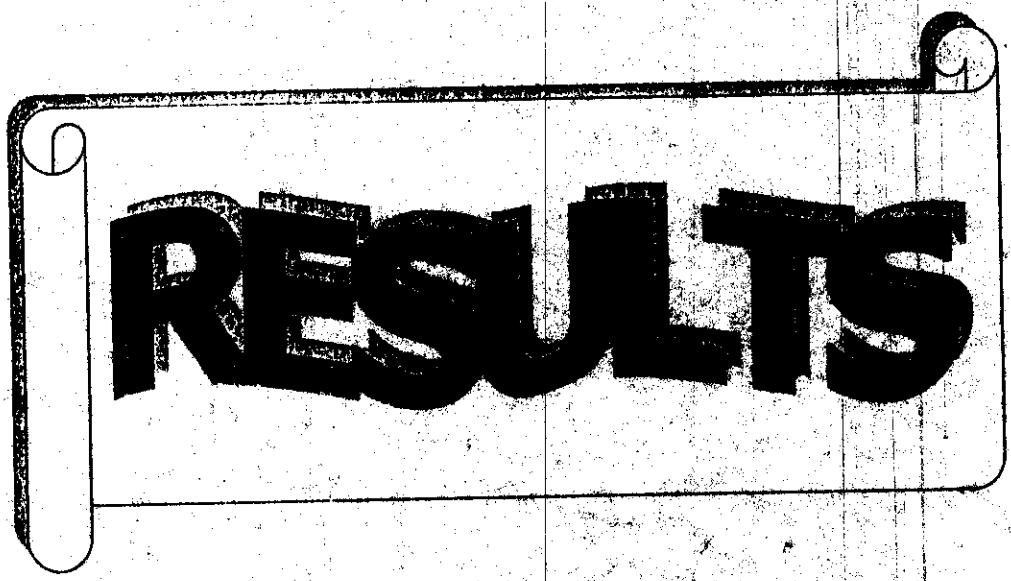

RESULTS

RESULTS

I-In vitro experiments:

1-1-Isolated rabbit's jejunum:

A-Effect of increasing doses of tianeptine and amitriptyline on the isolated rabbit's jejunum:

It was observed that addition of increasing doses of (2ug, 4ug, 8ug, 16u and 32ug/ml) of tianeptine produced statistically in significant inhibitory effect (P 0.05) in the tone and the amplitude of contraction of jejunal smooth muscle. While, the addition of increasing doses of amitriptyline of 2ug, 4ug, 8ug, 16ug and 32ug/ml produced statistically significant inhibitory effect ($P<0.05$) in the tone and amplitude of contraction of isolated rabbit jejunum by a percentage of 72%, 77%, 78.1%, 78.8% and 78.86% respectively (fig 3, 4, 5).

By comparing the inhibitory effect of tianeptine versus amitriptyline in the same doses, it was observed that tianeptine in a dose of (2, 4, 8, 16 and 32ug/ml) produced statistically in significant inhibitory effects less than amitriptyline. (table 1, figure 3).

Table (1): shows the inhibitory effects of tianeptine and amitriptyline on mean ± SE of tone and amplitude of isolated rabbit jejunum.

DOSES / Drugs	Control	2ug/ml	4ug/ml	8ug/ml	16ug/ml	32ug/ml
Tianeptine	4.4±0.27 {cm}	# 4.4±0.27 P1>0.05	# 4.3±0.22 P1>0.05	# 4.1±0.31 P1>0.05	# 3.9±0.35 P1>0.05	# 3.8±0.37 P1>0.05
Amitriptyline		* 1.2±0.47 P2<0.05	* 1.0±0.54 P2<0.05	* 0.96±0.51 P2<0.05	* 0.93±0.48 P2<0.05	* 0.93±0.49 P2<0.05

P1: compared the inhibitory effect of tianeptine on a doses of (2, 4, 8, 16 and 32ug/ml) on isolated rabbit jejunum with control value .

P2 : compared the inhibitory effect of amitriptyline on a doses of (2, 4, 8, 16 and 32ug/ml) on isolated rabbit jejunumwith control value.

N:B:

#: statistically insignificant inhibitory effect (P>0.05).

*: statistically significant inhibitory effect (P<0.05).

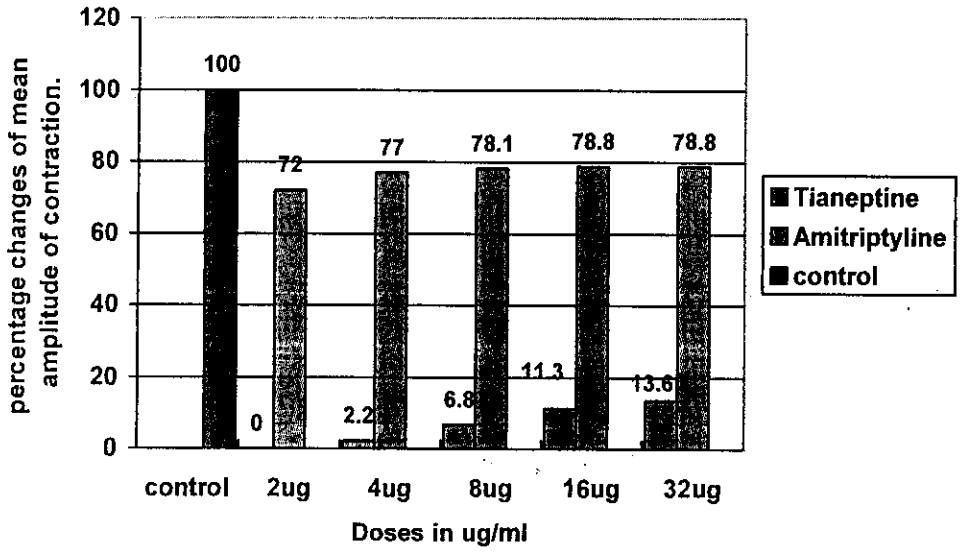


Fig. (3): histogram showing the percentage changes on mean amplitude of contraction of isolated rabbit jejunum, after addition of tianeptine and amitriptyline in a doses of (2, 4, 8, 16, and 32ug/ml) compared with control value..

It showed that tianeptine produced statistically insignificant inhibitory effect less than amitriptyline which produced statistically significant inhibitory effect in the same doses on mean amplitude of contraction of isolated rabbit jejunum.

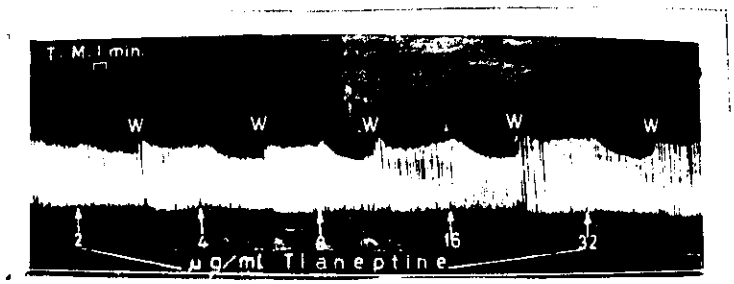


Fig.(4): A record showing the inhibitory effect of gradually increasing doses of (2ug, 4ug, 8ug, 16ug and 32ug/ml) of tianeptine on the isolated rabbit jejunum.

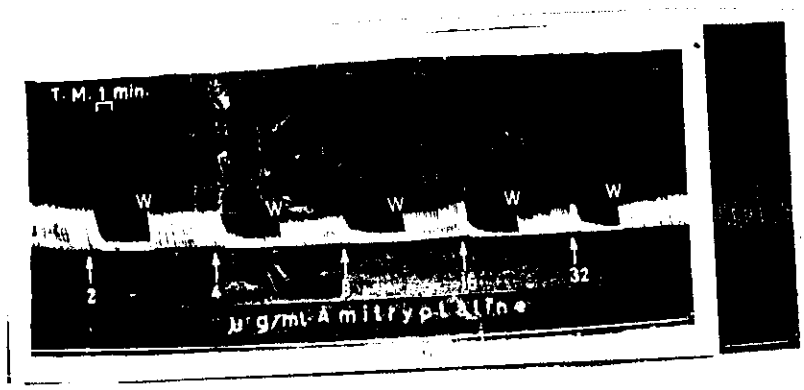


Fig. (5): A record showing the inhibitory effect of gradually increasing doses of (2ug, 4ug, 8ug, 16ug and 32ug/ml) of amitriptyline on the isolated rabbit jejunum.

B-Effect of tianeptine and amitriptyline on different receptors in isolated rabbit jejunum:

*** Effect of tianeptine and amitriptyline on alpha and beta receptors:**

It was observed that tianeptine added in a dose of (8ug/ml) produced statistically insignificant inhibitory effect ($p>0.05$) of the rhythmic jejunal contraction, after which adrenaline was added in a dose of (0.05 ug/ml) that produced an inhibitory effect of the rythmic contraction of isolated rabbit jejunum. Preincubation of the intestine by phentolamine and propranolol in a dose of (4ug/ml and 6ug/ml) respectively for 3 min. abolished the inhibitory effect of adrenaline, however it had no effect on tianeptine inhibitory effect. Fig. (6).

Amitriptyline added in a dose of 8ug/ml produced statistically significant inhibitory effect ($p<0.05$) of the rhythmic jejunal contraction, , after which adrenaline was added in a dose of (0.05 ug/ml) that produced an inhibitory effect of the rythmic contraction of isolated rabbit jejunum. Preincubation of the intestine by phentolamine and propranolol in a dose of (4ug/ml and 6ug/ml) respectively for 3 min. abolished the inhibitory effect of adrenaline, however it had no effect on amitriptyline inhibitory effect. (Fig. 7).

*** Effect of tianeptine and amitriptyline on dopaminergic receptors:**

It was observed that tianeptine added in a dose of (8ug/ml) produced statistically insignificant inhibitory effect ($p>0.05$) of the rythmic jejunal contraction, after which dopamine was added in a dose of 3ug/ml that produce an inhibition of the rythmic jejunal contraction. Preincubation of the intestine by metochlopramide in a dose of 6ug/ml for 3 min. duration abolished the inhibitory effect of dopamine; however, it had no effect on tianeptine inhibitory effect (fig. 8).

Amitriptyline in a dose of 8ug/ml produced statistically insignificant inhibitory effect ($p>0.05$) on the rythmic jejunal contraction, after which dopamine was added in a dose of 3ug/ml that produced an inhibition of the rythmic jejunal contraction. preincubation of the intestine by metochlopramide in a dose of 6ug/ml for 3 min. duration abolished the inhibitory effect of dopamine; however, it had no effect on amitriptyline inhibitory effect.(fig. 9).

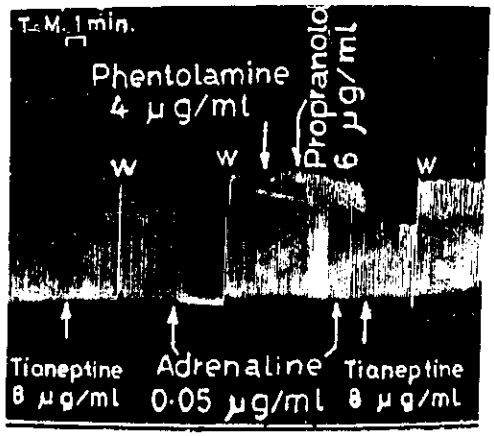


Fig. (6): A record showing the inhibitory effect of tianeptine on isolated rabbit jejunum which was not abolished after addition of alpha and beta blockers.

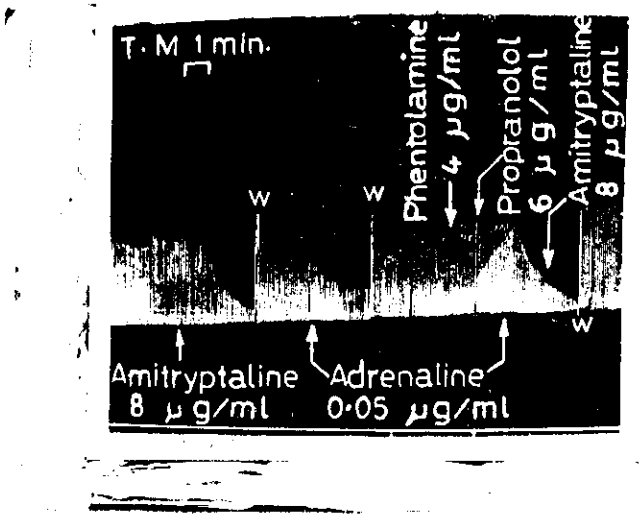


Fig. (7): A record showing the inhibitory effect of amitriptyline on isolated rabbit jejunum. Which was not abolished by phentolamine and propranolol (alpha and beta blockers) respectively

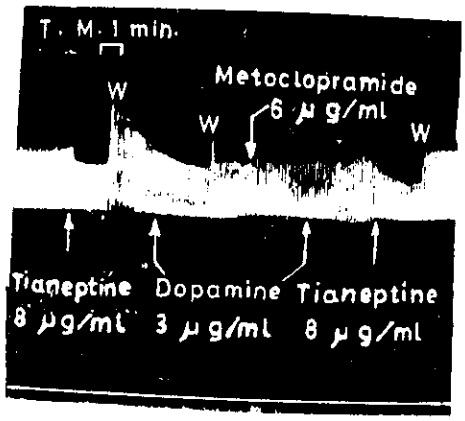


Fig. (8): a record showing the inhibitory effect of tianeptine which was not abolished after addition of metoclopramide on isolated rabbit jejunum.

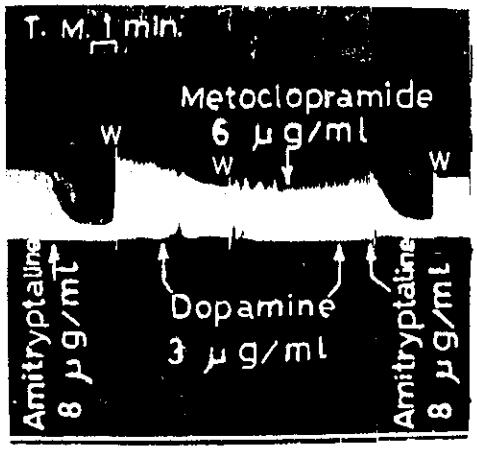


Fig. (9): A record showing the inhibitory effect of amitriptyline which not abolished after metoclopramide on isolated rabbit jejunm.

*** Effect of tianeptine and amitriptyline on muscarinic receptors:**

Regarding the interaction of tianeptine with A.ch. It was observed that preincubation of gradually increasing doses of tianeptine in a doses of (2ug, 4ug, 8ug, 16ug/ml) for 3 minutes before addition of A.ch.in a dose of (1ug/ml) produced statistically insignificant inhibition of A.ch. induced contractile response of the rabbit' s jejunum ($p>0.05$) in a dose related manner by a percentage of 1.8%, 3.6%., 7.2% and 10.9% respectively (fig. 10, 11, table 2).

whereas, preincubation of gradually increasing doses of amitriptyline (2ug, 4ug, 8ug, 16ug/ml) for 3 minutes prior to addition of acetylcholine in a dose of 1ug/ml produced significant inhibition of A.ch. induced contractile response of the rabbit' s jejunum ($p<0.05$)in a dose related manner by a percentage of 47.3%, 70.3%, 85.1% and 89.3% respectively (Fig.10, 12).

By comparing the effect of both drugs on muscarinic receptors it was observed that tianeptine had posses less anticholinergic effect than amitriptyline (fig. 10)

Table (2): showing the inhibitory effect of tianeptine and amitriptyline on mean ± SE of A.ch induced contraction in isolated rabbit jejunum.

Doses / Drugs	Control	2ug/ml	4ug/ml	8ug/ml	16ug/ml
A.ch. with tianeptine	5.5±0.21 {cm}	# 5.4±0.23 P1>0.05	# 5.3±0.28 P1>0.05	# 5.1±0.32 P1>0.05	# 4.9±0.33 P1>0.05
A.ch.with amitriptyline		* 2.9±0.54 P2<0.05	* 1.6±0.56 P2<0.05	* 1.2±0.58 P2<0.05	* 0.7±0.59 P2<0.05

P1: compared the inhibitory effect of tianeptine in a doses of (2ug, 4ug, 8ug,16ug and 32ug/ml) on mean amplitude of A.ch induced contraction of isolated rabbit jejunum in compared with control value.

P2: compared the inhibitory effect of amitriptyline in a doses of (2ug, 4ug, 8ug,16ug and 32ug/ml) on mean amplitude of A.ch induced contraction of isolated rabbit jejunum in compared with control value.

N:B:

: statistically insignificant inhibitory effect (P>0.05).

*: statistically significant inhibitory effect (P<0.05).

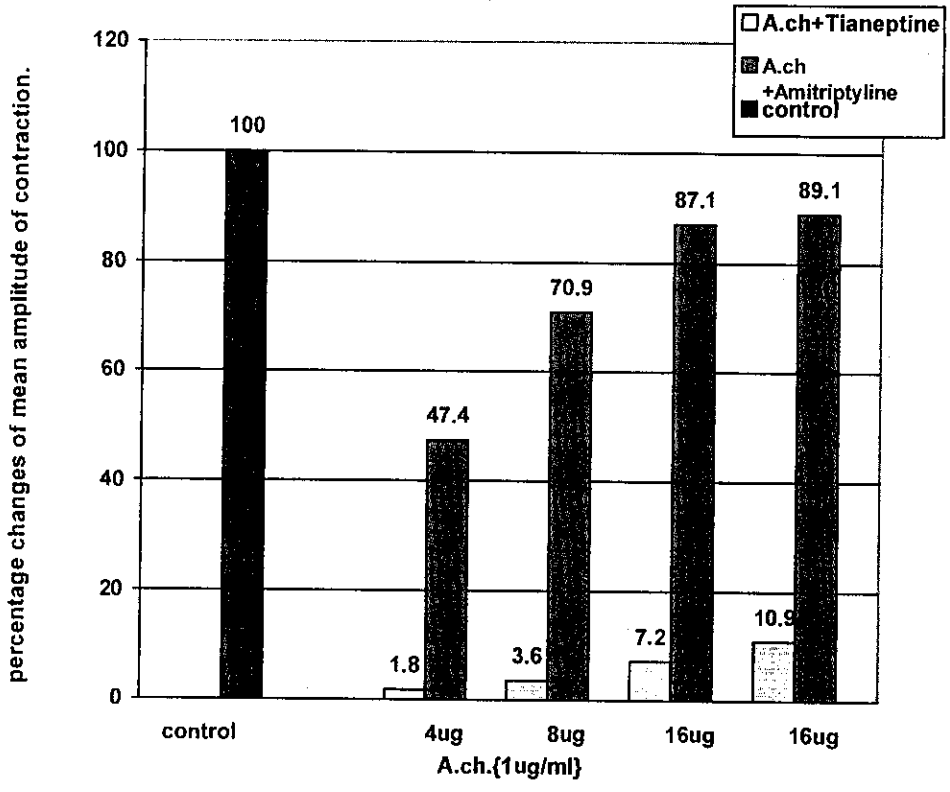


Fig. (12): histogram showing the percentage changes of inhibitory effect of tianeptine and amitriptyline on mean amplitude of A.ch. induced contraction on isolated rabbit jejunum compared with control value.

It showed that, Tianeptine produced inhibitory effect less than amitriptyline in the same doses.

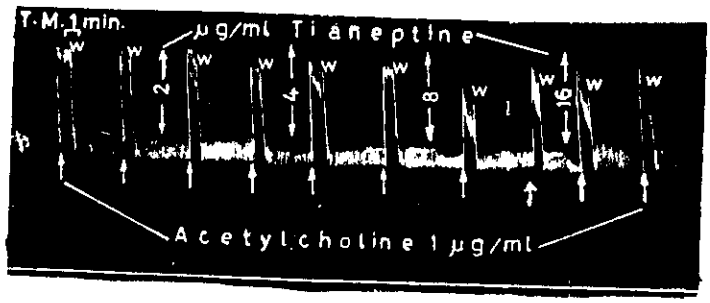


Fig. (11): A record showing the statistically in significant inhibitory effect of tianeptine on A.ch induced contraction on isolated rabbit jejunum.

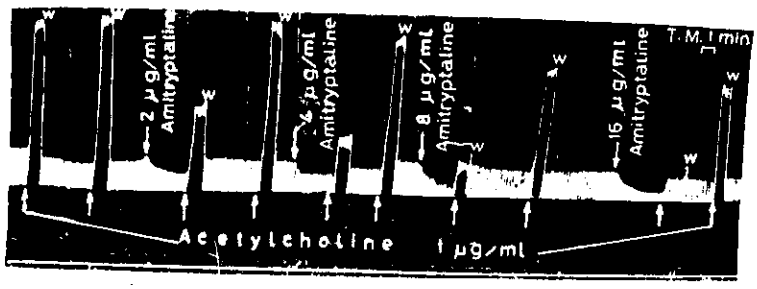


Fig. (12): A record showing the statistically significant inhibitory effect of amitriptyline on A.ch. induced contraction on the isolated rabbit jejunum.

I-2-Isolated rabbit heart:

***Effect of increasing doses of tianeptine and amitriptyline on isolated rabbit heart:**

It was observed that tianeptine added in doses of 2ug, 4ug, 8ug, 16ug and 32ug/ml produced a statisticlly insignificant change in the amplitude of contraction of isolated rabbit heart ($p>0.05$) when compared with control value(fig.13, 14).

While, amitriptyline added in doses of 2ug, 4ug, 8ug, 16ug and 32ug/ml produced insignificant decrease ($p>0.05$) in the amplitude of contractions in a dose-related manner by a percentage of 6.6%, 13.3%, 16.6%, 20% and 22.3% respectively compared with control value. (Fig.13, 15).

In comparing the effect of tianeptine in doses of (2,4, 8, 16, and 32ug/ml) with amitriptyline at the same doses it was observed that tianeptine had no significant changes on the mean amplitude of contraction of isolated rabbit heart in compared with the inhibitory effect of amitriptyline.(fig. 13).

***Effect of amitriptyline on muscarinic receptors:**

Amitriptyline was added in a dose of 8ugl/ml produced statistically in significant inhibition of cardiac contractility ($p>0.05$), after which A.ch. Was added in a dose of 1ug/ml that produced an inhibition in the amplitude of the heart contractility. Preincubation of the heart by atropine in a dose of 4ug/ml for 3 min. duration abolished the inhibitory effect of A.ch; however, it had no effect on amitriptyline inhibitory effect. (Fig.16).

***Effect of amitriptyline on nicotinic receptors:**

Amitriptyline was added in a dose of 8ug/ml produced statistically insignificant inhibition of cardiac contractility ($p>0.05$). Then NSD was added in a dose of 0.5ugl/ml induced similar decrease in the amplitude of the heart contractility. Preincubation of the heart with NLD in a dose of 0.1ugl/ml for 3 min. duration abolished the inhibitory effect of NSD; however, it had no effect on amitriptyline inhibitory effect. (Fig.17).

Table (3): showing the inhibitory effects of tianeptine and amitriptyline on mean ± SE of amplitude of contraction of isolated rabbit heart.

Doses / Drugs	control	2ug	4ug	8ug	16ug	32ug
Tianeptine	3±05.3 {cm}	# 3±0.14 P1>0.05	# 3±0.16 P1>0.05	# 3±0.03 P1>0.05	# 2.9±0.12 P1>0.05	# 2.9±0.07 P1>0.05
amitriptyline		# 2.8±.48 P2>0.05	# 2.7±.47 P2>0.05	# 2.5±.36 P2>0.05	# 2.4±.32 P2>0.05	# 2.3±.31 P2>0.05

P1: compared the inhibitory effect of tianeptine in doses of (2ug, 4ug, 8ug, 16ug and 32ug/ml) on mean amplitude of contraction of isolated rabbit heart compared with control value.

P2: compared the inhibitory effect of amitriptryline in doses of (2ug, 4ug, 8ug, 16ug and 32ug/ml) on mean amplitude of contraction of isolated rabbit heart compared with control value.

#: statistically insignificant inhiubitory effect (P>0.05).

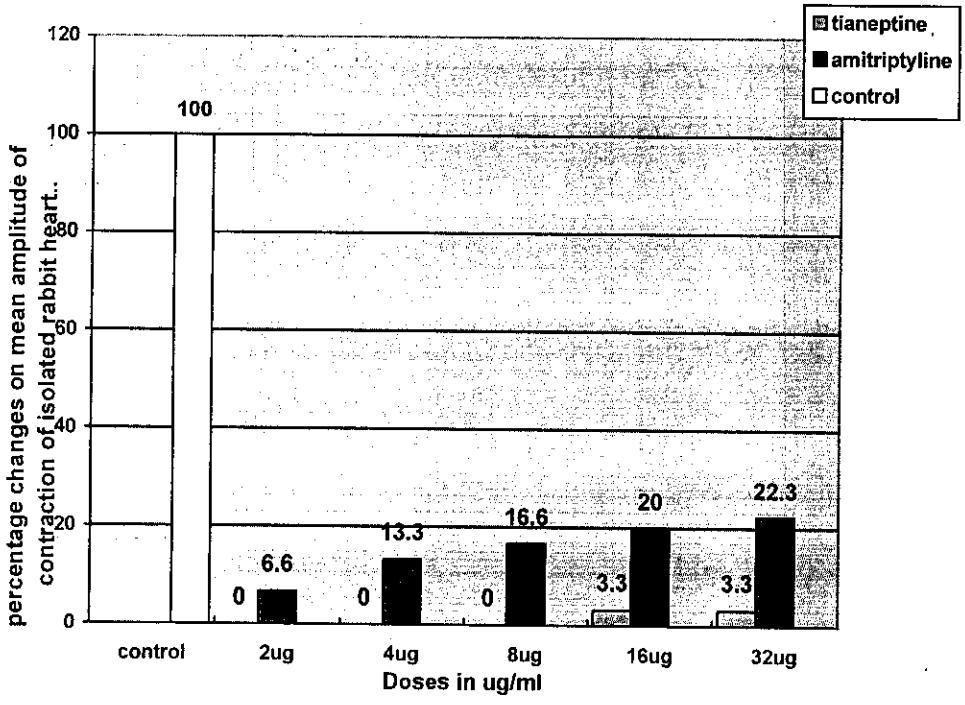


Fig. (13): histogram showing percentage changes on mean amplitude of contraction of isolated rabbit heart after addition of tianeptine and amitriptyline in a doses of (2, 4, 8, 16, and 32 ug/ml). It showed a statistically insignificant inhibitory effect of tianeptine and amitriptyline in doses of (2, 4, 8, 16 and 32ug/ml) on mean amplitude of contraction of isolated rabbit heart ($P>0.05$) compared with control value.

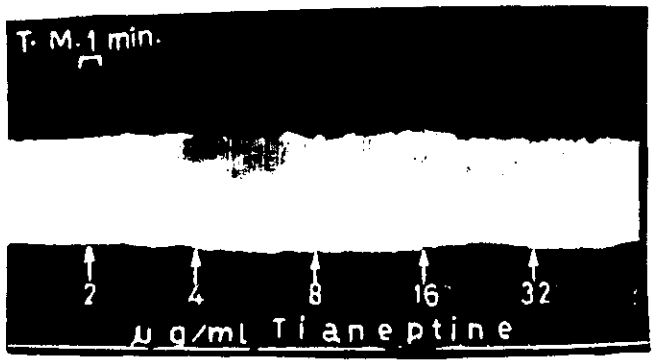


Fig. (14): A record showing the statistically insignificant changes of gradually increasing doses of (2, 4, 8, 16 and 32ug/ml) of tianeptine on mean amplitude of contraction of isolated rabbit heart.

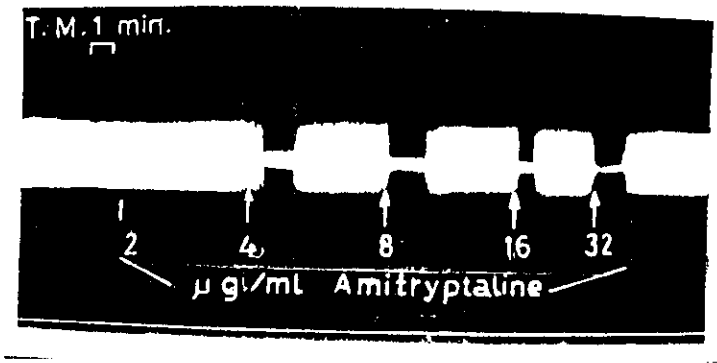


Fig. (15): A record showing the statistically insignificant inhibitory effect of gradually increasing doses of (2, 4, 8, 16, and 32ug/ml) of amitriptyline on mean amplitude of contraction of isolated rabbit heart.

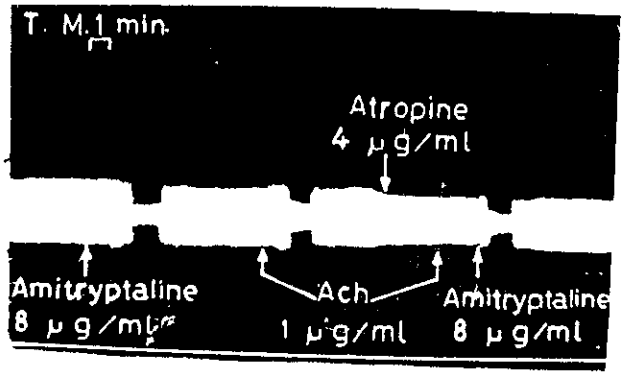


Fig. (16): A record showing the statistically insignificant inhibitory effect of (8ug/ml) amitriptyline which was not abolished after addition of atropine in a dose of (0.5ug/ml) on isolated rabbit heart.

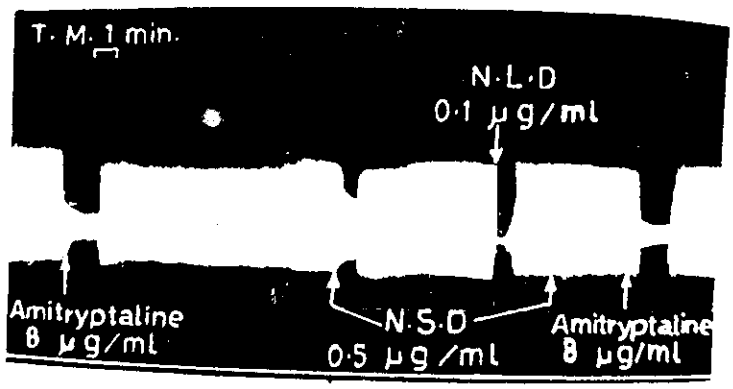


Fig. (17): A record showing the insignificant inhibitory effect of (8ug/ml) amitriptyline which was not abolished after addition of NLD in a dose of (0.1ug/ml) on isolated rabbit heart.

I-3-Isolated rabbit aorta:

*** Effect of increasing doses of tianeptine and amitriptyline on isolated rabbit aorta:**

It was observed that addition of both tianeptine and amitriptyline in dose of 2ug, 4ug, 8ug, 16ug and 32ug/ml. had no effect on the basal tone of isolated rabbit aorta. (table 4, Fig.18, 19, 20).

***Effects of tianeptine and amitriptyline on adrenergic receptors:**

It was observed that preincubation of tianeptine in a doses of 2ug, 4ug, 8ug , 16ug and 32ug/ml for 3 minutes before addition of norepinephrine in a dose of 5ug/ml produced statistically insignificant inhibition of the contractile response of the isolated rabbit aorta to norepinephrine ($p>0.05$) by a percentage of .00008%, 2.2%, 6.8%, 6.8% and 11.3% respectively.

on the other hand, preincubation of amitriptyline in a doses of 2ug, 4ug, 8ug, and 16ug/ml for 3 minutes before addition of norepinephrine in a dosc of 5ug/ml produced statistically insignificant inhibition ($p>0.05$) of the contractile response of the isolated rabbit aorta to norepinephrine by a percentage of 2.2, 4.5, 11.3, 13.63% respectively. while, preincubation of amitriptyline in a dose of 32ug/ml had statistically significant inhibitory effect on norepinephrine induced contractile response on isolated aortic rabbit strip by a percentage of 41.09%.(fig.19).

By comparing the tianeptine inhibitory effect on norepinephrine induced contraction of isolated rabbit aorta in doses of (2, 4, 8, 16, and 32ug/ml) and amitriptyline inhibitory effect on norepinephrine induced contraction on isolated rabbit aortic strip, it was observed that tianeptine

had statistically insignificant inhibitory effect in compared with amitripty.(fig. 18).

Table (4): showing the inhibitory effect of tianeptine and amitriptyline in doses of (2, 4, 8, 16, and 32ug) on mean ±SE of amplitude of norepinephrine induced contraction on isolated rabbit aorta.

Doses / Drugs	Control	2ug	4ug	8ug	16ug	32ug
Tianeptine		#	#	#	#	#
		4.4±0.32	4.3±0.25	4.1±0.43	4.1±0.45	3.9±0.51
	4.4±0.50	P1>0.05	P1>0.05	P1>0.05	P1>0.05	P1>0.05
Amitriptyline	{cm}	#	#	#	#	*
		4.3±.31	4.2±.42	3.9±.50	3.8±.48	2.7±.45
		P2>0.05	P2>0.05	P2>0.05	P2>0.05	P2<0.05

P1: compared the inhibitory effect of tianeptine in doses of (2, 4, 8, 16, and 32ug/ml) on mean amplitude of norepinephrine induced contraction on isolated rabbit aortic strip compared with control value.

P2: compared the inhibitory effect of amitriptyline in doses of (2, 4, 8, 16, and 32ug/ml) on mean amplitude of norepinephrine induced contraction on isolated rabbit aortic strip compared with control value.

N:B:

: statistically insignificant inhibitory effect (P>0.05).

*: stastistically significant inhibitory effect (P<0.05).

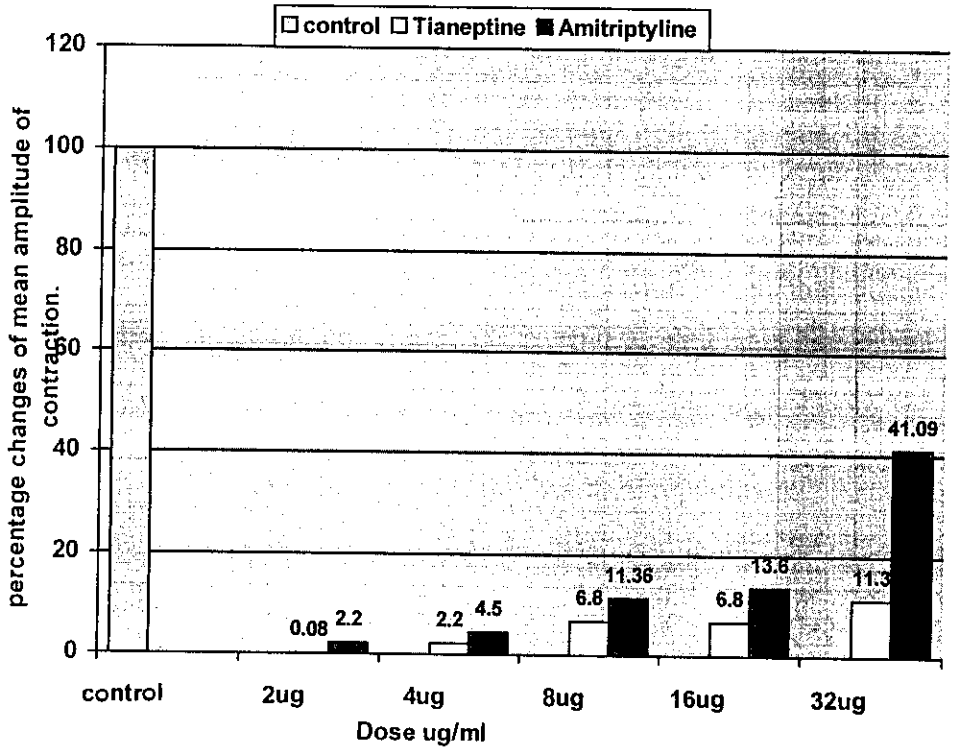


Fig.(18): histogram showing a percentage changes in mean amplitude of norepinphrine induced contraction on isolated rabbit aortic strip after addition of tianeptine in a doses of (2ug, 4ug, 8ug, 16ug, and 32ug/ml) and amitriptyline in the same doses.

It showed that tianeptine produced inhibitory effect less than amitriptyline in the same doses.

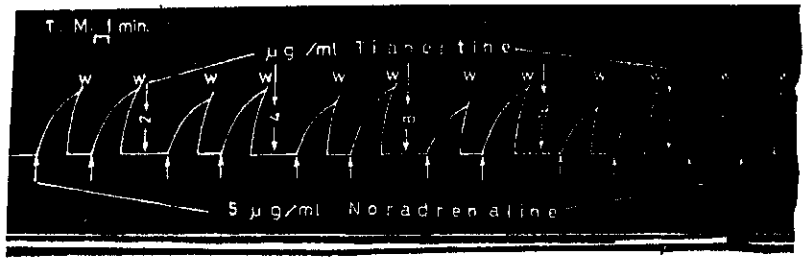


Fig. (19): a record showing the effect of gradually increasing doses of tianeptine (2, 4, 8, 16, 32ug/ml) on basal tone and amplitude of norepinephrine induced contraction on isolated rabbit aortic strip.

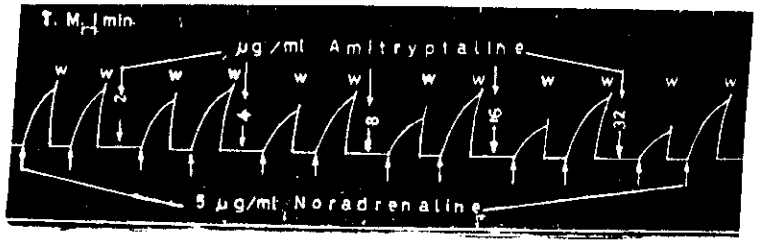


Fig. (20): a record showing the effect of gradually increasing doses of amitriptyline (2, 4, 8, 16, 32ug/ml) on basal tone and amplitude of norepinephrine induced contraction on isolated rabbit aortic strip.

In vivo experiments:

II-1- Effect on mean systolic blood pressure:

a) Effect of acute administration of tianeptine on mean systolic blood pressure:

The mean systolic blood pressure (SBP) at the start of the experiment (0 time) Was 125.83±1.49mmHg, after 15 min. after tianeptine injection, it was 125.76±2mmHg, after 30 min. it was125.66±1.66mmHg, after 60 min. it was 124.83±2.01mmHg and after 90 min. it was 124.66±1.60mmHg when these values were compared to control (0 time), there were statistically insignificant decrease in mean systolic blood pressure ($P>0.05$) (table 5, fig 21, 22).

b) Effect of acute administration of amitriptyline on mean systolic blood pressure:

The mean systolic blood pressure (SBP) at the start of the experiment (0 time) was 125.33±5.37mmHg, after15min. after amitriptyline injection it was 125.6±7.48mmHg, after 30min. it was 123.2±5.57mmHg , after 60min. it was 123.2±10.07mmHg and after 90 min. it was 122.4±6.01mmHg.When these values were compared to control (0 time) , there were statistically insignificant decrease in mean systolic blood pressure ($P<0.05$) (Table 5, fig. 21 ,23).

By comparing the effect of tianeptine with amitriptyline on mean systolic blood pressure there was no statistically difference between effect of both drugs.

Table (5): showing the effects of tianeptine and amitriptyline on mean systolic blood pressure and ±SE of mean.

Time / Groups	(0 time) control	15 min.	30 min.	60 min.	90 min.
Tianeptine group	125.83±1.49 mmHg	# 125.73±2 mmHg P1>0.05	# 125.66±1.66 mmHg P1>0.05	# 124.83±2.01 mmHg P1>0.05	# 124.66±1.6 mmHg P1>0.05
Amitriptyline group		# 125.6±7.48 mmHg P2>0.05	# 123.2±5.57 mmHg P2>0.05	# 123.4±10.0 mmHg P2>0.05	# 122.4±6.0 mmHg P2>0.05

P1: compared the effect of tianeptine on mean systolic blood pressure after 15 min.,30 min. ,60 min., and after 90 min.of acute I.P. administration of 10mg/kg with control value.

P2: compared the effect of amitriptyline on mean systolic blood pressure after 15 min.,30 min. ,60 min., and after 90 min.of acute I.P. administration of 10mg/kg with control value.

N:B:

#: insignificant decrease in mean systolic blood pressure (P>0.05).

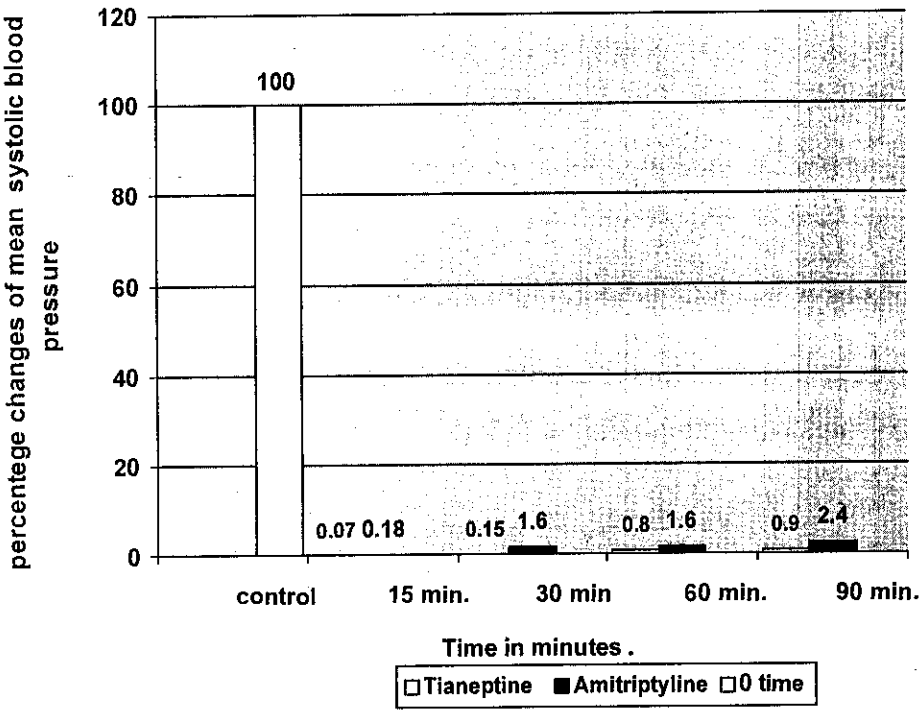
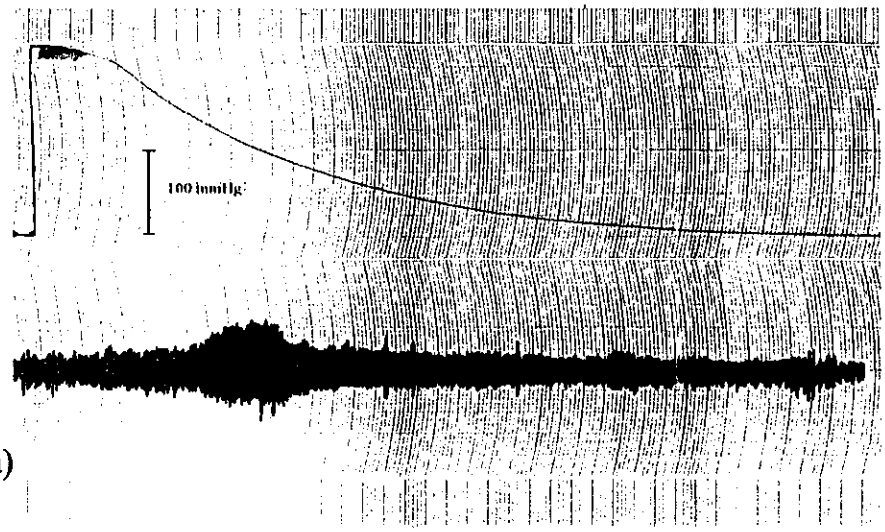
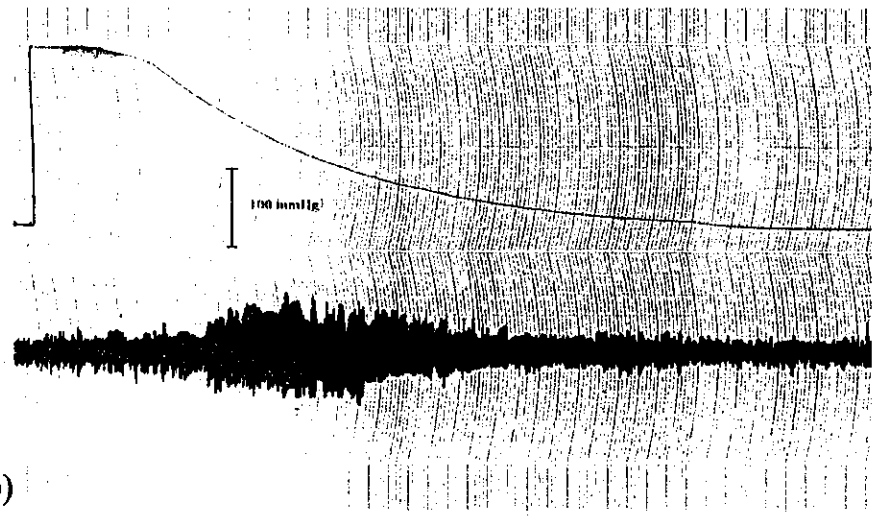


Fig.(21): histogram showing the percentage changes on mean systolic blood pressure after intraperitoneal injection of 10mg/k of tianeptine and amitriptyline. It shows statistically insignificant decrease in mean systolic blood pressure compared with control value and there were statistically no difference between the effect of both drugs on mean systolic blood pressure.



(a)



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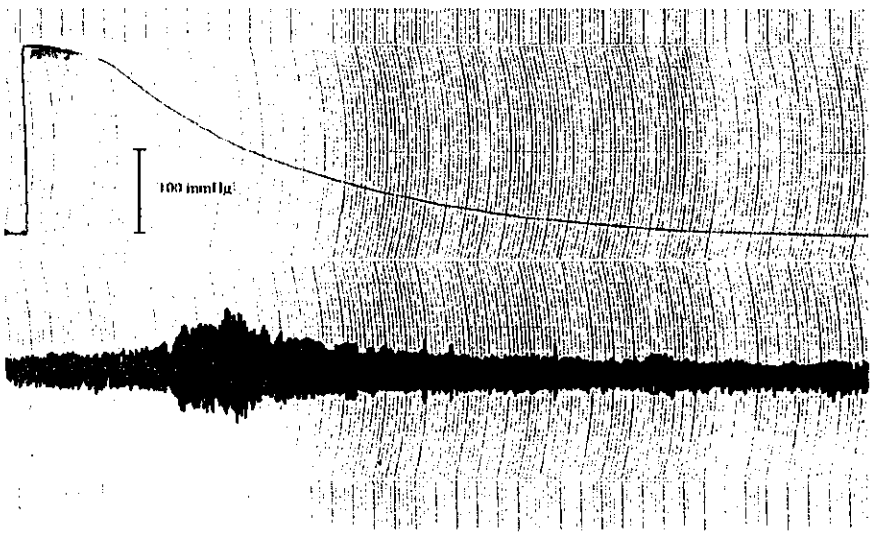


(c)

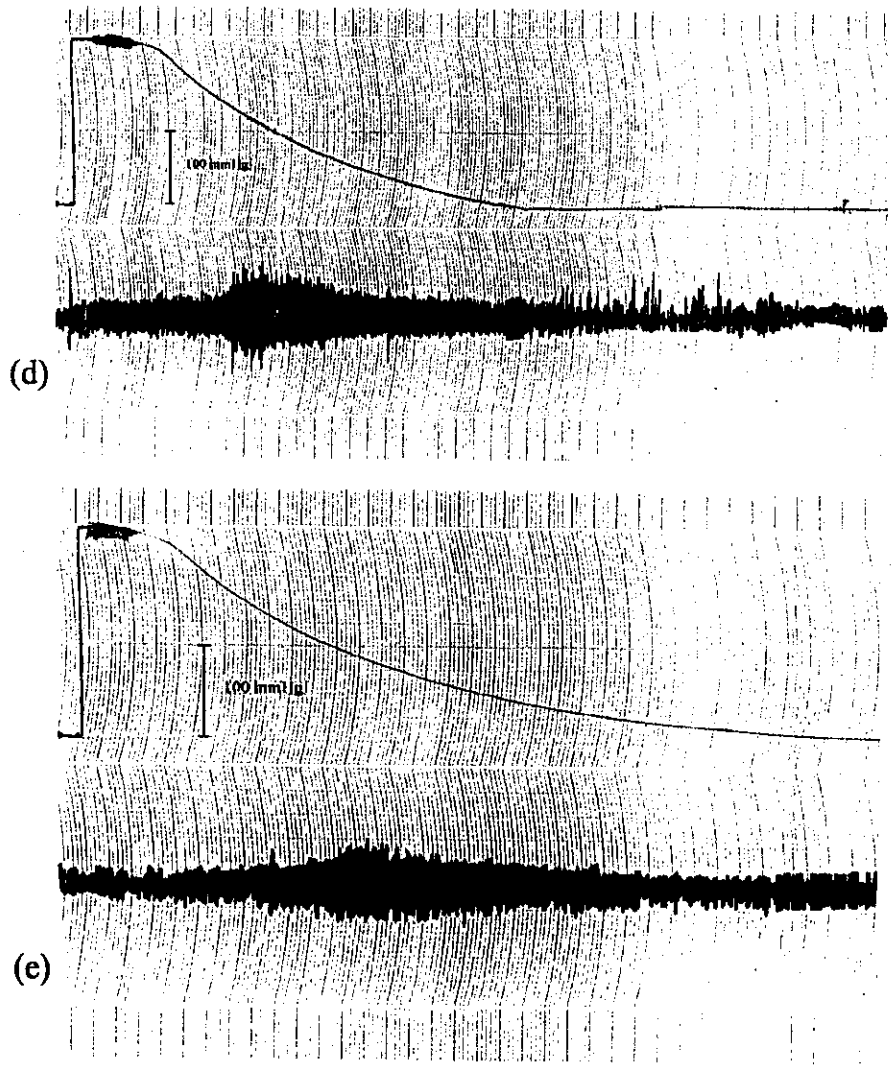
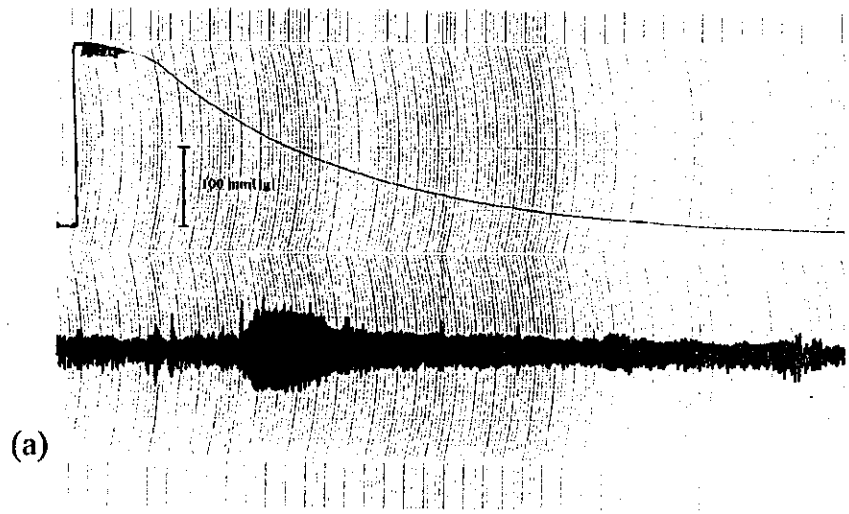


Fig. (22): the effect of acute I.P. injection of tianeptine in a dose of 10 mg/ kg on systolic blood pressure of rat.

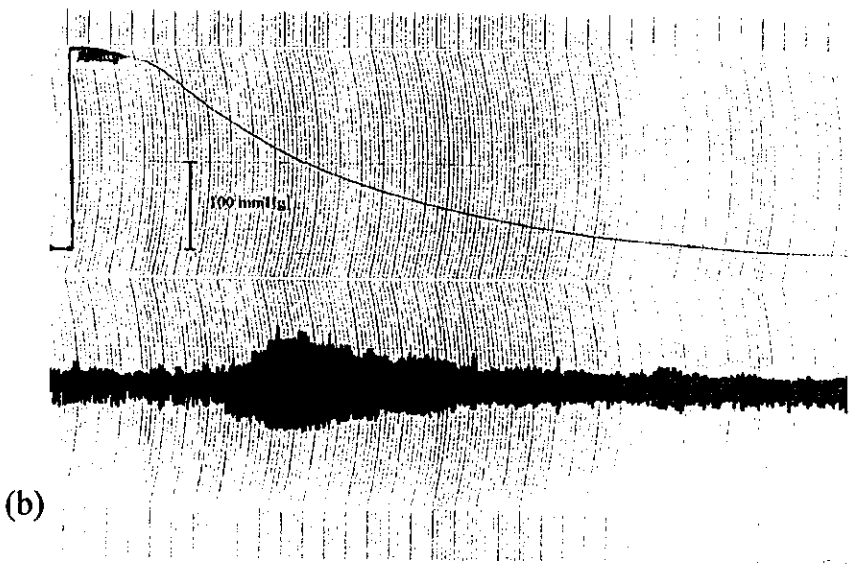
(a) Control (0 time : without drug.
(b) After (15 min.) of acute I.P. injection of 10 mg / kg of tianeptine.
(c) After (30 min.) of acute I.P. injection of 10 mg / kg of tianeptine.
(d) After (60 min.) of acute I.P. injection of 10 mg / kg of tianeptine.
(e) After (90 min.) of acute I.P. injection of 10 mg / kg of tianeptine.

- Lower trace represents pulse blood flow.
- Upper trace represents cuff pressure.

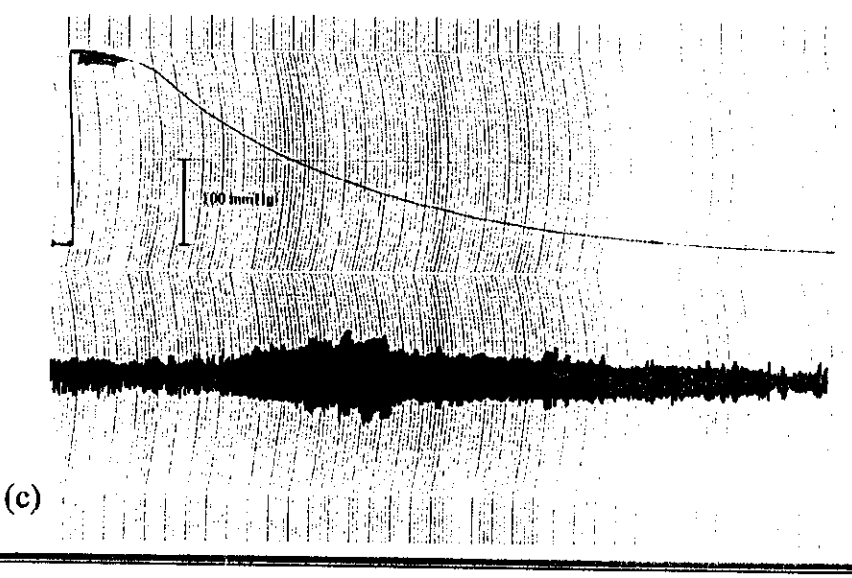
The systolic blood pressure measured at the startof pulsation and referenced to the pressure curve.



(a)



(b)



(c)

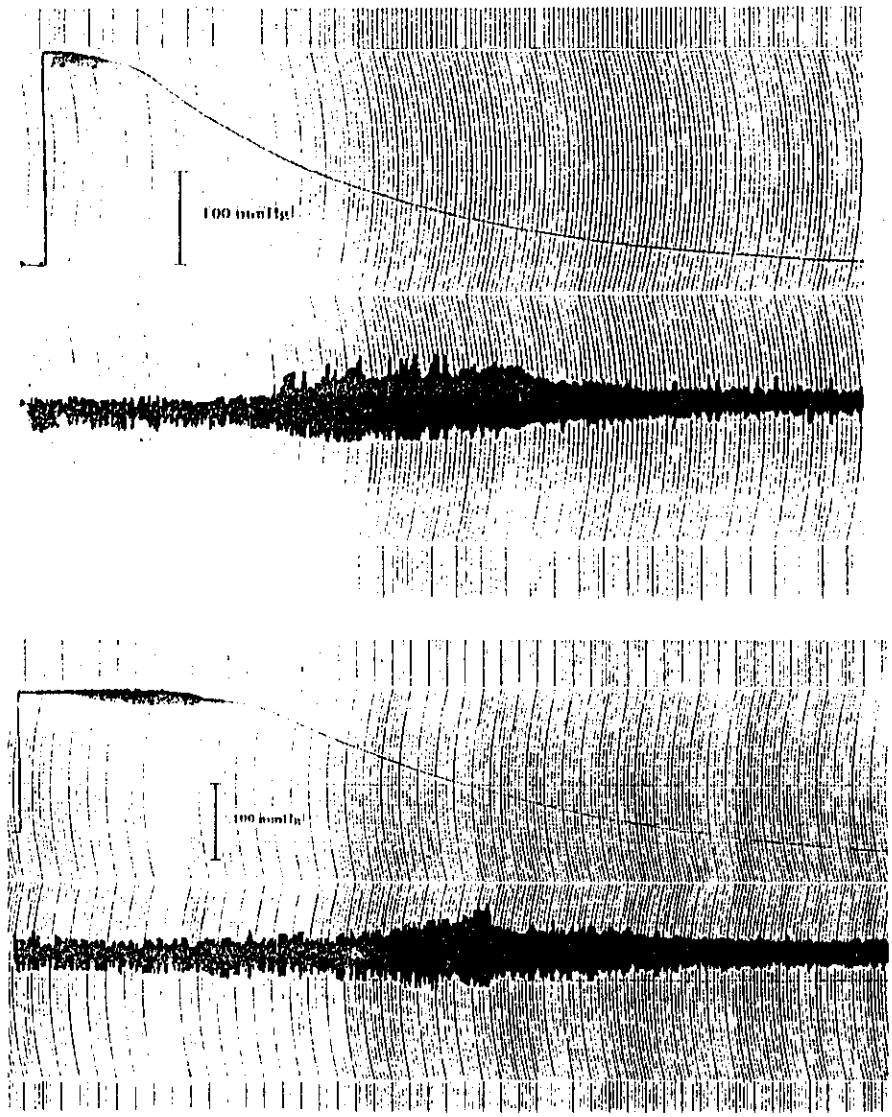


Fig. (23) : the effect of acute I.P. injection of amitriptyline in a dose of 10 mg/ kg on systolic blood pressure of rat.

(a) Control (0 time : without drug.
(b) After (15 min.) of acute I.P. injection of 10 mg / kg of amitriptyline.
(c) After (30 min.) of acute I.P. injection of 10 mg / kg of amitriptyline.
(d) After (60 min.) of acute I.P. injection of 10 mg / kg of amitriptyline.
(e) After (90 min.) of acute I.P. injection of 10 mg / kg of amitriptyline.

- Lower trace represents pulse blood flow.
- Upper trace represents cuff pressure.

The systolic blood pressure measured at the startof pulsation and referenced to the pressure curve.

II-2 -Effect on ECG:

***Heart rate:**

1- Tianeptine group:

The mean heart rate at the start of experiment (0 time) was 363.8±21,after15 min. of acute I.P. administration of tianeptine in a dose of 10mg/kg it was 360.5±18 and after 30 min. it was 360.6±21 after 60 min. it was 359±5 and after 90 min. it was 359.3±22 when these values were compared to control (0 time), there were statistically insignificant change in the heart rate ($p>0.05$). (Table 6,Fig. 23, 24).

b) Amitriptyline group:

Mean heart rate at the start of the experiment it was 363.8±21, after 15 min. of acute I.P. administration of amitriptyline in a dose of 10mg/kg it was 356.1±18, after 30 min. it was 349.5±17, after 60 min. 342.1±23 and after 90 min. it was 338.6±21 when these value were compared to control (0 time) there were statistically insignificant decrease in the heart rate ($P>0.05$) (Table 6, Fig 23, 25).

By comparing the effect of tianeptine on mean rat heart rate and amitriptyline after intraperitoneal injection of the same dose (10mg/kg) there was statistically insignificant difference between both drugs.

Table(6): shows effect of intraperitoneal injection of (10mg/ml) tianeptine and amitriptyline on mean heart rate and ±SE of mean {beat/minute}compared with control value.

Time / Groups	O time (control)	15 min.	30 min.	60 min.	90 min.
Tianeptine group		# 363.5±18 P1>0.05	# 360.6±21 P1>0.05	# 359.5±22 P1>0.05	# 359.3±22 P1>0.05
Amitriptyline group	363.8±21	# 356.1±18 P2>0.05	# 349.5±17 P2>0.05	# 342.1±23 P2>0.05	# 338.6±21 P2>0.05

P1: compared the mean heart rate after 10mg/kg injection of tianeptine, which showed statistically insignificant changes in mean heart rate with control value.

P2: compared the mean heart rate after injection of amitriptyline (10mg/kg), which showed statistically insignificant changes in mean heart rate with control value

#: statistically insignificant decrease in mean heart rate (P>0.05).

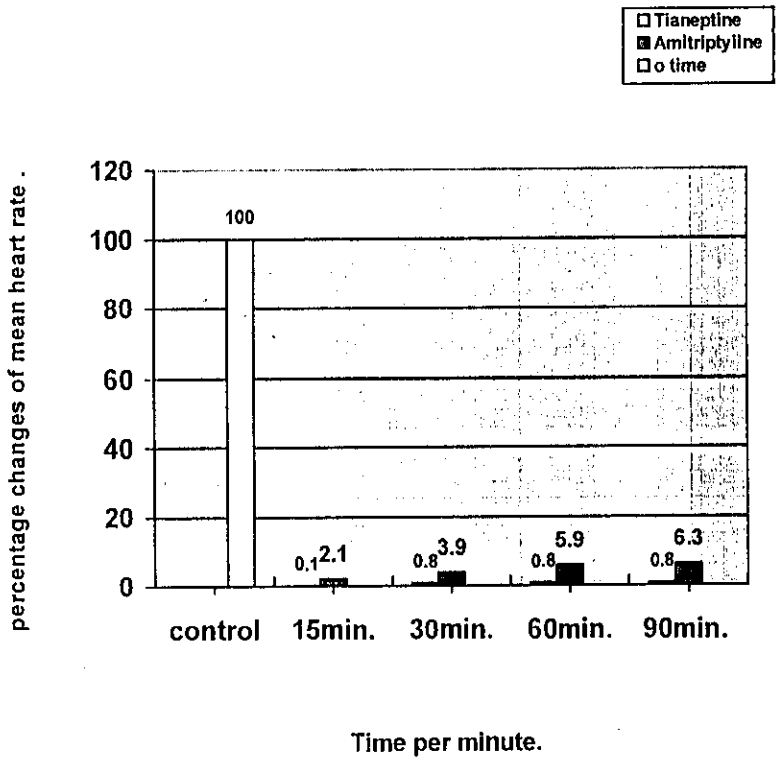


Fig.(21): histogram showing the percentage changes of mean heart rate of anesthetized rat after intraperitoneal injection of 10mg/kg of tianeptine and amitriptyline.

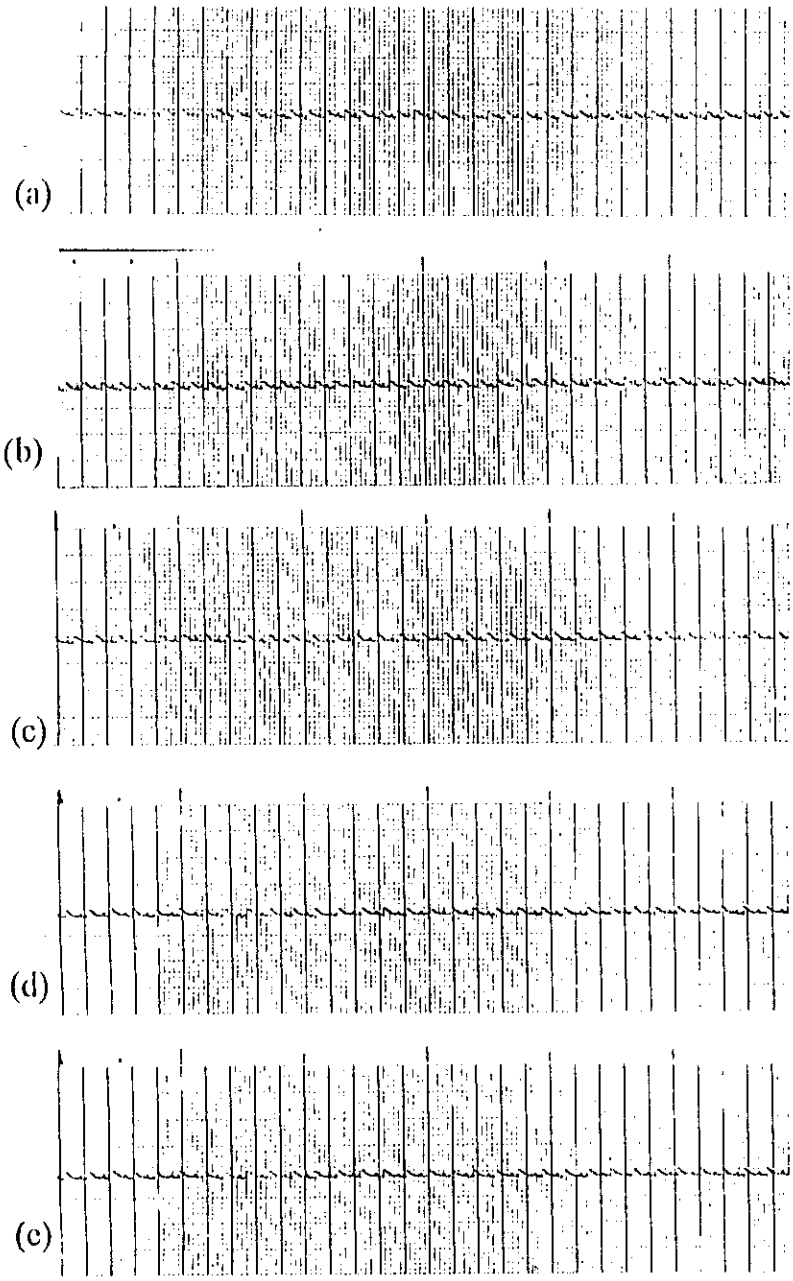


Fig. (25) ECG traces demonstrating the effect of acute I.P. injection of tianeptine on heart rate of urethane anesthetized rats:

(a) Control (0 time): record with no drug.
(b) After (15 min.) of acute I.P. injection of 10 mg / kg of tianeptine.
(c) After (30 min.) of acute I.P. injection of 10 mg / kg of tianeptine.
(d) After (60 min.) of acute I.P. injection of 10 mg / kg of tianeptine.
(e) After (90 min.) of acute I.P. injection of 10 mg / kg of tianeptine.

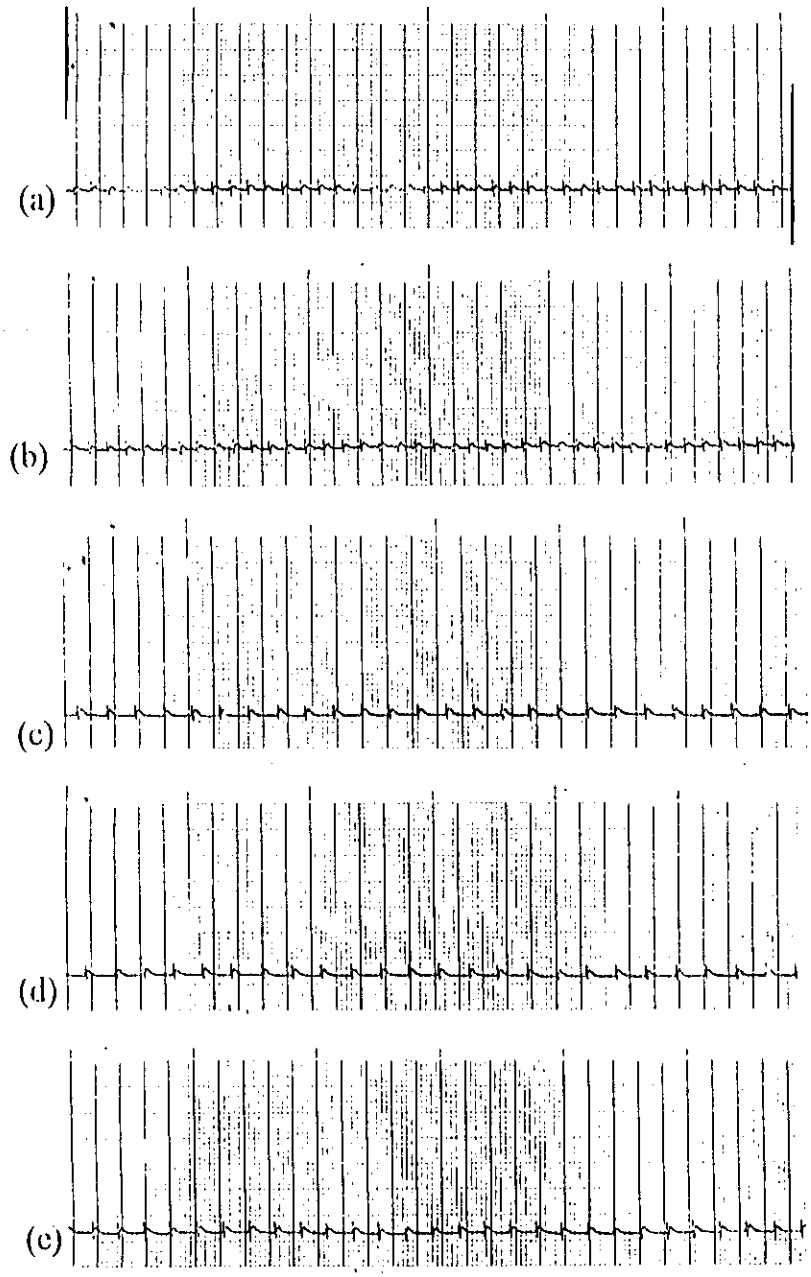


Fig. (26) ECG traces demonstrating the effect of acute I.P. injection of amitriptyline on heart rate of urethane anesthetized rats:

(a) Control (0 time): record with no drug.
(b) After (15 min.) of acute I.P. injection of 10 mg / kg of amitriptyline.
(c) After (30 min.) of acute I.P. injection of 10 mg / kg of amitriptyline.
(d) After (60 min.) of acute I.P. injection of 10 mg / kg of amitriptyline.
(e) After (90 min.) of acute I.P. injection of 10 mg / kg of amitriptyline .

C-Analgesic effect of tianeptine:-

The acute administration of tianeptine in a dose of 10mg/kg body weight, induced an analgesic effect as measured by analgesimeter.The reading at 0 time was310.83±22.7 force(g),after15 min.it was 490.16±19.8, after 30 min.it was 580.33±50.1, after 60 min. it was 630.8±22.7 and after 90 min. the reading was 680.8±12.5force(g), when compared these values with control, there were statistically significant analgesic effect of tianeptine.(Table7, fig 27).

While, the acute administration of amitriptyline I.P bolus dose of 10mg/kg body weight, induced an analgesic effect as measured by analgesimeter. The reading at 0 time was 310.83±33.2 force(g), after 15 min. the reading was 510.17±56.1force(g) , after 30 minutes it was 614.19±19.6, after 60 min.it was 710.1±27.3 and after 90 min. it was 769.2±22.1when we compare these value with control (0 time), there were statistically significant analgesic effect of amitriptyline ($P<0.05$).(Table 7, 27).

By comparing the analgesic effect of tianeptine versus amitriptyline after intraperitoneal injection of 10mg/kg of tianeptine and amitriptyline it was found statistically insignificant difference between both drugs.

Table (7): showing the statistically significant analgesic effect of tianeptine and amitriptyline and ±SE of mean.{force (g)}.

Time / Groups	0 time	15min.	30min	60min.	90min.
Tianeptine group	310.83±22.7 force{g}	* 490.16±19.8 p1<0.05	* 580.33±50.1 p1<0.05	* 630.8±22.7 p1<0.05	* 680.8±12.5 p1<0.05
Amitriptyline group		* 510.17±56.1 P2<0.05	* 614.19±19.6 P2<0.05	* 710.1±27.3 P2<0.05	* 769.2±22.1 P2<0.05

P1: compared the analgesic effect of tianeptine after acute I.P. administration of 10mg/kg to rats with control value.

P2: compared the analgesic effect of amitriptyline after acute I.P. administration of 10mg/kg to rats with control value.

N.B:

*: statistically significant analgesic effect (P<0.05).

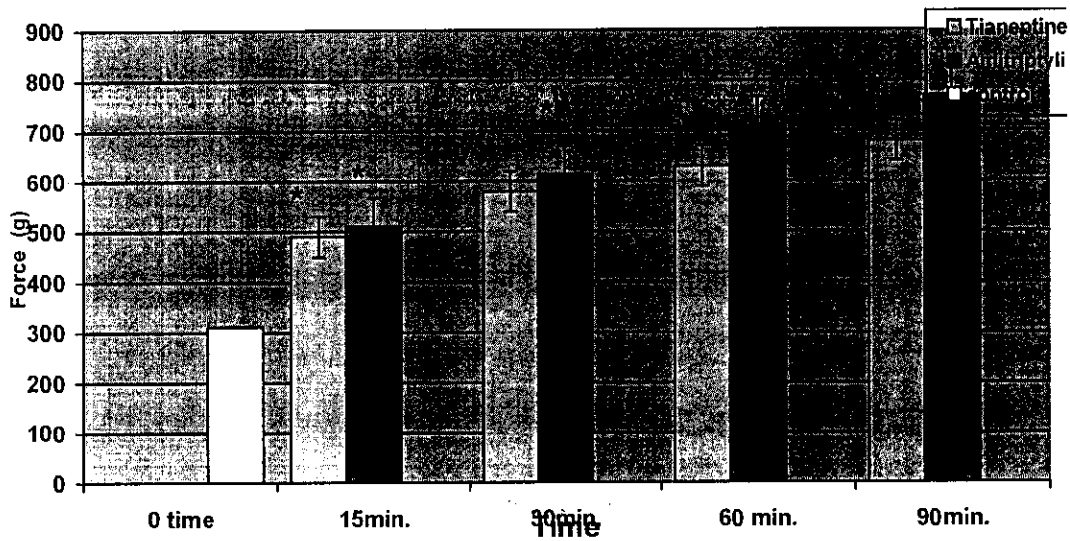


Fig. (27): histogram showing the statistically significant analgesic effect of tianeptine and amitriptyline compared with control value.

N:B

*significant analgesic effect ($P<0.05$).