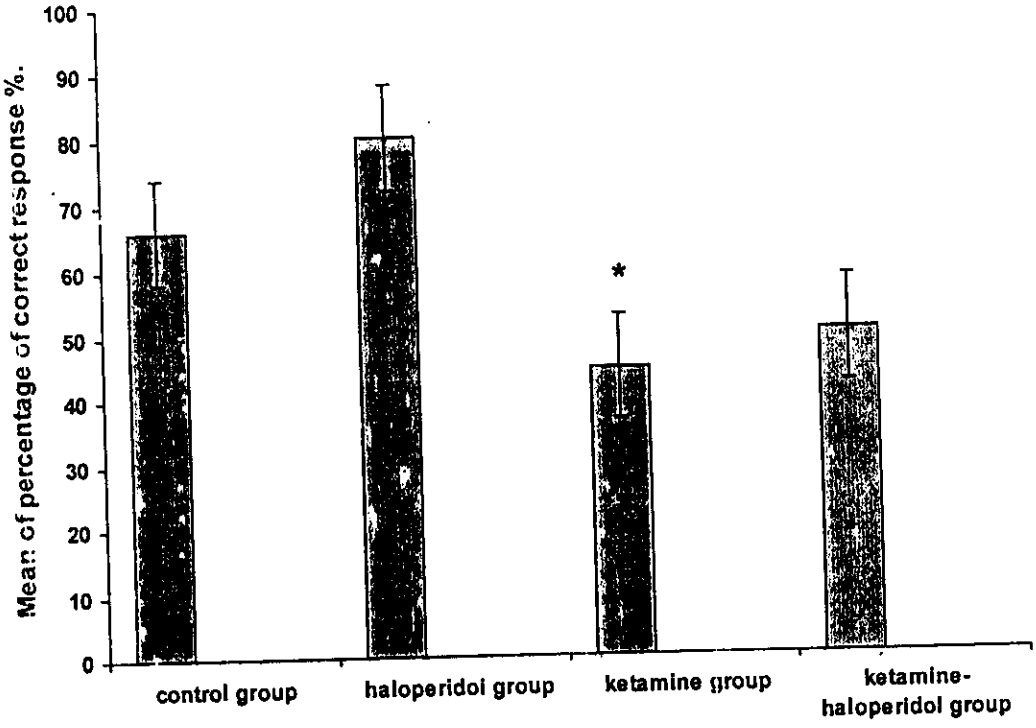

Fig. (45): Histogram showing the effect of haloperidol on the holeboard learning task in rats.

N.B. * Significant ($P<0.05$) compared to control group.

Vertical lines represent SE of mean.

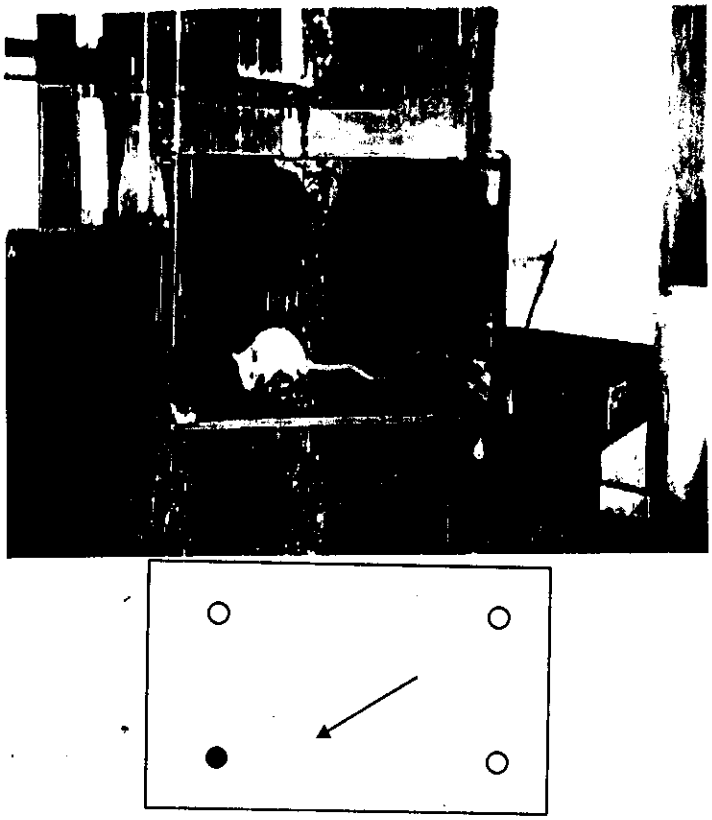

Fig. (46): **A photo and a diagram showing a rat could go directly to the hole that contained food during acquisition.**

N. B. The rat starts from the middle of the holebaord.

● food

○ no food

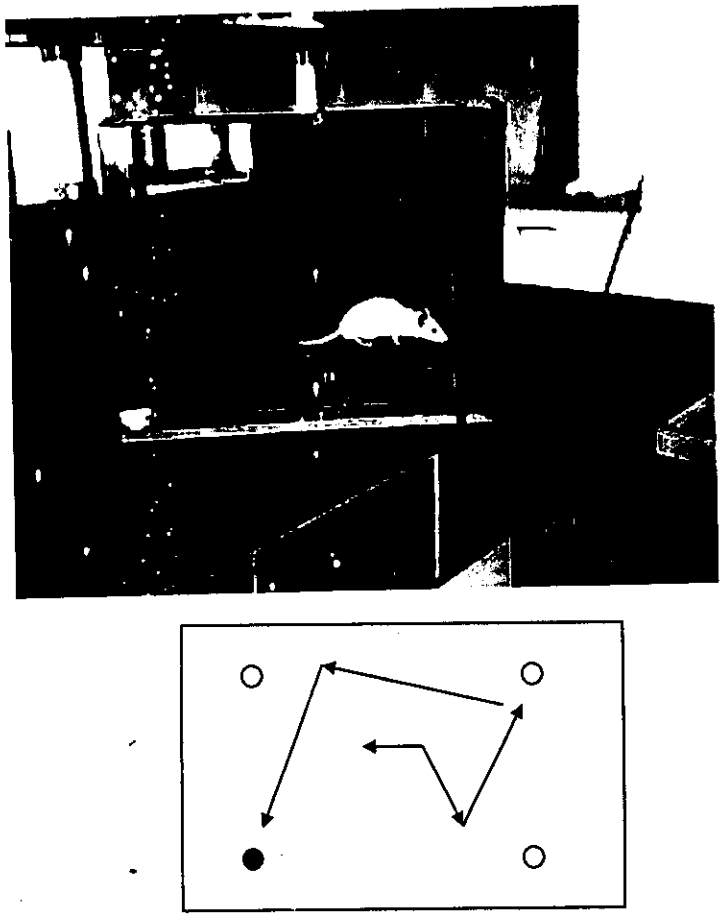

Fig. (47): **A photo and a diagram showing a rat failed to go directly to hole that contained food during acquisition.**

N. B. The rat starts from the middle of the holeboard.

● food

○ no food