RESULTS

I. In vivo experiments:

A-Effect of pretreatment of atorvastatin (10mg/kg p.o) 2 hours before and / or pioglitazone (10mg/kg p.o) 2 hours before experimentally induced acute myocardial infarction induced by isoprenaline (150mg/kg s.c) in non diabetic and L-fructose induced diabetic albino rats:

Data was analysed 4 hrs after induction of myocardial infarction.

1.Heart rate changes:

In infracted non diabetic rats, there was significant increase ($p<0.05$) in heart rate in infracted group compared to control group, while in atorvastatin pretreated group, pioglitazone pretreated group and combination group(atorvastatin+ pioglitazone) pretreated group there was significant reduction ($p<0.05$)in heart rate compared to infracted group but it was still at significant higher level ($p<0.05$) if compared to control group (Table 1, Figure 1, 7 ,8, 9, 10, 11).

In infracted diabetic rats there was significant increase ($p<0.05$) in heart rate in diabetic-infarcted group compared to control diabetic group, while there was significant reduction ($p<0.05$)in heart rate in atorvastatin pretreated group, pioglitazone pretreated group and combination (atorvastatin+pioglitazone) pretreated group compared to diabetic-infarcted but its level still significantly elevated ($p<0.05$) if compared to control group. (Table 2 , Figure 4, 12, 13, 14, 15, 16).

2.ST segment elevation changes:

In infracted non diabetic rats, there was significant increase($p<0.05$) in ST segment elevation in infracted group compared to

control group, while in atorvastatin pretreated group, there was significant decrease in ST segment elevation compared to infracted group infarcted but it was still at significant higher level ($p<0.05$) if compared to control group, In pioglitazone pretreated group and combination (atorvsatatin+ pioglitazone) pretreated group there was significant decrease ($p<0.05$) in ST segment elevation compared to infracted and atorvastatin pretreated groups but its level still significantly elevated ($p<0.05$) if compared to control group (Table 1, Figure 2, 7, 8, 9, 10, 11).

In infracted diabetic rats there was significant increase ($p<0.05$)in ST segment elevation in diabetic-infarcted group compared to control diabetic group, while there was significant decrease ($p<0.05$) in ST segment elevation in atorvastatin pretreated group and pioglitazone pretreated group compared to diabetic-infarcted and combination (atorvastatin+ pioglitazone) pretreated groups but its level still significantly elevated ($p<0.05$) if compared to control group, also there was significant decrease ($p<0.05$) in ST segment elevation in combination(atorvastatin+ pioglitazone) pretreated group compared to diabetic-infarcted while it was still at significant higher level($p<0.05$) if compared to control diabetic group. (Table 2, Figure 5, 12, 13, 14, 15, 16).

3.CPK-MB changes:

In infracted non diabetic rats there was significant increase ($p<0.05$)in CPK-MB fraction in infracted group compared to control group, while in atorvastatin pretreated group there was significant decrease ($p<0.05$) in CPK-MB fraction ($p<0.05$) compared to infracted group while it was still at significant higher level($p<0.05$) if compared to control group. pre-treatment of infarcted rats of group IV with pioglitazone and group V combination (atorvastatin+ pioglitazone)

decrease CPK-MB level significantly (P < 0.05) compared to infracted and atorvastatin pretreated groups but it was still at significant higher level (p<0.05) if compared to control group (Table 1, Figure 3).

In infracted diabetic rats there was significant increase (P < 0.05) in CPK-MB level compared to control diabetic group (group I), While pre-treatment of infracted-diabetic rats of group III with atorvastatin decreases CPK-MB level significantly (P < 0.05) compared to diabetic-infarcted group but it was still significantly high (p<0.05) if compared to control diabetic group (Table 2, Figure 6).

Pre-treatment of diabetic-infarcted rats of group IV with pioglitazone and group V with atorvastatin and pioglitazone decrease CPK-MB level significantly (P < 0.05) compared to diabetic-infarcted and atorvastatin pretreated groups but it its level still significantly elevated (p<0.05) if compared to control diabetic group (Table 2, Figure 6).

4. Histopathological studies data analysis among groups with acute myocardial infarction:

Normal myocardium stains pink ,while the injured myocardium stains pale pink .The sections were examined by the ordinary light microscope.

Histopathological examination of the heart for detection of signs of acute ischemia and inflammation was done at the end of the experiment with comparison of signs of acute infarction (changes in cardiomyocyte bundles, nuclear shape and nuclear cytoplasm) in different groups**.**

Histopathology indicates that in infracted non diabetic rats pioglitazone pre-treated group had the little signs of acute infarction

,followed by the combination (atorvastatin+pioglitazone) pre-treated group. But atorvastatin pre-treated group showed the most evident signs of acute infarction (Fig17, 18, 19, 20, 21).

While in infracted diabetic rats combination (atorvastatin+pioglitazone) pre-treated group had the little signs of acute infarction ,followed by pioglitazone pre-treated group. But atorvastatin pre-treated group showed the most evident signs of acute infarction **(**Fig 22, 23, 24, 25, 26).

Table (1): Effect of Mean ± SEM of atorvastatin (10mg/kg p.o) 2 hours before and / or pioglitazone (10mg/kg p.o) 2 hours before infarction on heart rate (b/min), ST segment elevation (mm) and CPK-MB (u/l) in acute myocardial infarction induced by isoprenaline (150mg/kg s.c) in albino rats:

Parmeter / Groups	Heart rate (b/min)	ST segment elevation (mm)	CPK-MB (u/l)
Control group	301±8	0	1452±18.6
Infracted group Percent change %	596±15.17[a] 100%	11.6 ± 0.39[a] 100%	3170±21.2[a] >100%
Ator pre-treated group Percent change %	499±18[a,b] ↓16.27%	7.25 ± 0.32[a,b] ↓ 37.5	2666±16.4[a,b] ↓15.89%
Pioglitazone pre-treated group Percent change %	437±19[a,b] ↓26.67%	4.5 ±0.32[a,b,c] ↓ 61.2	1980±11.3[a,b,c] ↓ 37.53%
Ator+Pioglitazone pre-treated group Percent change %	428±11[a,b] ↓28.18%	4.35 ±0.19[a,b,c] ↓ 62.5	1965±13.6[a,b,c] ↓38.01%

a: Significant difference versus control at $p<0.05$

b: Significant difference versus infarcted group at $p<0.05$

c: Significant difference versus atorvastatin group at $p<0.05$

N.B: % change is calculated in relation to infracted group.

Table (2): Effect of Mean ± SEM of atorvastatin(10mg/kg p.o) 2 hours before and / or pioglitazone (10mg/kg p.o) 2 hours before infarction on acute myocardial infarction induced by isoprenaline (150mg/kg s.c) on heart rate (b/min), ST segment elevation (mm) and CPK-MB (u/l) in experimentally-induced diabetic albino rats by administration of 10%l-fructose solution in drinking water for 8 weeks:

Parmeter / Groups	Heart rate (b/min)	ST segment elevation (mm)	CPK-MB (u/l)
Diabetic group	310 ± 13	0	1685±17.3
Diabetic- infracted group Percent change %	603±20[a] 100%	12.1 ± 0.56[a] 100%	3880±32.5[a] 100%
Ator pre-treated group Percent change %	415 ± 13[a,b] ↓14.75	7.8±0.38[a,b,d] ↓35.5	3118±19.6[a,b] ↓ 19.63%
Pioglitazone pre-treated group Percent change %	450 ± 8[a,b] ↓ 25.37	7.4±0.34[a,b,d] ↓38.8	2713±22.8 [a,b,c] ↓ 30.7%
Ator+Pioglitazone pre-treated group Percent change %	406 ± 10[a,b] ↓32.66	5.72±0.39[a,b] ↓ 52.7	2805±17.5 [a,b,c] ↓ 27.7%

a: Significant difference versus diabetic group at $p<0.05$.

b: Significant difference versus diabetic infracted group at $p<0.05$.

c: Significant difference versus diabetic-infarcted+atorvastatin group at $p<0.05$.

d: Significant difference versus diabetic-infarcted+atorvastatin+pioglitazone group at $p<0.05$.

N.B: % change is calculated in relation to infracted group.

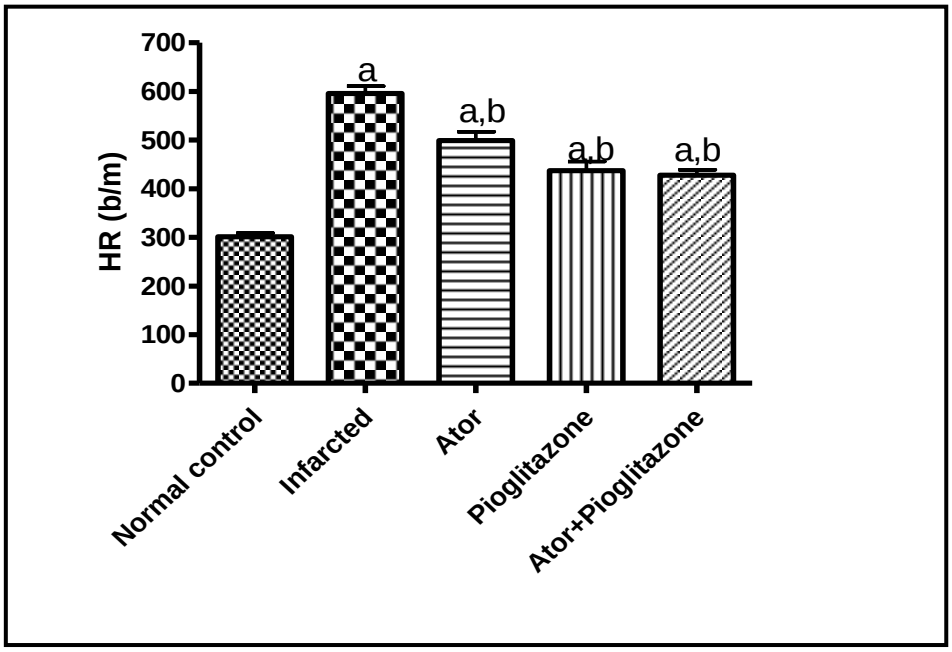


Fig. (1): Effect of atorvastatin(10mg/kg p.o) 2 hours before and / or pioglitazone(10mg/kg p.o) 2 hours before infarction on heart rate in acute myocardial infarction induced by isoprenaline (150mg/kg s.c) in albino rats.

Data are presented as mean ± SEM

a: Significant difference versus control at $p<0.05$

b: Significant difference versus infarcted group at $p<0.05$

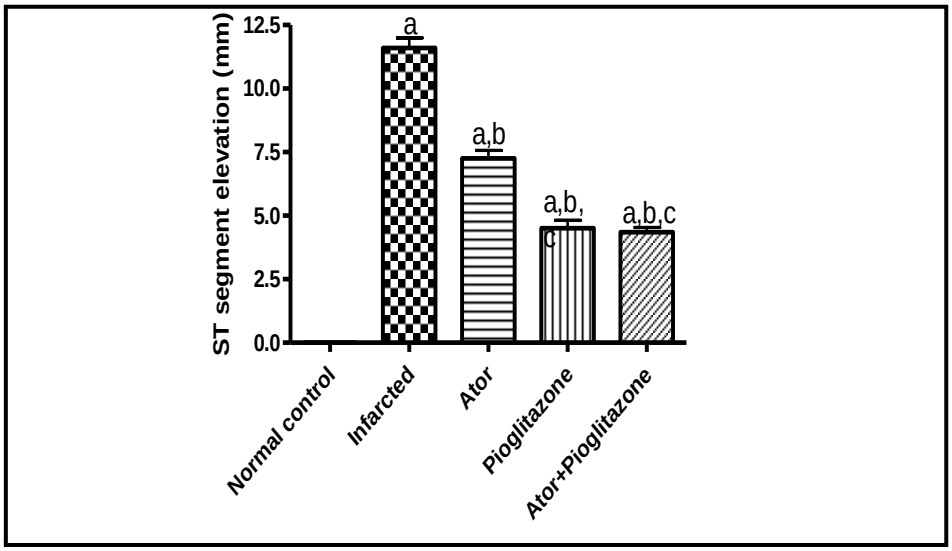


Fig. (2): Effect of atorvastatin(10mg/kg p.o) 2 hours before and / or pioglitazone(10mg/kg p.o) 2 hours before infarction on ST segment elevation in acute myocardial infarction induced by isoprenaline (150mg/kg s.c) in albino rats.

Data are presented as mean ± SEM

a: Significant difference versus control at $p<0.05$

b: Significant difference versus infarcted group at $p<0.05$

c: Significant difference versus atorvastatin group at $p<0.05$

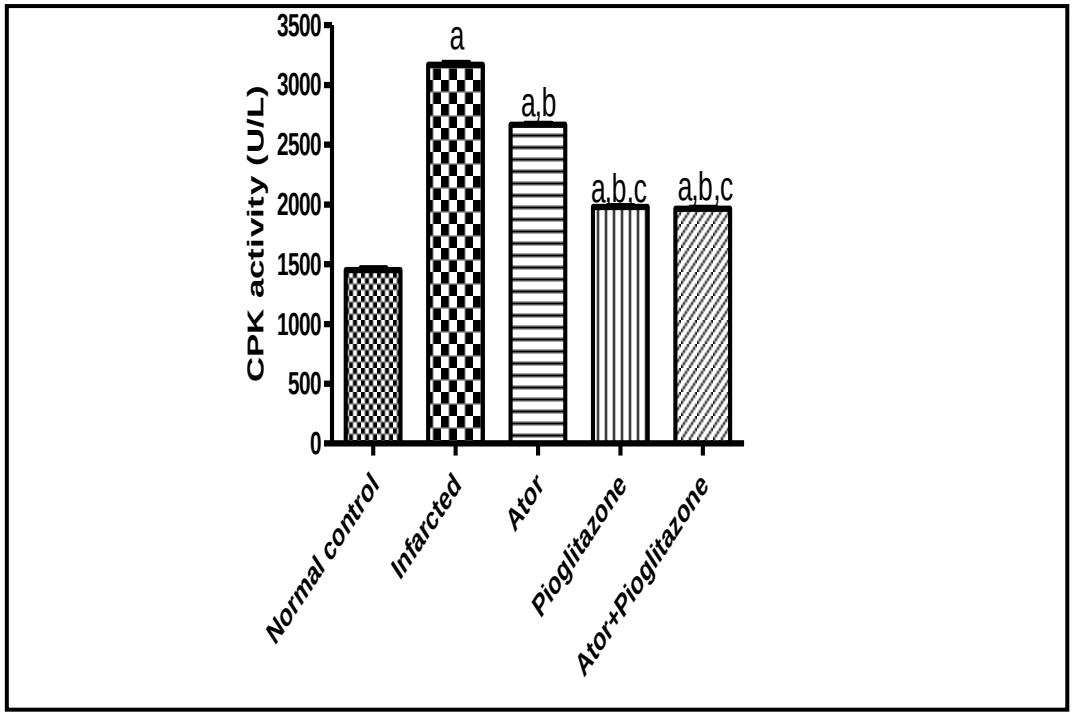


Fig. (3): Effect of atorvastatin(10mg/kg p.o) 2 hours before and /or pioglitazone(10mg/kg p.o) 2 hours before infarction on CPK-MB in acute myocardial infarction induced by isoprenaline (150mg/kg s.c) in albino rats.

Data are presented as mean ± SEM

a: Significant difference versus control at $p<0.05$

b: Significant difference versus infarcted group at $p<0.05$

c: Significant difference versus atorvastatin group at $p<0.05$

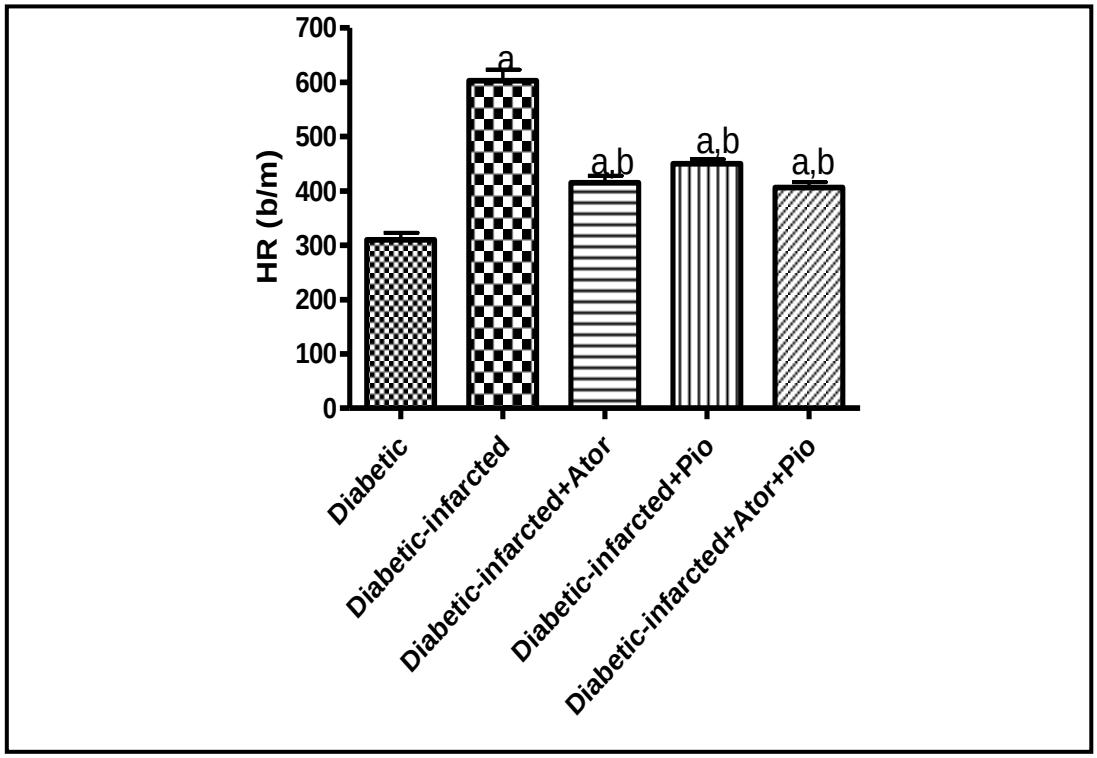


Fig. (4): Effect of atorvastatin(10mg/kg p.o) 2 hours before and / or pioglitazone(10mg/kg p.o) 2 hours before infarction on acute myocardial infarction induced by isoprenaline (150mg/kg s.c) on heart rate in experimentally- induced diabetic albino rats by administration of 10%l-fructose solution in drinking water for 8 weeks.

Data are presented as mean ± SEM .

a: Significant difference versus diabetic group at $p<0.05$.

b: Significant difference versus diabetic infracted group at $p<0.05$.

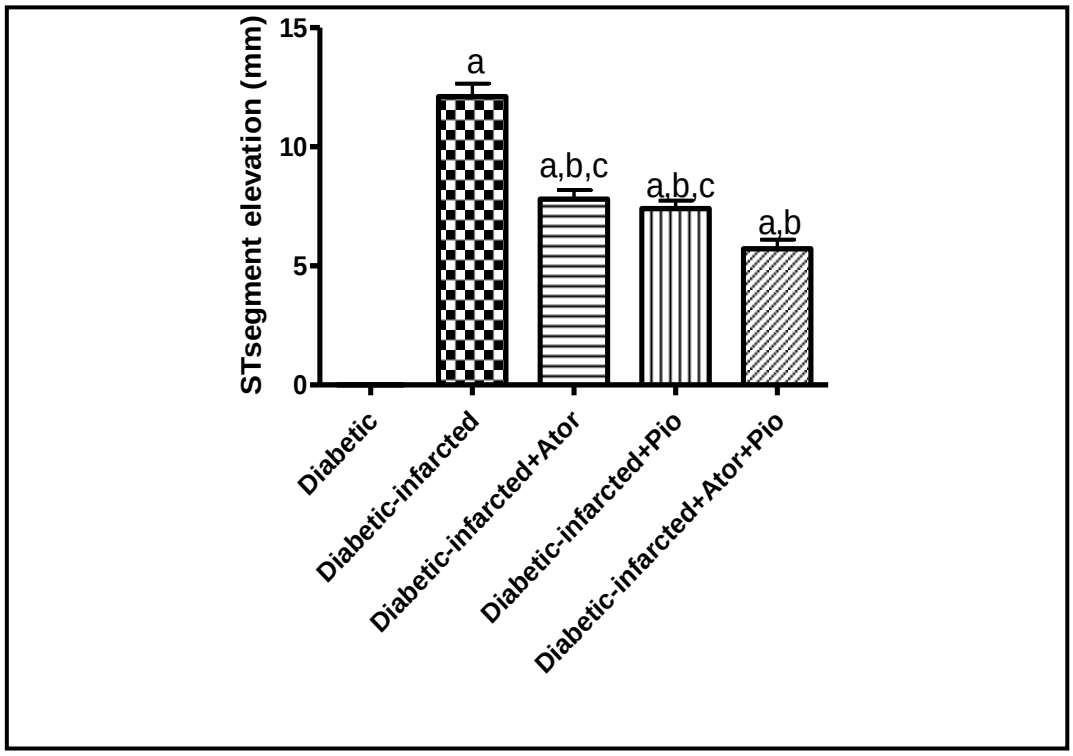


Fig. (5): Effect of atorvastatin(10mg/kg p.o) 2 hours before and / or pioglitazone (10mg/kg p.o) 2 hours before infarction on acute myocardial infarction induced by isoprenaline (150mg/kg s.c) on ST segment elevation in experimentally-induced diabetic albino rats by administration of 10%l-fructose solution in drinking water for 4 weeks.

Data are presented as mean ± SEM .

a: Significant difference versus diabetic group at $p<0.05$.

b: Significant difference versus diabetic infracted group at $p<0.05$.

d: Significant difference versus diabetic-infarcted+atorvastatin+pioglitazone group at $p<0.05$.

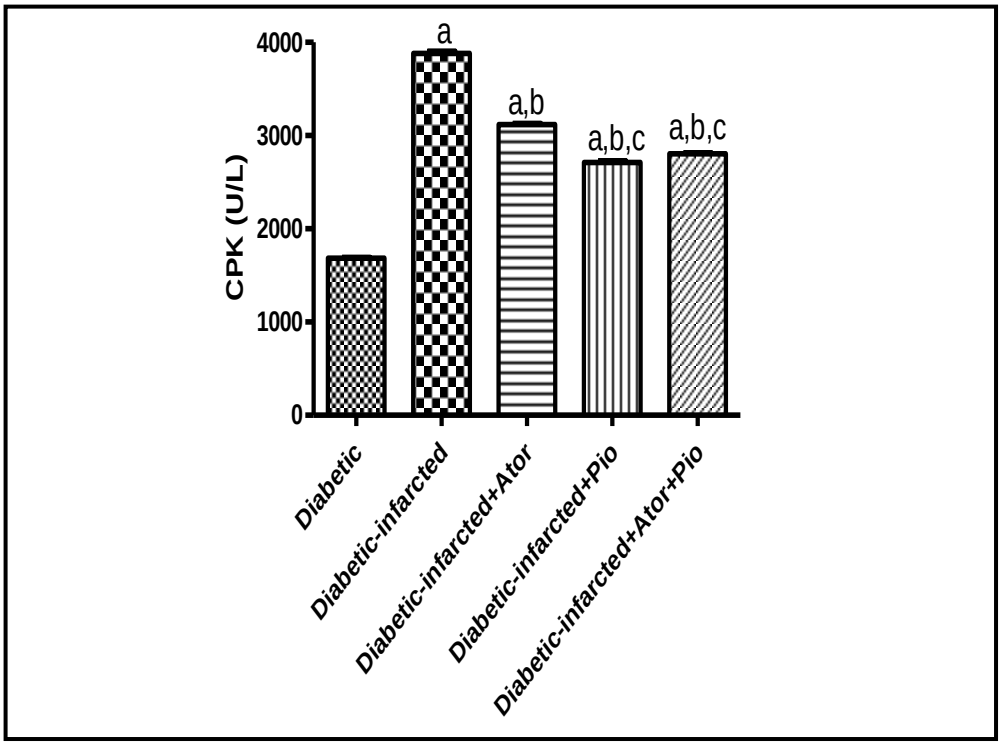


Fig.(6): Effect of atorvastatin(10mg/kg p.o) 2 hours before and / or pioglitazone(10mg/kg p.o) 2 hours before infarction on acute myocardial infarction induced by isoprenaline (150mg/ kg s.c) on CPK-MB in experimentally-induced diabetic albino rats by administration of 10%l-fructose solution in drinking water for 4 weeks.

Data are presented as mean ± SEM .

a: Significant difference versus diabetic group at $p<0.05$.

b: Significant difference versus diabetic infracted group at $p<0.05$.

c: Significant difference versus diabetic-infarcted+Ator group at $p<0.05$.

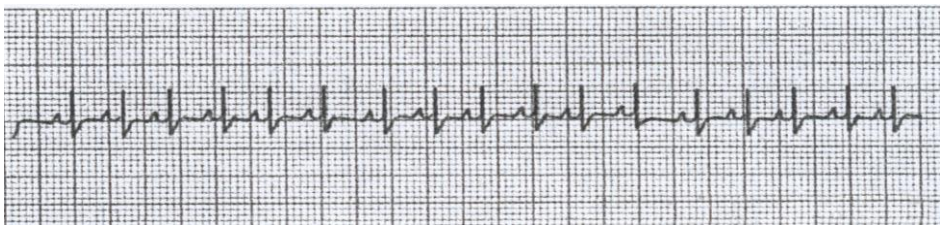


Fig.(7): ECG Tracing (lead II) of control normal rat (after 4 hours).

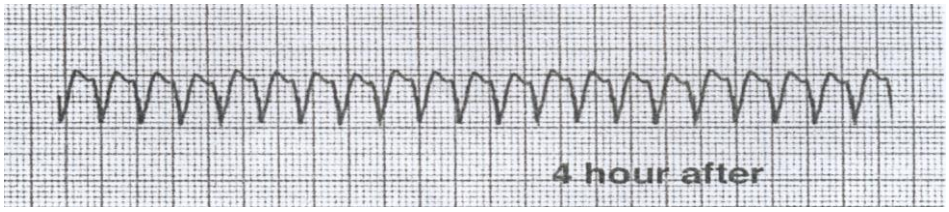


Fig.(8): ECG Tracing (lead II) of infarcted non pre-treated rat received isoprenaline s.c injection (after 4 hours after isoprenaline).

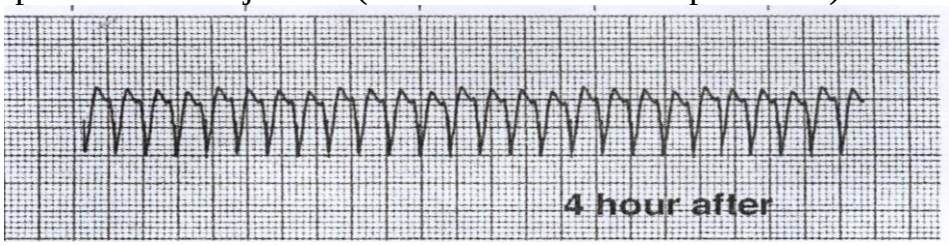


Fig.(9): ECG Tracing (lead II) of infarcted atorvastatin pre-treated rat received isoprenaline s.c injection (after 4 hours after isoprenaline).

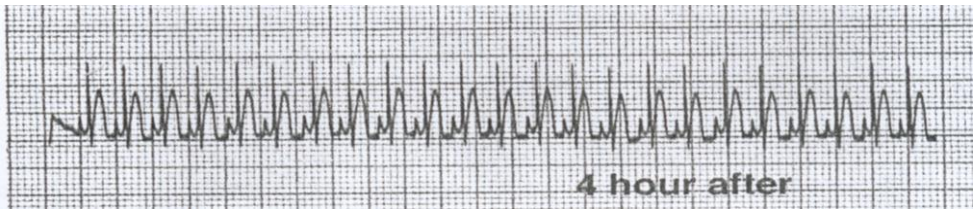


Fig.(10): ECG Tracing (lead II) of infarcted pioglitazone pre-treated rat received isoprenaline s.c injection (after 4 hours after isoprenaline).

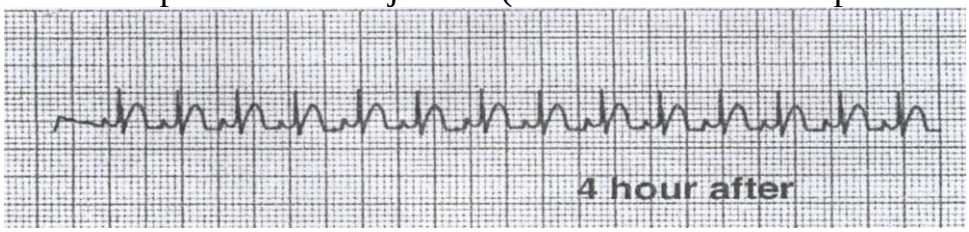


Fig.(11): ECG Tracing (lead II) of infarcted atorvastatin +pioglitazone pre-treated rat received isoprenaline s.c injection (after 4 hours after isoprenaline).

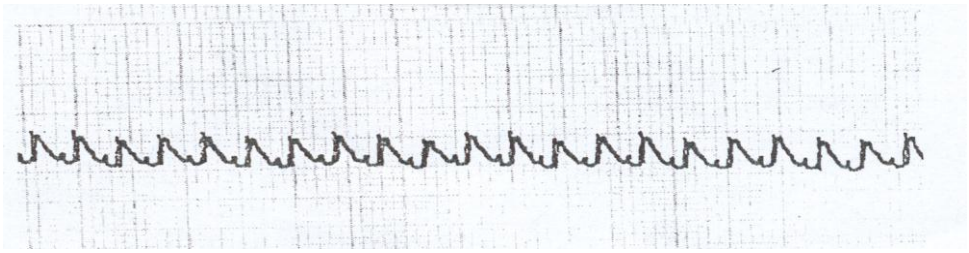


Fig.(12): ECG Tracing (lead II) of control diabetic rat (after 4 hours).

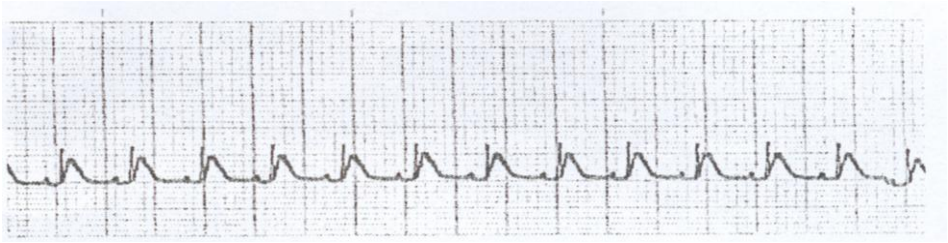


Fig.(13): ECG Tracing (lead II) of infracted-diabetic non pre-treated rat received isoprenaline s.c injection (after 4 hours after isoprenaline).

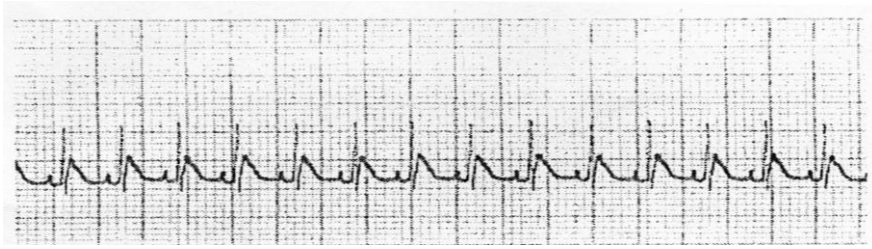


Fig.(14): ECG Tracing (lead II) of infracted-diabetic atorvastatin pre-treated rat received isoprenaline s.c injection (after 4 hours after isoprenaline).

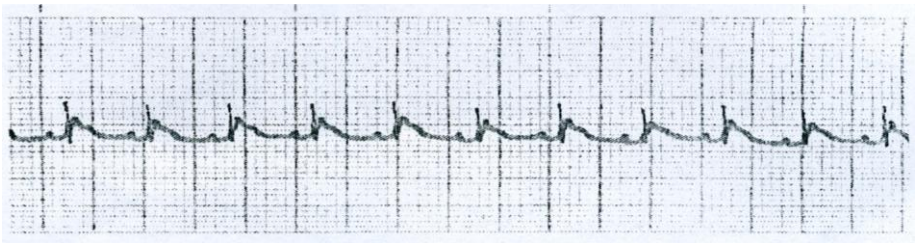


Fig.(15): ECG Tracing (lead II) of infracted- diabetic pioglitazone pre-treated rat received isoprenaline s.c injection (after 4 hours after isoprenaline).

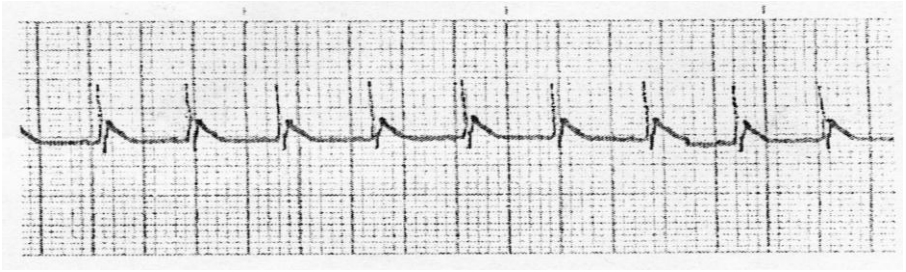


Fig.(16): ECG Tracing (lead II) of infarcted- diabetic atorvastatin +pioglitazone pre-treated rat received isoprenaline s.c injection (after 4 hours after isoprenaline).

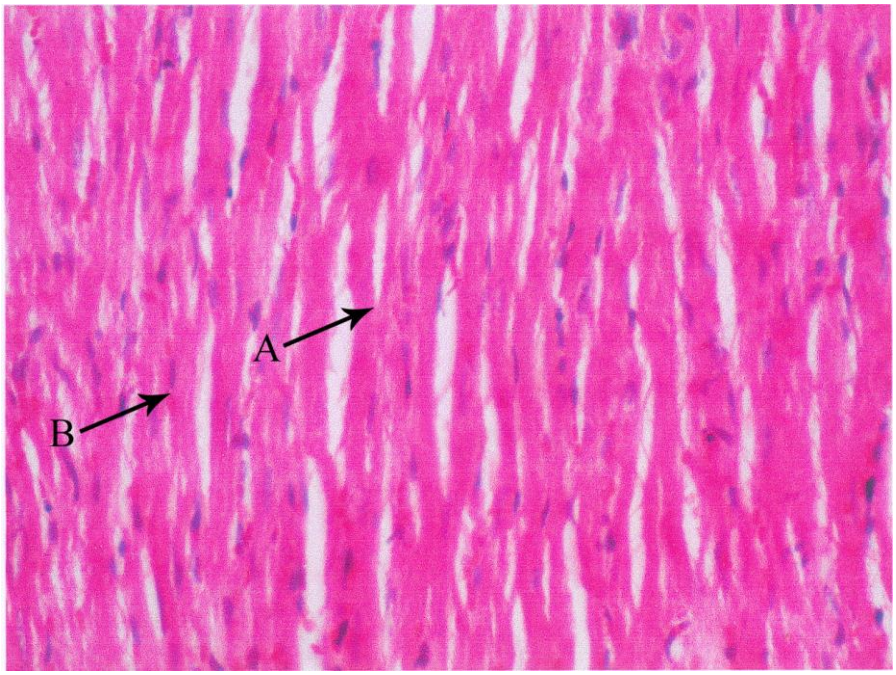


Fig.(17): A photomicrograph of a cut section in the heart of a control rat (group I) Showing interlacing (a) bundles of cardiomyocytes with (b) spindle shaped nucleus with abundant eosinophilic cytoplasm.(H&Ex40).

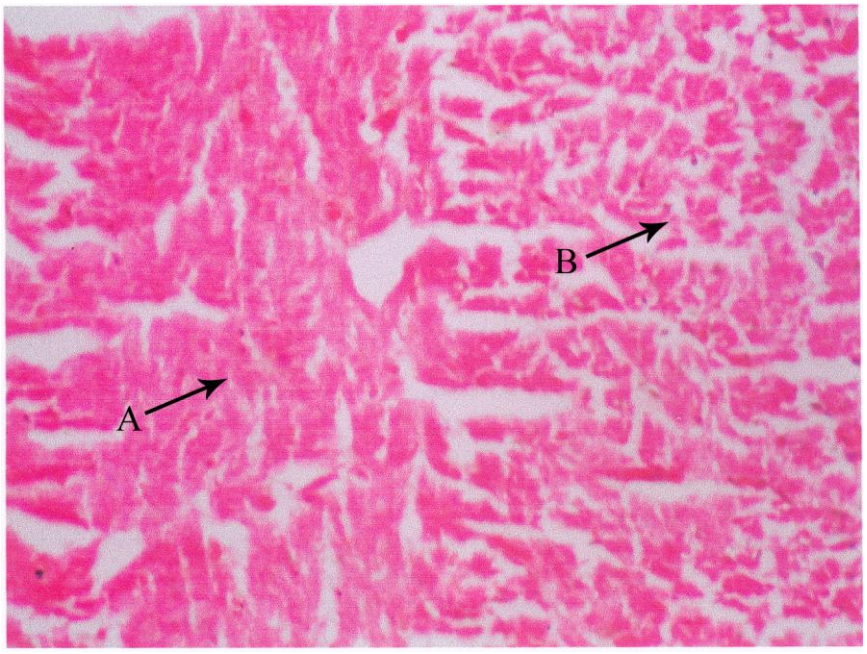


Fig.(18): A photomicrograph of a cut section in the heart of an infarcted rat (group II) Showing (a) ghosts of cardiomyocytes with cellular details. (b) nuclei showing pyknotic changes. (H&Ex40).

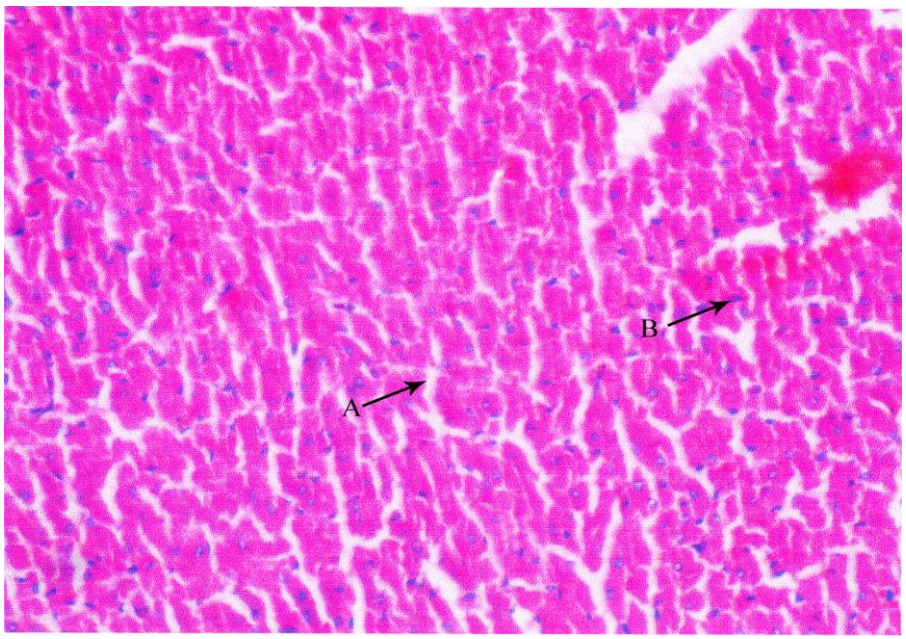


Fig.(19): A photomicrograph of a cut section in the heart of a pioglitazone pretreated rat (group VI) Showing reversal of infarction changes with (a) interlacing bundles of cardiomyocytes with (b) spindle shaped nucleus and abundant eosinophilic cytoplasm. (H&Ex40).

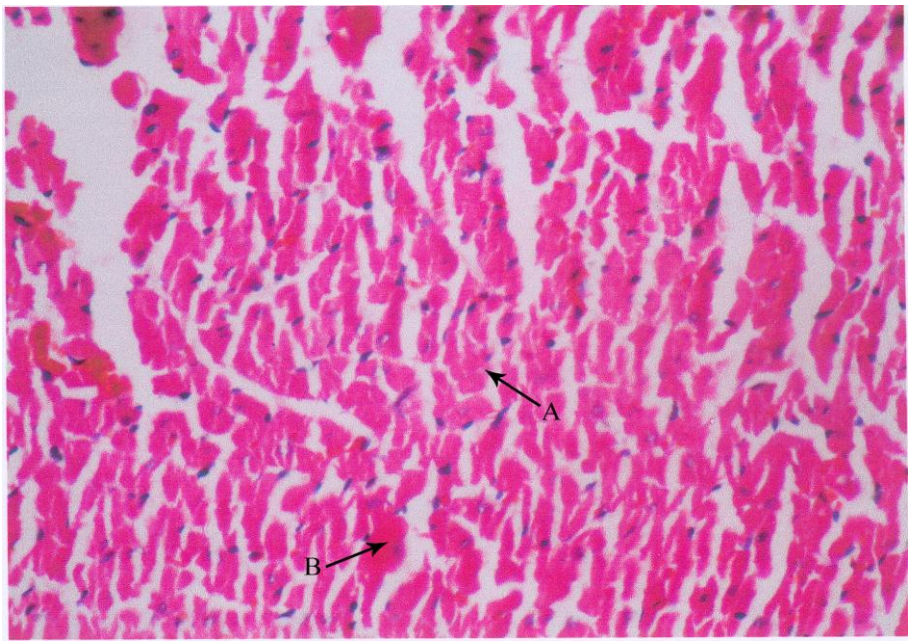


Fig.(20): A photomicrograph of a cut section in the heart of a atorvastatin+pioglitazone pretreated rat (group V) Showing (a) normal appearing cardiomyocytes with (b) scatterd foci of necrotic areas. (H&Ex40).

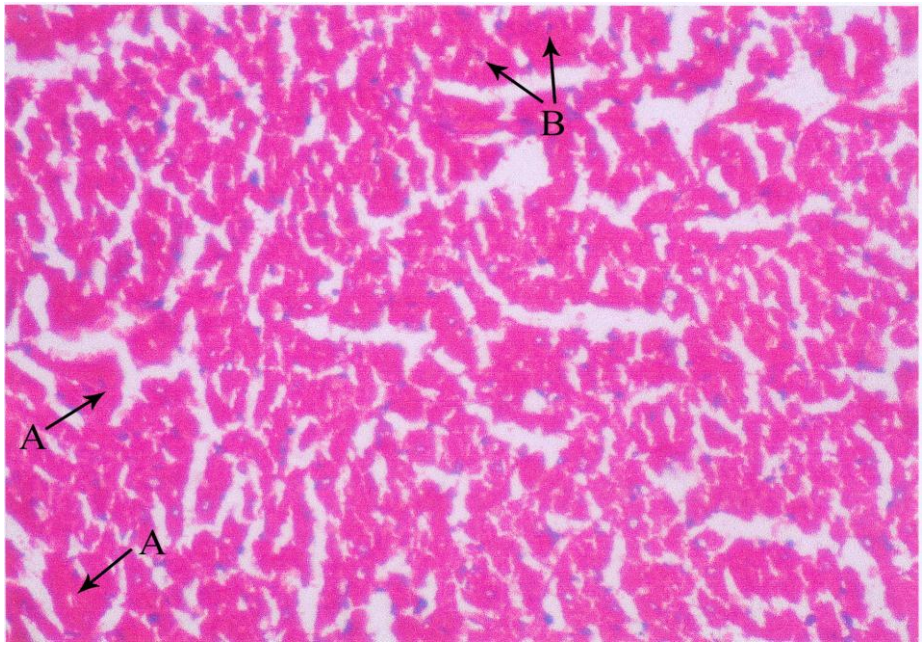


Fig.(21): A photomicrograph of a cut section in the heart of a atorvastatin pretreated rat (group III) Showing (a) wide area of necrotic cardiomyocytes and (b) pyknotic nuclei. (H&Ex40).

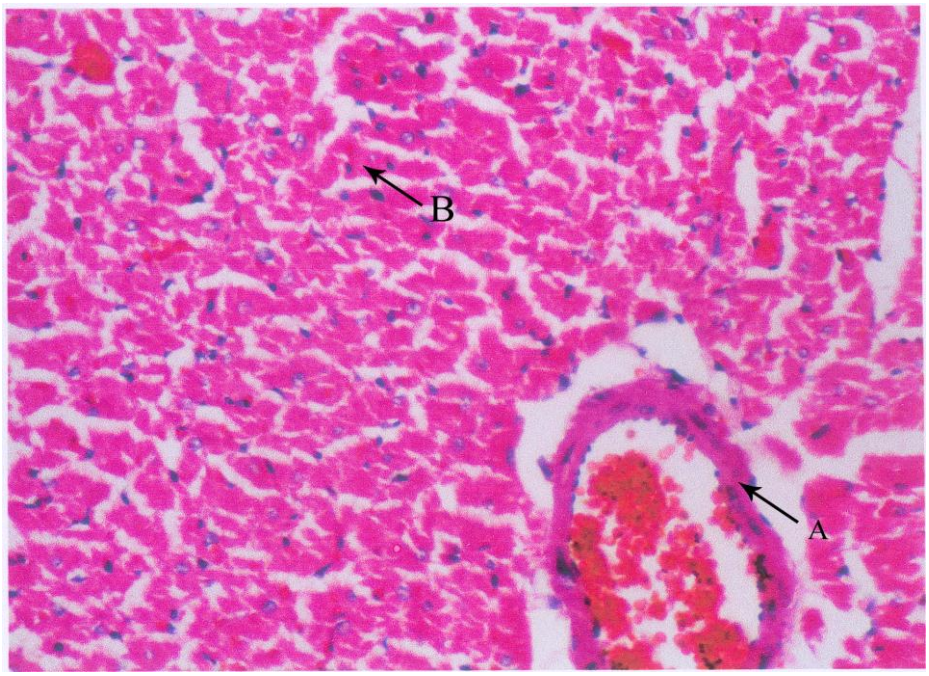


Fig.(22): A photomicrograph of a cut section in the heart of a control diabetic rat (group I) Showing (a) some hyalinosis and scelerosis of blood vessel wall with (b) slight atrophic cardiomyocytes. (H&Ex40).

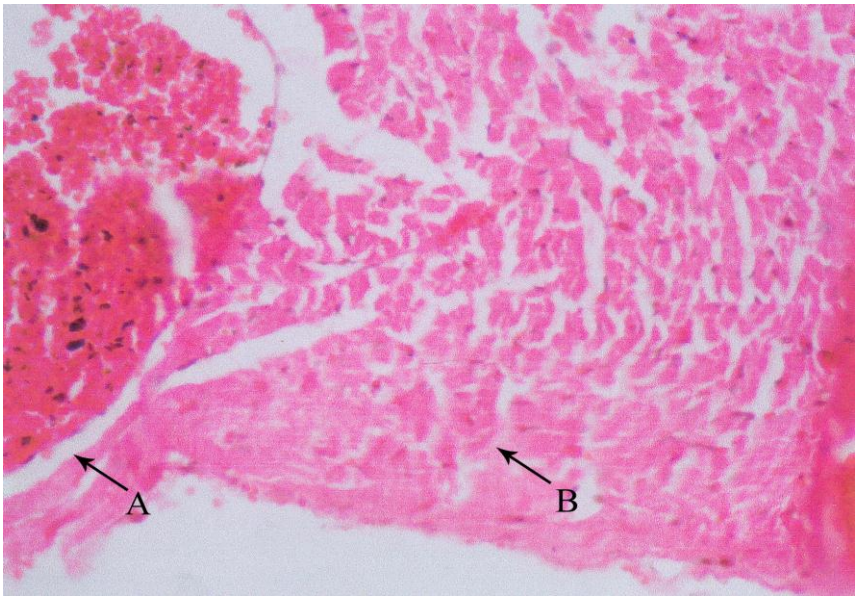


Fig.(23): A photomicrograph of a cut section in the heart of a diabetic rat with acute infarction (group II)Showing (a) necrotic areas with loss of cellular detailes and pyknotic nuclei. (b) Adjacent areas showing hyalinosis and scelerosis of blood vessel wall. (H&Ex40).

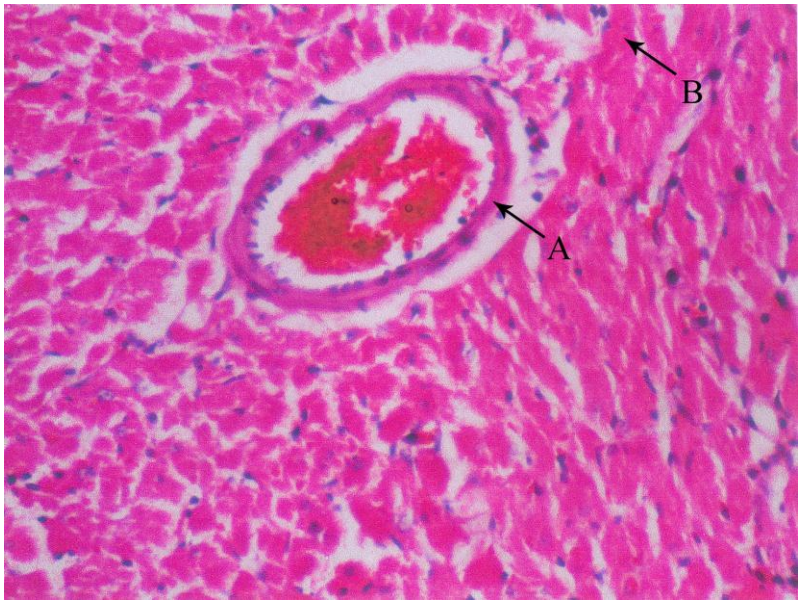


Fig.(24): A photomicrograph of a cut section in the heart of a diabetic rat with acute infartion received atorvastatin+pioglitazone pretreatment (group V)Showing (a) some hylinosis and scelerosis of the blood vessel wall with (b) slight atrophic cardiomyocytes. (H&Ex40).

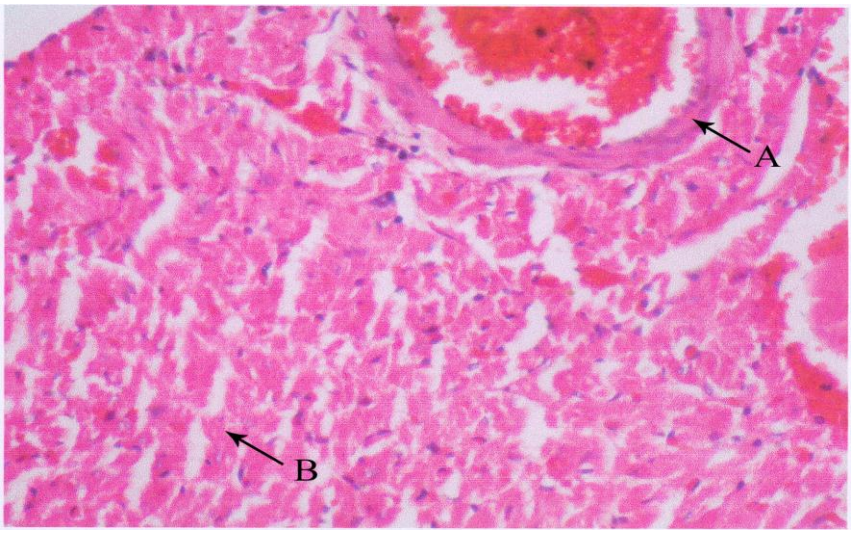


Fig.(25): A photomicrograph of a cut section in the heart of a diabetic rat with acute infartion received pioglitazone pretreatment (group IV) Showing (a) some hylinosis and scelerosis of the blood vessel wall and (b) focal areas of necrotic cardiomyocytes with pycnotic nuclei. (H&Ex40).

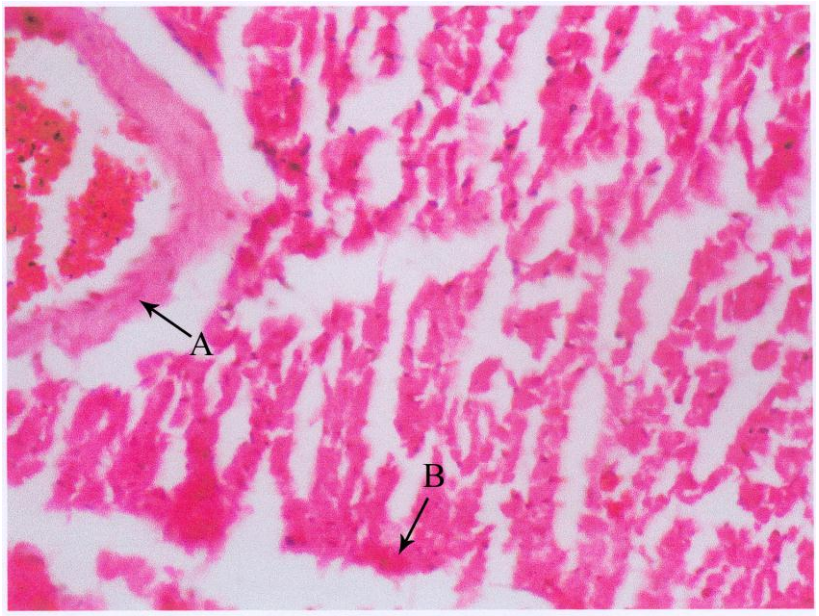


Fig.(26): A photomicrograph of a cut section in the heart of a diabetic rat with acute infartion received atorvastatin pretreatment(group III)Showing (a) necrotic area with loss of cellular details and pycnotic nuclei. (b) Adjacent areas showing hyalinosis and scelerosis of blood vessels. (H&Ex40).

B-Effect of atorvastatin (10mg/kg p.o for 2 weeks) and / or pioglitazone (10mg/kg p.o for 2 weeks)on experimentally induced type II diabetes mellitus (by administration of 10%L-fructose solution in drinking water for 4 weeks).

1.Arterial blood pressure changes:(Fig: 35, 36, 37, 38, 39)

In non treated diabetic group there was significant increase($p<0.05$) in mean arterial blood pressure compared to control group.The current work also demonstrated statistically significant reduction ($p<0.05$) in mean arterial blood pressure in atorvastatin pretreated group, pioglitazone pretreated group and combined group (atorvastatin+pioglitazone) pretreated group compared to diabetic non treated group (Table 3, Figure 27).

2.Lipid profile changes:

2-1.Total cholesterol level changes:

L-fructose administration resulted in statistically significant increase ($p<0.05$) in total cholesterol level in diabetic non treated group compared to control group. Treatment of diabetic group of rats with atorvastatin and also in pioglitazone treated group reduced total cholesterol level significantly ($p<0.05$) compared to diabetic non treated group but it was still at significant higher level ($p<0.05$) if compared to control group. By using combined drugs (atorvastatin+pioglitazone) there was significant reduction ($p<0.05$) of total cholesterol level compared to atorvastatin treated and diabetic non treated groups but it its level still significantly elevated ($p<0.05$) if compared to control group (Table 4, Figure 28).

2-2.Triglycerid level changes:

Concerning triglycerid level statistically significant elevation ($p<0.05$) was observed in diabetic group compared to control group. The present study demonstrated a significant reduction in triglycerid level in atorvastatin treated group ($p<0.05$) compared to diabetic non treated and control groups, while treatment of diabetic rats with pioglitazone and using drugs as combination (atorvastatin+pioglitazone) resulted in significant reduction of triglycerid level ($p<0.05$) compared to atorvastatin treated and diabetic non treated groups but it was still at significant higher level ($p<0.05$) if compared to control group. (Table 4, Figure 29).

2-3.High density lipoprotein cholesterol(HDL-C) level changes:

Regarding HDL-C level there was statistically significant reduction of HDL-C level ($p<0.05$) in diabetic non treated group compared to control group. Treatment of diabetic group with atorvastatin resulted in significant increase in HDL-C ($p<0.05$)compared to diabetic non treated group but it was still at significant lower level ($p<0.05$) if compared to control group, while treatment of diabetic rats with pioglitazone and in the group of combined drugs resulted in significant increase of HDL-C level ($p<0.05$)compared to atorvastatin treated and diabetic non treated groups (Table 4, Figure 30).

2-4. Low density lipoprotein cholesterol(LDL-C) level changes:

Regarding LDL-C level there was statistically significant increase of LDL-C level ($p<0.05$) in diabetic non treated group compared to control group.Treatment of diabetic group with atorvastatin resulted in significant reduction in LDL-C ($p<0.05$) compared to control group while treatment of diabetic rats with pioglitazone and in the group of combined drugs resulted in significant decrease of LDL-C level ($p<0.05$) compared

to atorvastatin treated and diabetic non treated groups but it was still at significant higher level ($p<0.05$) if compared to control group (Table 4, Figure 31).

3. Plasma insulin level changes:

Concerning plasma insulin level statistically significant elevation ($p<0.05$) was observed in diabetic group compared to control group. The current work demonstrated significant reduction($p<0.05$) in plasma insulin level in atorvastatin treated group compared to diabetic non treated group but it was still at significant higher level($p<0.05$) if compared to control group (Table 5, Figure 32), while treatment of diabetic rats with either pioglitazone or combined drugs (atorvastatin+pioglitazone) resulted in significant reduction($p<0.05$) of plasma insulin level compared to atorvastatin treatedgroup and diabetic non treated group (Table 5, Figure 32).

4. Plasma glucose level changes:

In diabetic non treated group there was statistically significant increase ($p<0.05$) of plasma glucose level compared to control group. Treatment of diabetic group with atorvastatin resulted in significant reduction ($p<0.05$)in plasma glucose level compared to diabetic non treated group but it was still at significant higher level ($p<0.05$) if compared to control group. While in groups of either pioglitazone or group of combined drugs resulted in significant decrease of plasma glucose level ($p<0.05$)compared to atorvastatin treated and diabetic non treated groups while it was still at significant higher level($p<0.05$) if compared to control group (Table 5, Figure 33).

5. HOMA IR index changes:

Regarding HOMA IR index there was statistically significant increase ($p<0.05$) of HOMA IR index in diabetic non treated group compared to control group. Treatment of diabetic group with atorvastatin resulted in significant decrease ($p<0.05$)in HOMA IR index compared to diabetic non treated group while it was still at significant higher level ($p<0.05$) if compared to control group. On the other hand treatment of diabetic rats with pioglitazone and also in the group of combined drugs the result was significant decrease ($p<0.05$) of HOMA IR index compared to atorvastatin treated and diabetic non treated groups (Table 5, Figure 34).

Table (3): Effect Mean±SEM of atorvastatin (10mg/kg p.o for 2 weeks) and / or pioglitazone (10mg/kg p.o for 2 weeks) on mean arterial blood pressure in experimentally induced type II diabetes mellitus (by administration of 10%L-fructose solution in drinking water for 4 weeks):

	Mean arterial blood pressure (mm/Hg)
Control group	83.59±2.9
Diabetic group **Percent change%**	126.6±2.8[a] 100%
Ator treated group **percent change %**	92.77±3.8[b] ↓26.72%
Pioglitazone treated group **percent change%**	85.27±3.6[b] ↓32.64%
Ator+Pioglitazone treated group **percent change%**	84.1±2.1[b] ↓33.49%

a: Significant difference from control at $p<0.05$.

b: Significant difference from diabetic group at $p<0.05$**.**

N.B: % change is calculated in relation to diabetic group.

Table (4): Effect of Mean±SEM of atorvastatin and / or pioglitazone on total cholesterol level, triglycerids, HDL-C and LDL-C in experimentally induced type II diabetes mellitus (by administration of 10%L-fructose solution in drinking water for 4 weeks):

	Total cholesterol mg/dl	**Triglycerids mg/dl**	**HDL-C mg/dl**	**LDL-C mg/dl**
Control group	110±5.9	115±5.3	38±1.2	49±1.8
Diabetic group	159±4.2[a]	260±0.55[a]	18±0.9[a]	107±2.9[a]
Percent change	100%	100%	100%	100%
Ator treated group	140±3.1[a,b]	198±6.9[a,b]	25±0.62[a,b]	100.4±3.1[a]
Percent change	↓ 11.94%	↓ 23.84%	↑ 38.88%	↓ 6.16%
Pioglitazone treated group	129±2.9[a,b]	163±4.5[a,b,c]	33±1.01[b,c]	96.4±2.6[a,b,c,d]
Percent change	↓ 18.86%	↓ 37.3	↑ 83.33%	↓ 9.9%
Ator+Pioglitazone treated group	133±4.1[a,b,c]	159±6.2[a,b,c]	36±2.3[b,c]	65.2±3.1[a,b,c]
Percent change	↓ 16.35%	↓ 38.84%	>100%	↓ 39.06%

a: Significant difference versus control group at $p<0.05$.

b: Significant difference versus diabetic group at $p<0.05$.

c: Significant difference versus atorvastatin group at $p<0.05$.

d: Significant difference versus diabetic-infarcted+atorvastatin+pioglitazone group at $p<0.05$.

N.B: % change is calculated in relation to diabetic group.

Table (5): Effect of Mean±SEM of atorvastatin and / or pioglitazone on plasma insulin level, blood glucose level and HOMA IR index in experimentally induced type II diabetes mellitus (by administration of 10%L-fructose solution in drinking water for 4 weeks):

	plasma insulin level µIU/ml	**Blood glucose mg/dl**	**HOMA IR index**
Control group	49±1.6	76±2.1	9.19±0.83
Diabetic group	82±2.9[a]	169±3.1[a]	34.21±0.64[a]
Percent change	100%	100%	100%
Ator treated group	6.2±1.2[a,b]	147±2.3[a,b]	22.5±0.92[a,b]
Percent change	↓ 24.39%	↓ 13.01%	↓ 34.22%
Pioglitazone treated group	53±1.1[b,c]	138±1.9[a,b,c]	18.05±0.68[a,b,c]
Percent change	↓ 35.36%	↓ 18.34%	↓47.23%
Ator+Pioglitazone treated group	51±1.4[b,c]	136±1.8[a,b,c]	17.1±0.39[a,b,c]
Percent change	↓ 37.8%	↓ 19.52%	↓ 50%

a: Significant difference versus control group at $p<0.05$.

b: Significant difference versus diabetic group at $p<0.05$.

c: Significant difference versus atorvastatin group at $p<0.05$.

N.B: % change is calculated in relation to diabetic group.

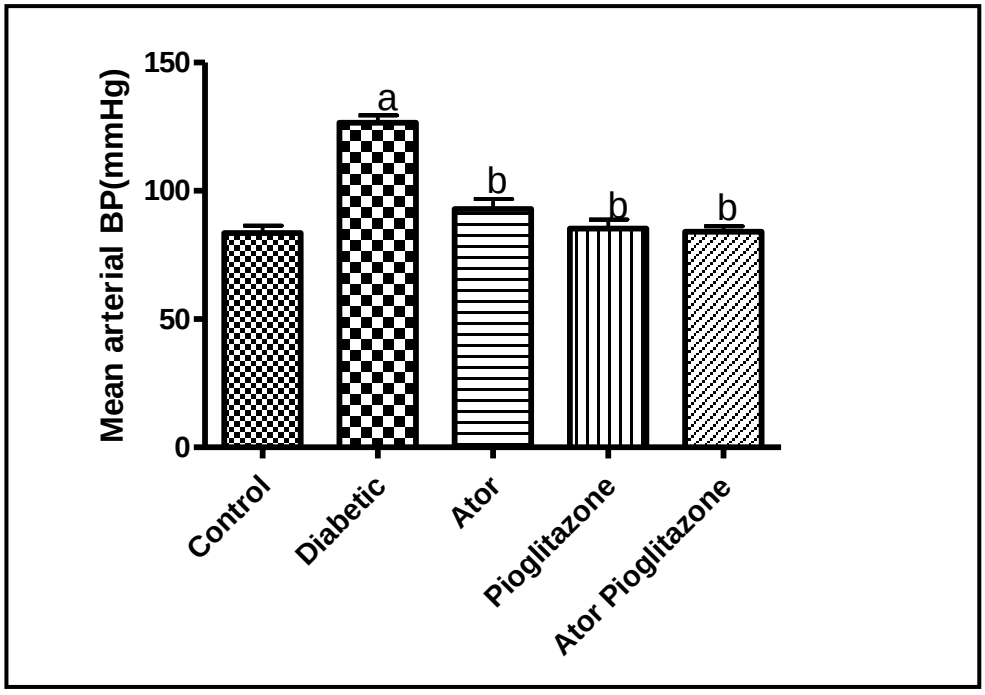


Fig. (27): Effect of atorvastatin(10mg/kg p.o for 2 weeks) and / or pioglitazone(10mg/kg p.o for 2 weeks)on mean arterial blood pressure in experimentally induced type II diabetes mellitus(by administration of 10%L-fructose solution in drinking water for 4 weeks).

Data are presented as mean ± SEM

a: Significant difference versus control group at $p<0.05$.

b: Significant difference versus diabetic group at $p<0.05$.

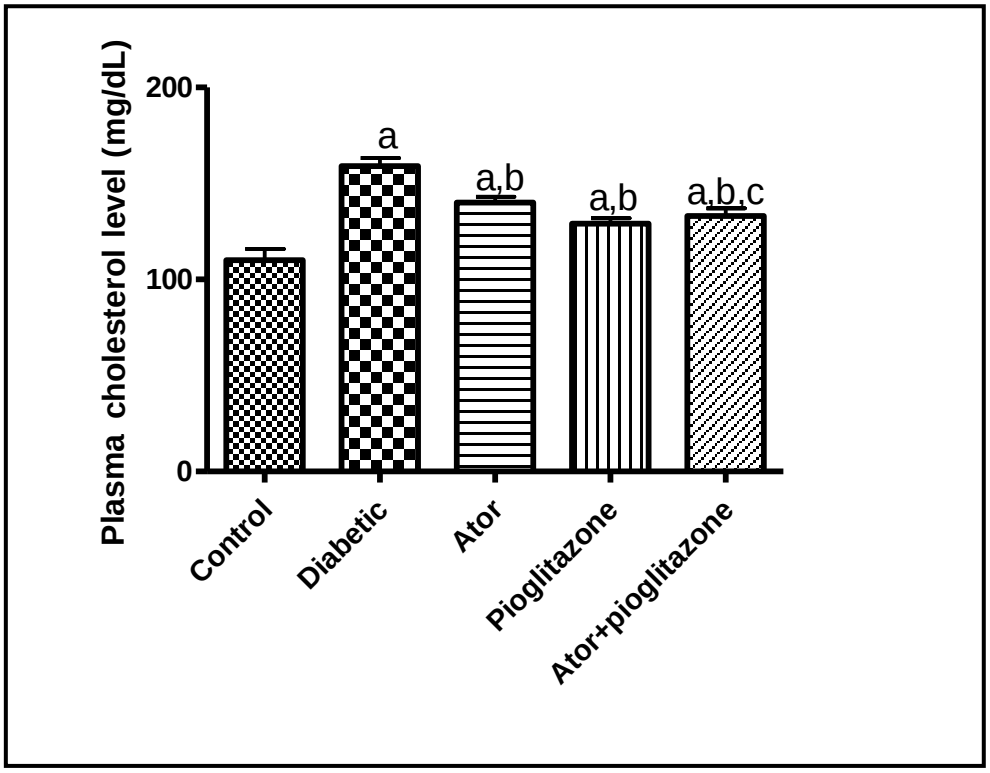


Fig. (28): Effect of atorvastatin(10mg/kg p.o for 2 weeks) and / or pioglitazone (10mg/kg p.o for 2 weeks)on serum total cholesterol level in experimentally induced type II diabetes mellitus(by administration of 10%L-fructose solution in drinking water for 4 weeks).

Data are presented as mean ± SEM

a: Significant difference versus control group at $p<0.05$.

b: Significant difference versus diabetic group at $p<0.05$.

c: Significant difference versus atorvastatin group at $p<0.05$.

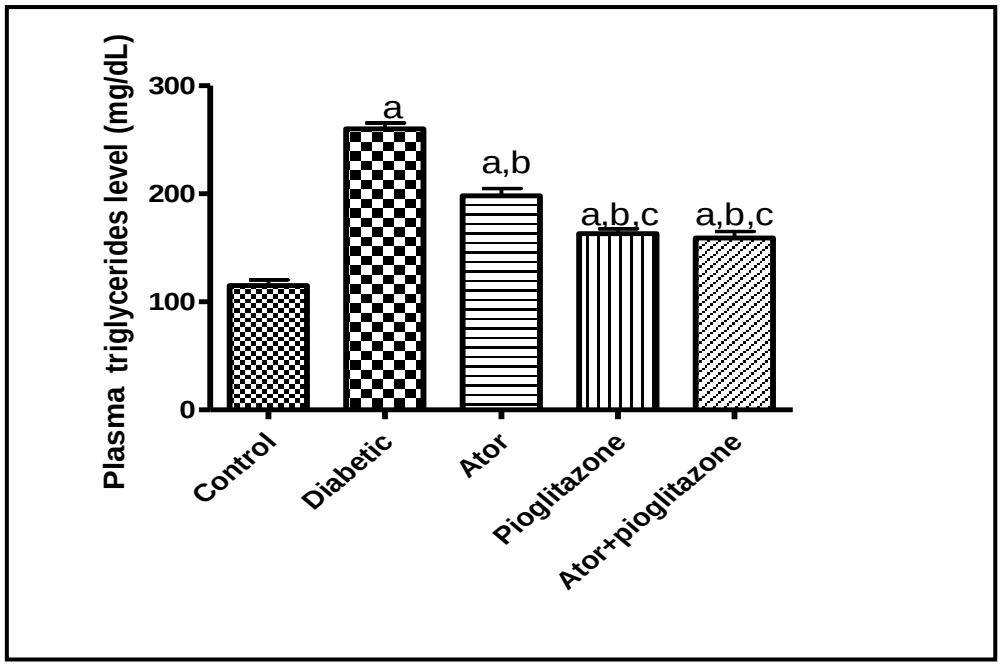


Fig. (29): Effect of atorvastatin(10mg/kg p.o for 2 weeks) and / or pioglitazone (10mg/kg p.o for 2 weeks) on serum triglyceride level in experimentally induced type II diabetes mellitus (by administration of 10%L-fructose solution in drinking water for 4 weeks).

Data are presented as mean ± SEM

a: Significant difference versus control group at $p<0.05$.

b: Significant difference versus diabetic group at $p<0.05$.

c: Significant difference versus atorvastatin group at $p<0.05$.

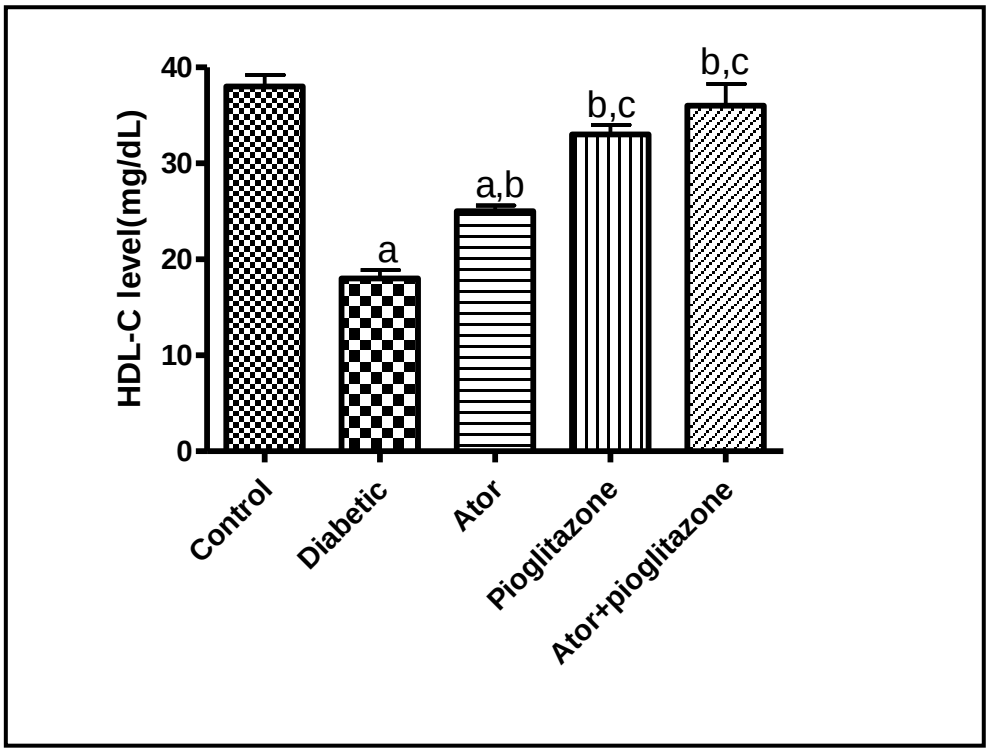


Fig. (30): Effect of atorvastatin(10mg/kg p.o for 2 weeks) and / or pioglitazone (10mg/kg p.o for 2 weeks) on high density lipoprotein cholesterol (HDL-C) level in experimentally induced type II diabetes mellitus (by administration of 10%L-fructose solution in drinking water for 4 weeks).

Data are presented as mean ± SEM

a: Significant difference versus control group at $p<0.05$.

b: Significant difference versus diabetic group at $p<0.05$.

c: Significant difference versus atorvastatin group at $p<0.05$.

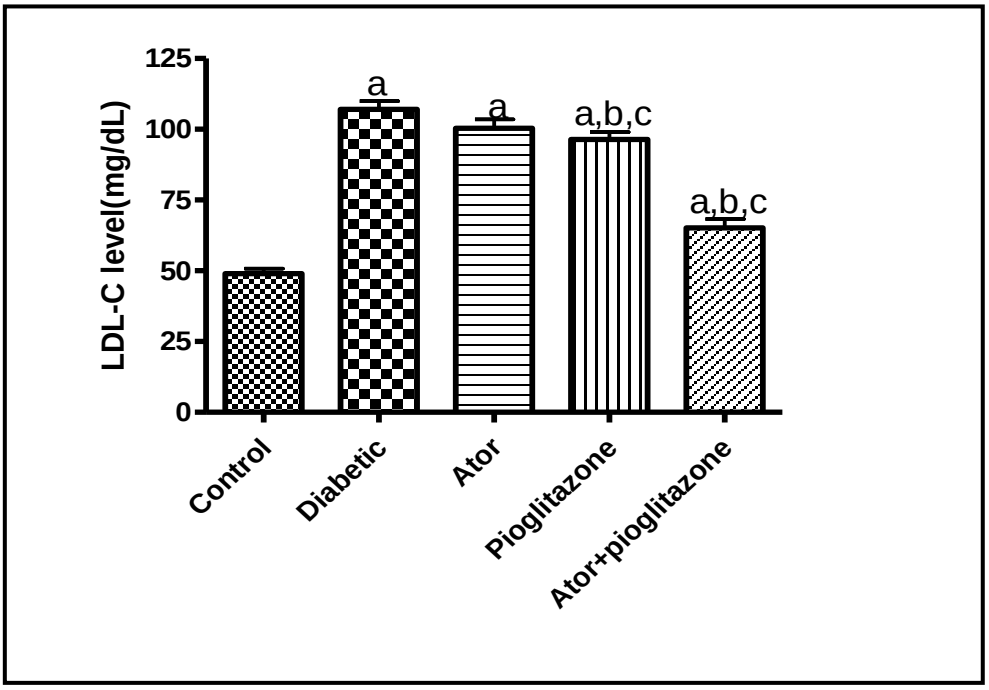


Fig. (31): Effect of atorvastatin (10mg/kg p.o for 2 weeks) and / or pioglitazone (10mg/kg p.o for 2 weeks) on Low density lipoprotein cholesterol (LDL-C) level in experimentally induced type II diabetes mellitus (by administration of 10%L-fructose solution in drinking water for 4 weeks).

Data are presented as mean ± SEM

a: Significant difference versus control group at $p<0.05$.

b: Significant difference versus diabetic group at $p<0.05$.

c: Significant difference versus atorvastatin group at $p<0.05$.

d: Significant difference versus diabetic-infarcted+atorvastatin+pioglitazone group at $p<0.05$.

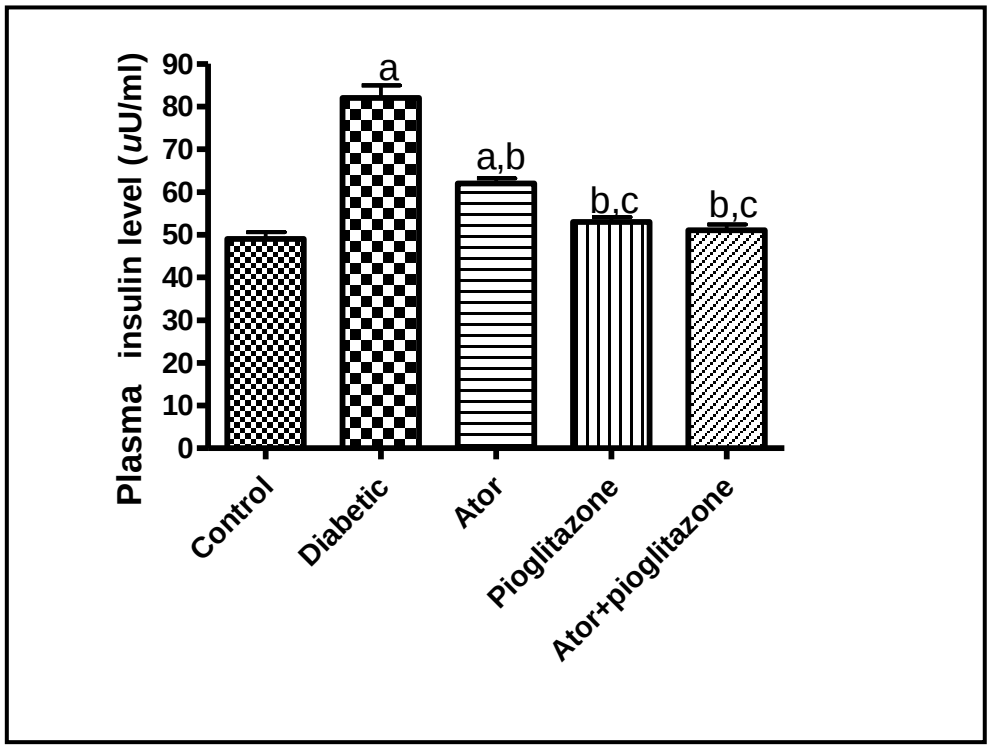


Fig. (32): Effect of atorvastatin(10mg/kg p.o for 2 weeks) and / or pioglitazone(10mg/kg p.o for 2 weeks)on plasma insulin level in experimentally induced type II diabetes mellitus (by administration of 10%L-fructose solution in drinking water for 4 weeks).

Data are presented as mean ± SEM

a: Significant difference versus control group at $p<0.05$.

b: Significant difference versus diabetic group at $p<0.05$.

c: Significant difference versus atorvastatin group at $p<0.05$.

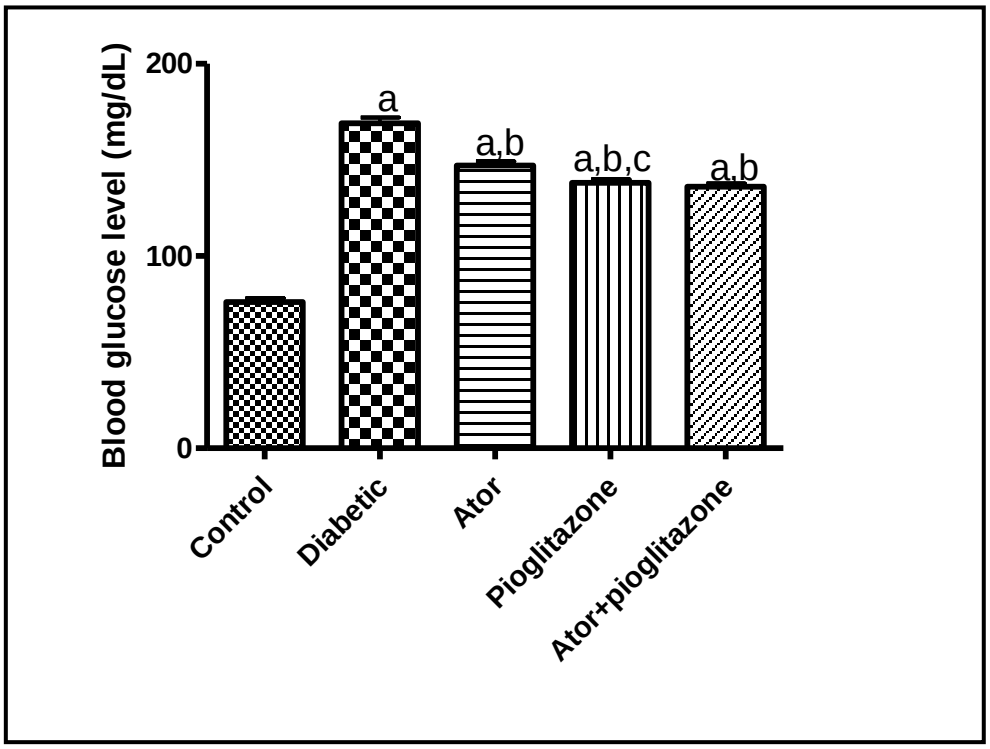


Fig. (33): Effect of atorvastatin(10mg/kg p.o for 2 weeks) and / or pioglitazone(10mg/kg p.o for 2 weeks)on plasma glucose level in experimentally induced type II diabetes mellitus (by administration of 10%L-fructose solution in drinking water for 4 weeks).

Data are presented as mean ± SEM

a: Significant difference versus control group at $p<0.05$.

b: Significant difference versus diabetic group at $p<0.05$.

c: Significant difference versus atorvastatin group at $p<0.05$.

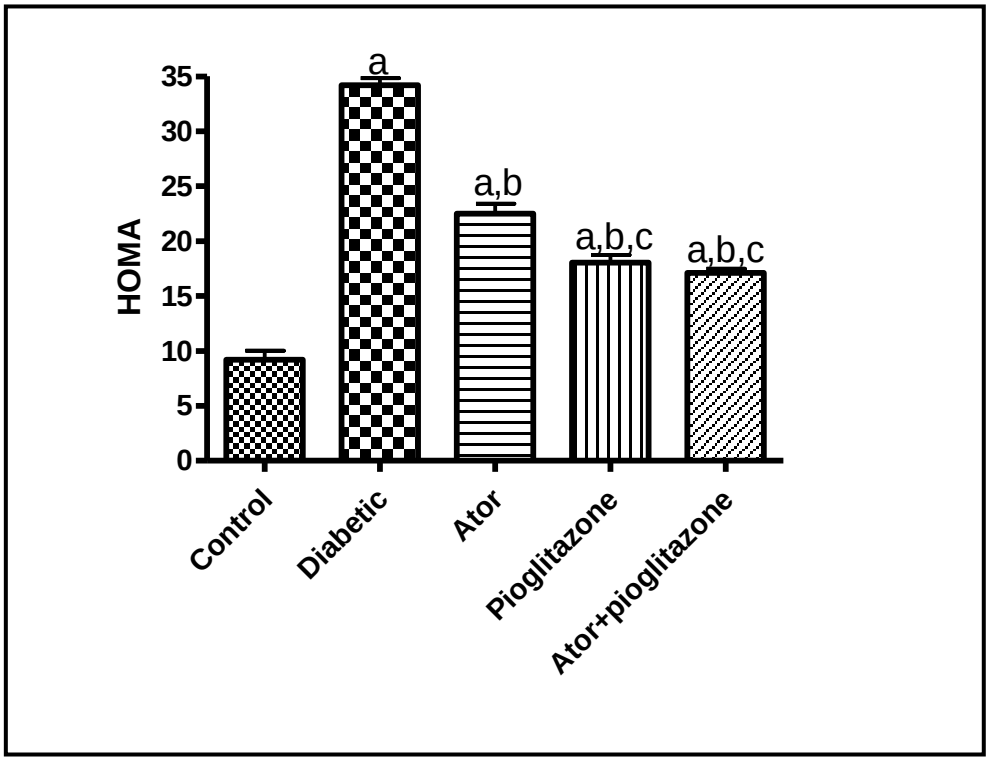


Fig.(34): Effect of atorvastatin(10mg/kg p.o for 2 weeks) and / or pioglitazone (10mg/kg p.o for 2 weeks) on HOMA IR index in experimentally induced type II diabetes mellitus (by administration of 10%L-fructose solution in drinking water for 4 weeks).

Data are presented as mean ± SEM

a: Significant difference versus control group at $p<0.05$.

b: Significant difference versus diabetic group at $p<0.05$.

c: Significant difference versus atorvastatin group at $p<0.05$.

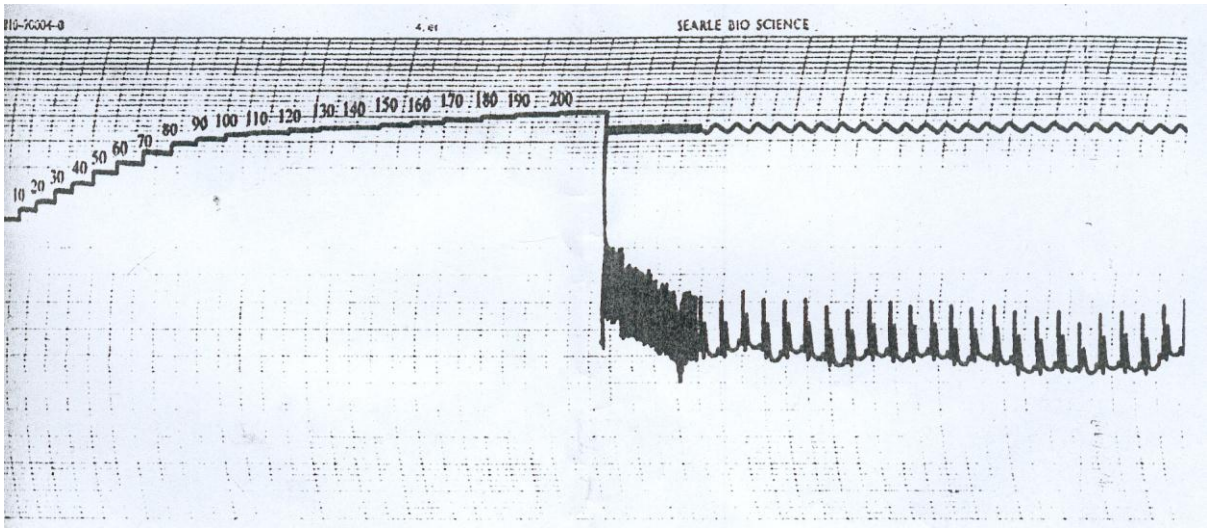


Fig. (35): Blood pressure Tracing of control normal rat.

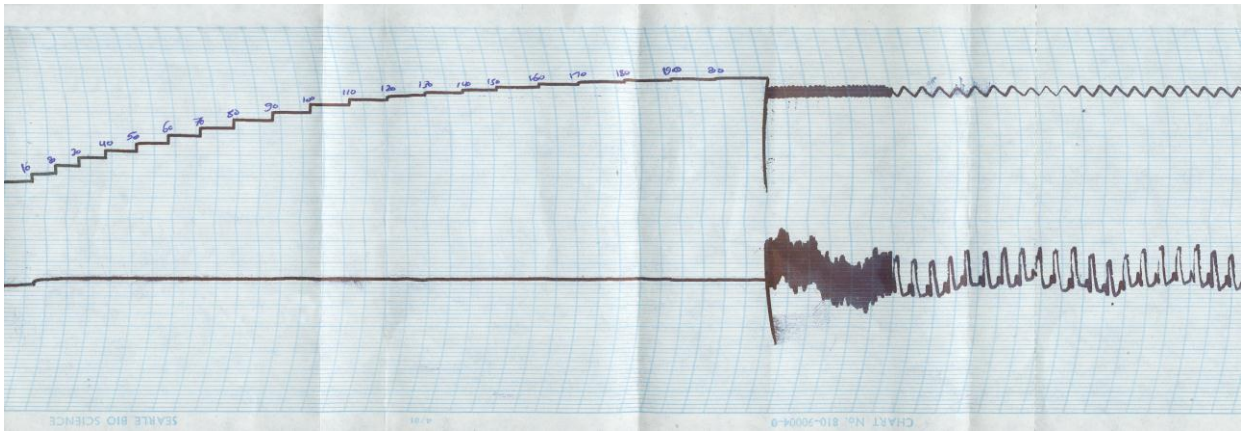


Fig .(36): Blood pressure Tracing of diabetic rat.

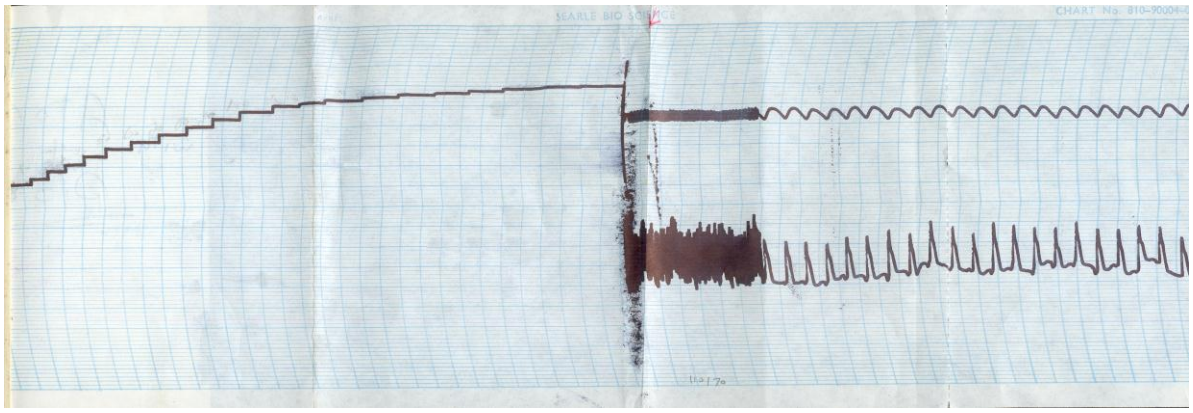


Fig. (37): Blood pressure Tracing of atorvastatin treated rat.

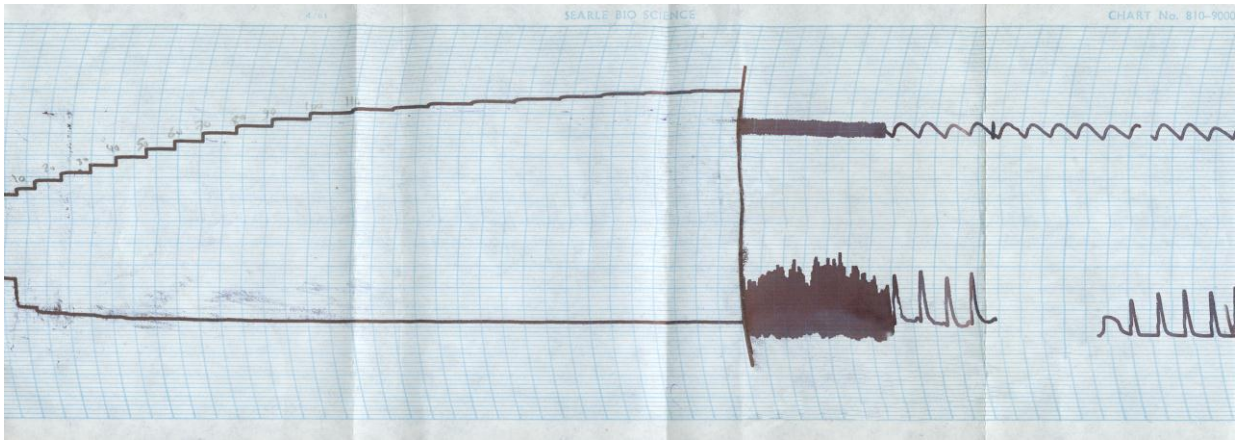


Fig. (38): Blood pressure Tracing of pioglitazone treated rat.

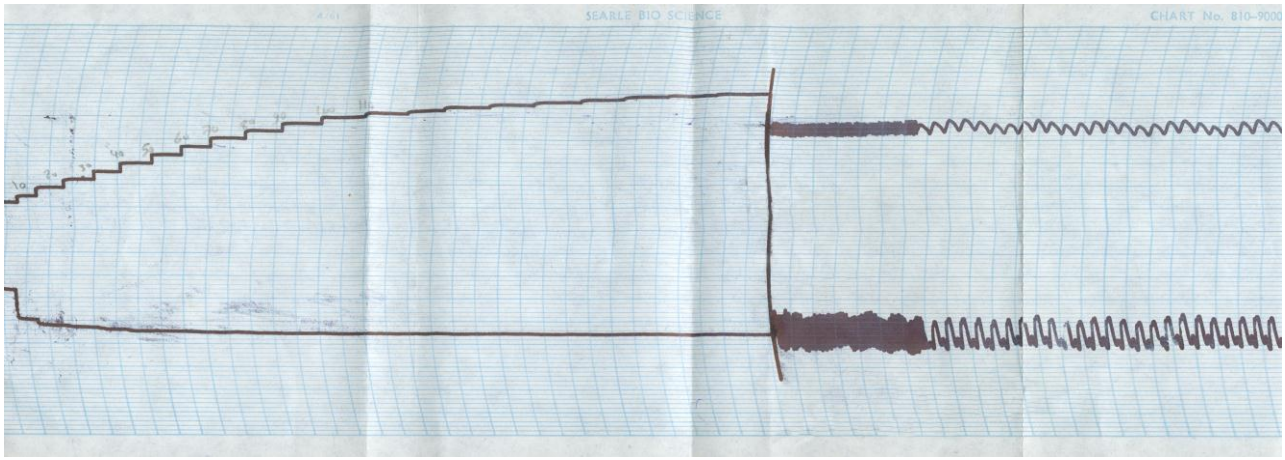


Fig. (39): Blood pressure Tracing of atorvastatin+pioglitazone treated rat

II.In vitro experiments:

To show the effect of atorvatatin on isolated rabbit aortic strip it was added in gradually increasing doses (10,30,100,300,1000 ug/20ml organ bath) it was observed that atorvastatin produced no effect on the isolated aortic strip. (Fig 41).

Also the drug had no effect on nor adrenaline precontracted isolated rabbit aortic strip (40 ug/20ml organ bath) by increasing doses of the drug. (Fig 42).

By adding atorvatatin on isolated rabbit heart in gradually increasing doses (10,30,100,300,1000 ug) it was observed that atorvastatin produced no effect on the isolated heart. (Fig.43).

To explore the effect of pioglitazone rabbit aortic strip it was added in gradually increasing doses(10,30,100,300,1000 ug/20ml organ bath) it was noted that increasing doses of pioglitazone induced significant relaxation (reduction) in nor adrenaline precontracted isolated rabbit aortic strip (40 ug/20ml organ bath). (Table 6, Fig 40, 44).

By adding pioglitazone on isolated rabbit aortic strip in an increasing doses (10,30,100,300,1000 ug/20ml organ bath) there was no change in aortic contraction (Fig 45).

Adding pioglitazone on isolated rabbit heart in an increasing doses(10,30,100,300,1000 ug) there was no effect on the isolated heart (Fig 46).

Atorvastatin and pioglitazone were dissolved in methanol (Fig 47, 48).

Table (6): Effect of pioglitazone (10,30,100,300,1000 ug/20ml organ bath) on nor adrenaline precontracted isolated rabbit aortic strip (40 ug/20ml organ bath).

	Nor Ardrendine (40 ug/20ml organ bath)	**Pioglitazone (dose μg)**				
		10 μg	**30 μg**	**100 μg**	**300 μg**	**1000 μg**
Response (cm)	6.6 ± 0.39^{b}	6.4 ± 0.13^{a}	6.1 ± 0.46^{a}	$5.8 \pm 0.78^{a,b}$	$4.4 \pm 0.68^{a,b}$	$3.6 \pm 0.46^{a,b}$
% reduction	100%	3 ±0.03%	8±0.25%	12±0.2%	18±0.17%	45 ± 1.7%

Data are presented as mean ± SEM.

Groups having the same symbol are significantly different from each other $p<0.05$.

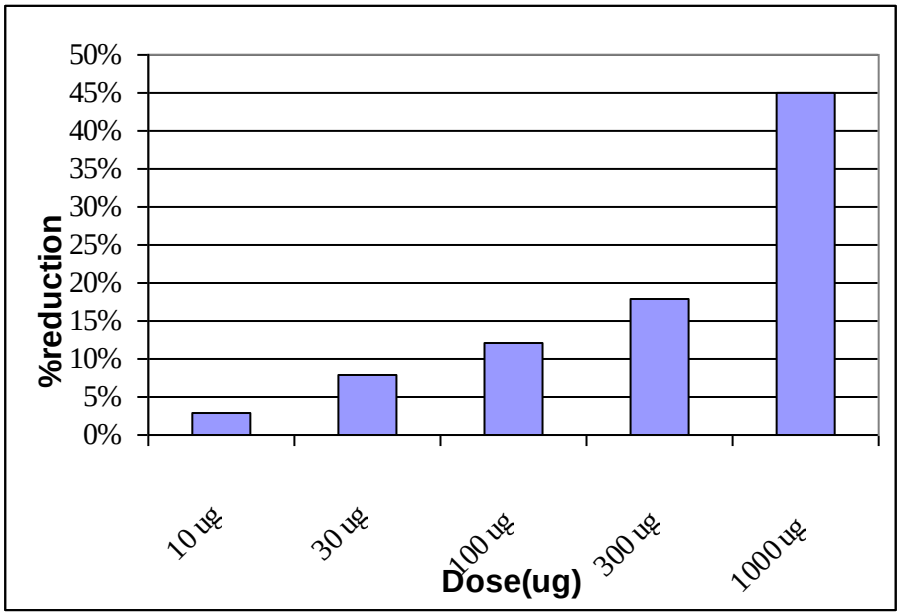


Fig. (40): Effect of pioglitazone (10,30,100,300,1000 ug/20ml organ bath) on nor adrenaline precontracted isolated rabbit aortic strip (40 ug/20ml organ bath).

Data are presented as mean ± SEM.

Groups having the same symbole are significantly different from each other $p<0.05$.

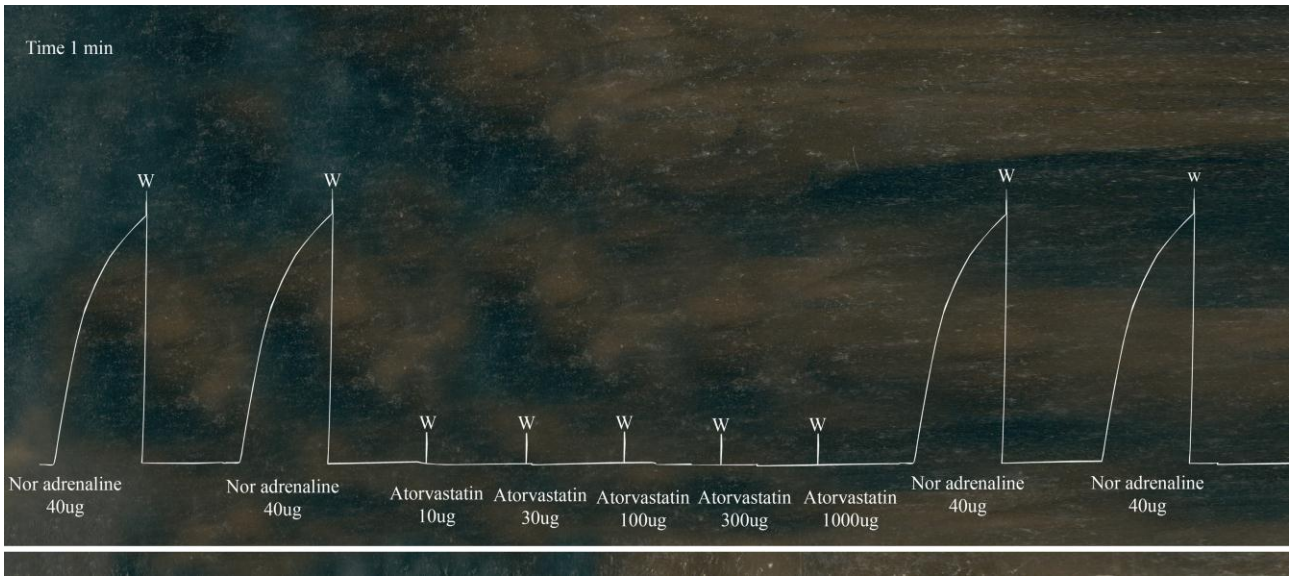


Fig. (41): A record demonstrating the effect of atorvastatin on isolated rabbit's aortic spiral strip.

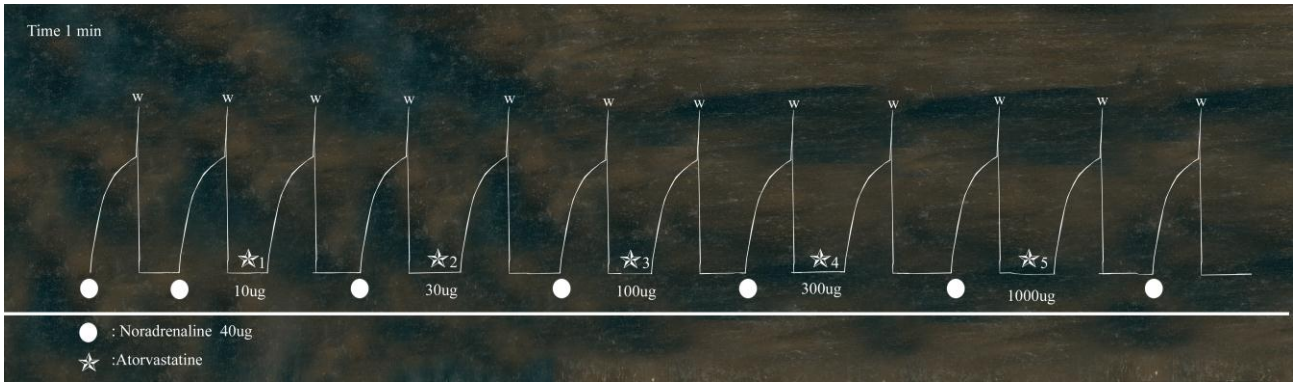


Fig. (42): A record demonstrating the effect of atorvastatin on nor adrenaline precontracted isolated rabbit aortic strip.

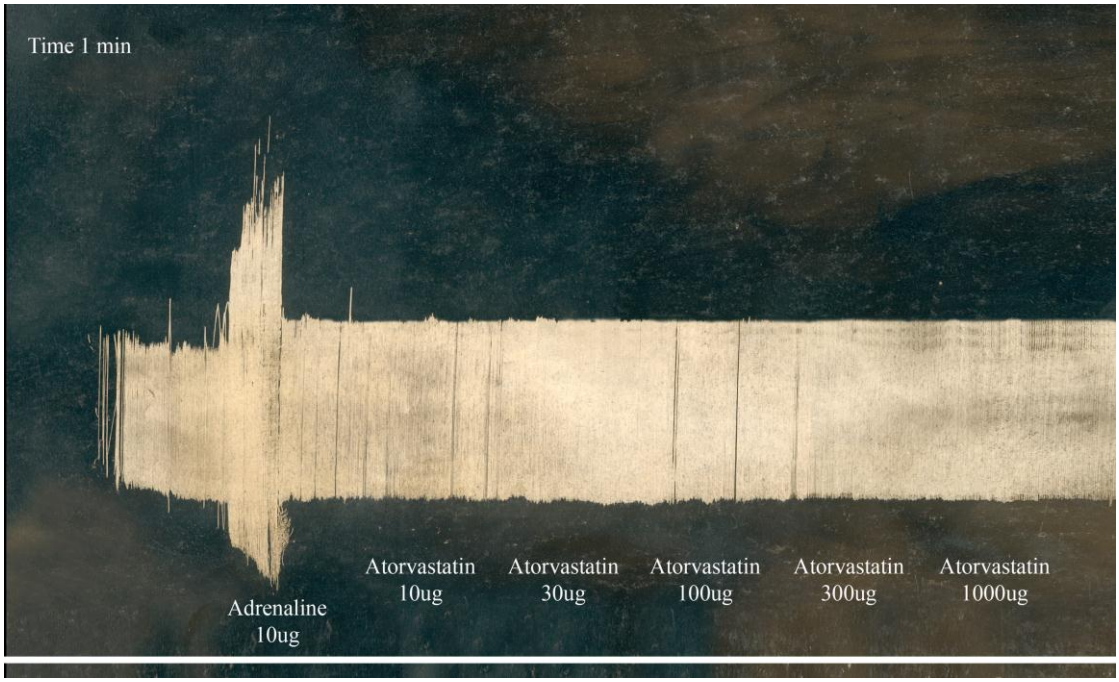


Fig. (43): A record demonstrating the effect of gradually increasing doses of atorvastatin on the isolated perfused rabbit's heart contractions.

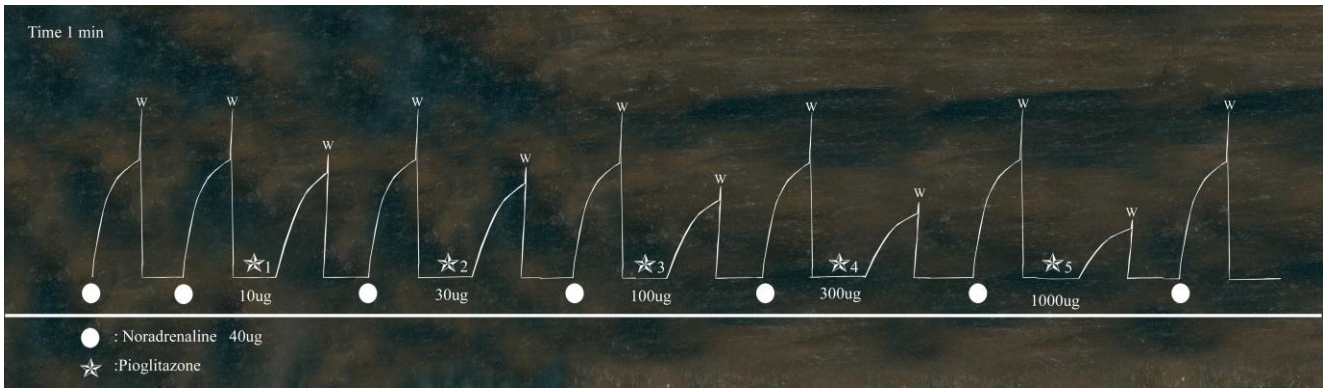


Fig. (44): A record demonstrating the effect of pioglitazone on nor adrenaline precontracted isolated rabbit aortic strip.

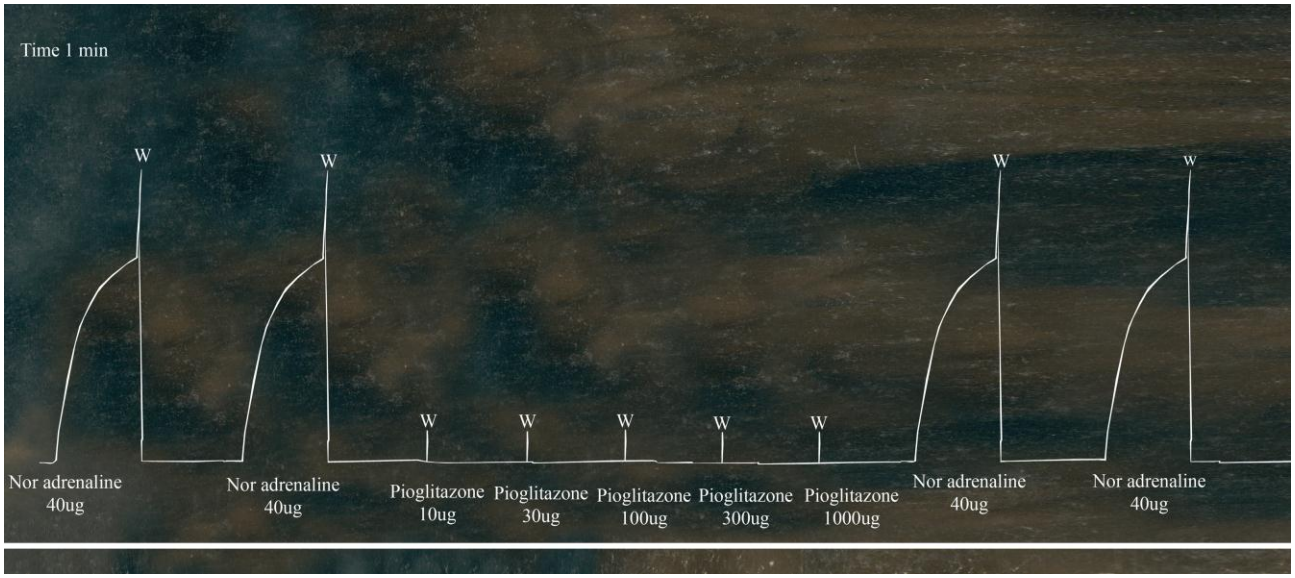


Fig. (45): A record demonstrating the effect of pioglitazone on isolated rabbit's aortic spiral strip.

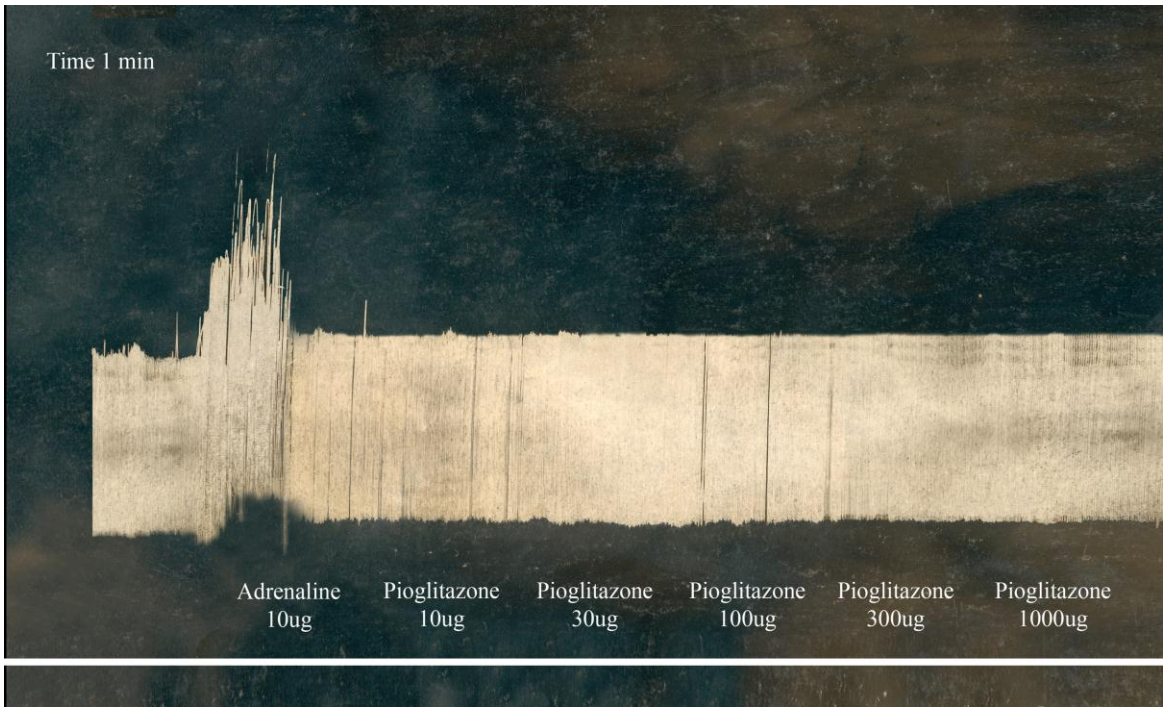
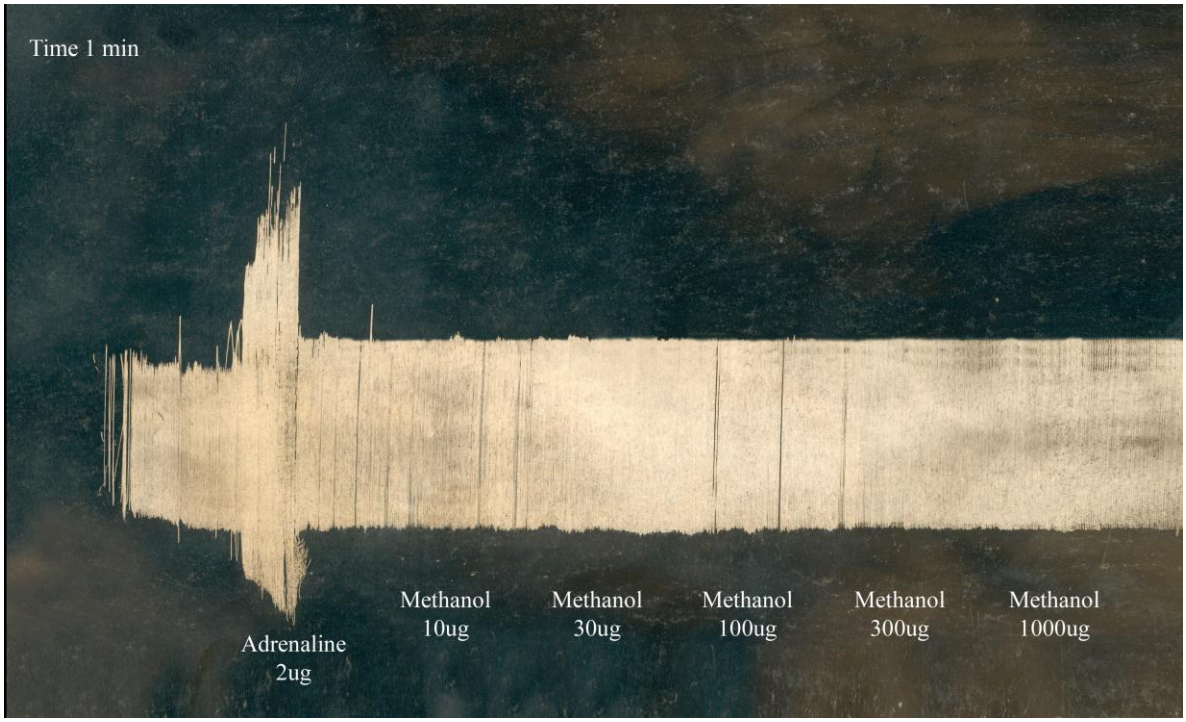


Fig. (46): A record demonstrating the effect of gradually increasing doses of pioglitazone on the isolated perfused rabbit's heart contractions.



Fig, (47): A record demonstrating the effect of gradually increasing doses of methanol on the isolated perfused rabbit's heart contractions.

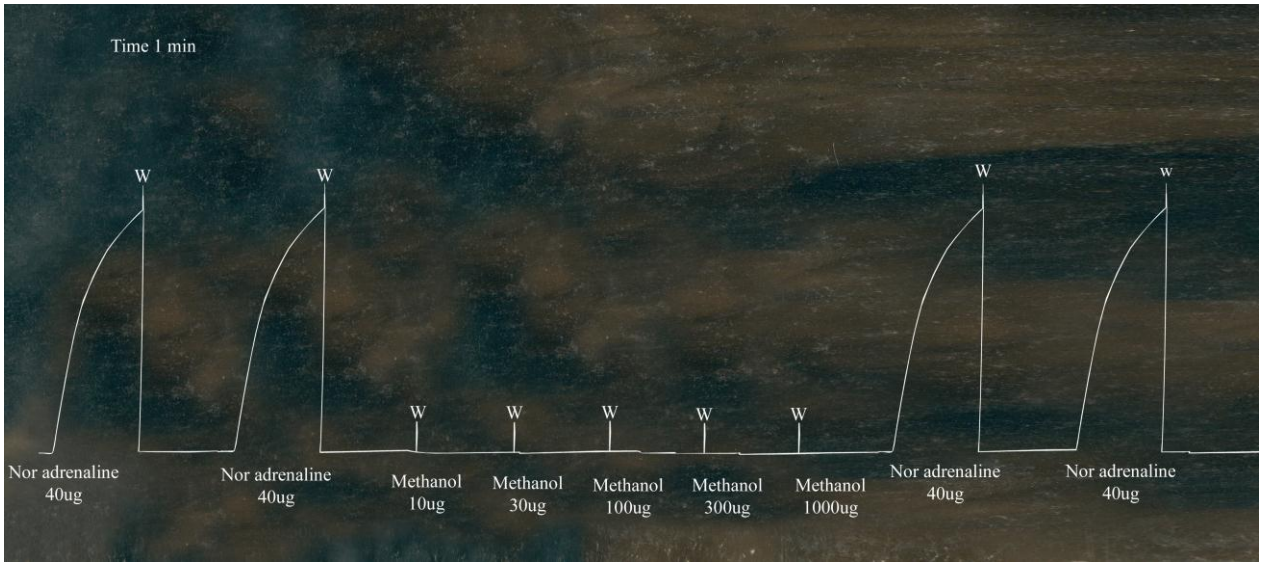


Fig. (48): A record demonstrating the effect of methanol on isolated rabbit's aortic spiral strip.