CHAPTER - 4

RESULTS

4.1 BIOCHEMICAL INVESTIGATIONS

Changes observed in lipid peroxidation product, endogenous antioxidants and enzymes after 30 days exposure to 10,30 and 100 ppm of cadmium chloride.

4.1.1 GENERAL OBSERVATIONS

There was no significant change in the body weight of animals of group 2 (10CD) and group 3 (30CD) compared to group 1 (control). However there was a significant ($p<0.001$) decrease in the body weight of animals during thirty days exposure to 100 ppm cadmium chloride group 4 (100CD) compared to group 1 (control) **(Fig: 4.1).**

4.1.2 TISSUE ESTIMATIONS

4.1.2.1.1 Changes in the levels of Malondialdehyde (MDA)

The MDA levels was not increased significantly in any of the tissues in group 2 (10CD) compared to group1 (control). The MDA levels as a marker of lipid peroxidation were increased significantly in brain, lung and kidney of group 3 (30CD) compared to group 1 (control) ($p<0.05$) in brain, ($p<0.05$) in lung and ($p<0.01$) in kidney. No significant increase was found in the MDA levels in liver and heart of group 3 (30CD) compared to group 1.It was also significantly increased in all tissues in group 4 (100CD) compared to control ($p<0.001$) in liver, kidney, lung and brain and ($p<0.01$) in heart **(Fig: 4.2)**.

4.1.2.2 Changes in the levels of Endogenous Antioxidants

4.1.2.2.1 Changes in the levels of Superoxide dismutase (SOD)

The SOD levels were not decreased significantly in any of the organs in group 2 (10CD) compared to group (control). The SOD levels in group 3 (30CD) was decreased significantly in all the tissues compared to group 1 (control) except in the heart and brain where it was not significantly decreased. It was significantly decreased in liver, kidney and lung ($p<0.05$). In group 4 (100CD) SOD levels were decreased significantly in all the tissues i.e. liver, kidney, lung, heart and brain ($p<0.001$) **(Fig 4.3)**.

4.1.2.2.2 Changes in the levels of Catalase (CAT)

The CAT levels in liver, lung, heart and brain were decreased significantly ($p<0.001$),in kidney($p<0.01$) in group 4 (100CD) as compared to group 1 (control). In the group 3 (30CD) the CAT levels were significantly decreased in kidney ($p<0.01$), lung ($p<0.05$), heart ($p<0.05$) and brain ($p<0.05$) compared to control. No significant decrease was found in the CAT levels in liver of group 3 (30CD). No significant decrease was found in the CAT levels in any of the organs of group 2 (10CD) **(Fig 4.4)**.

4.1.2.2.3 Changes in the levels of Reduced glutathione (GSH)

The Reduced glutathione (GSH) levels in liver, lung and heart were decreased significantly ($p<0.001$) in group 4 (100 CD) as compared to group 1 (control). In kidney and brain it was decreased significantly ($p<0.01$) in group 4 (100CD) compared to group 1 (control). It was significantly decreased ($p<0.01$) in group 3 (30CD) in kidney and also in heart ($p<0.05$) and liver ($p<0.05$) compared to group 1 (control). No significant decrease was found in the levels of reduced glutathione in brain and lung in group 3 (30CD). A significant decrease ($p<0.05$) was found in the levels of GSH in kidney in group 2 (10CD) compared to group 1 (control). No significant decrease in GSH levels was found in any other organs in group 2 (10 CD) **(Fig 4.5)**.

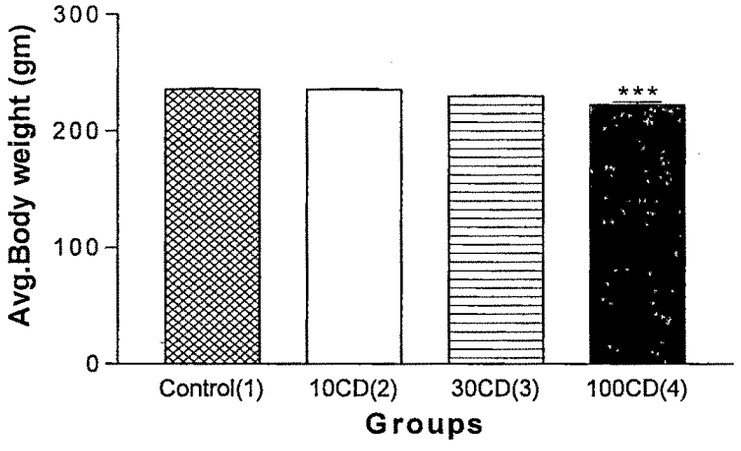


Fig: 4.1. Effect of cadmium chloride (CD-10, 30,100ppm) exposure for 30 days on body weights of rats.

Values are expressed as mean ± SEM for six animals in each group.
Group 2, 3, 4 compared with group 1.
$^{*}p<0.05$, $^{**}p<0.01$, $^{***}p<0.001$.

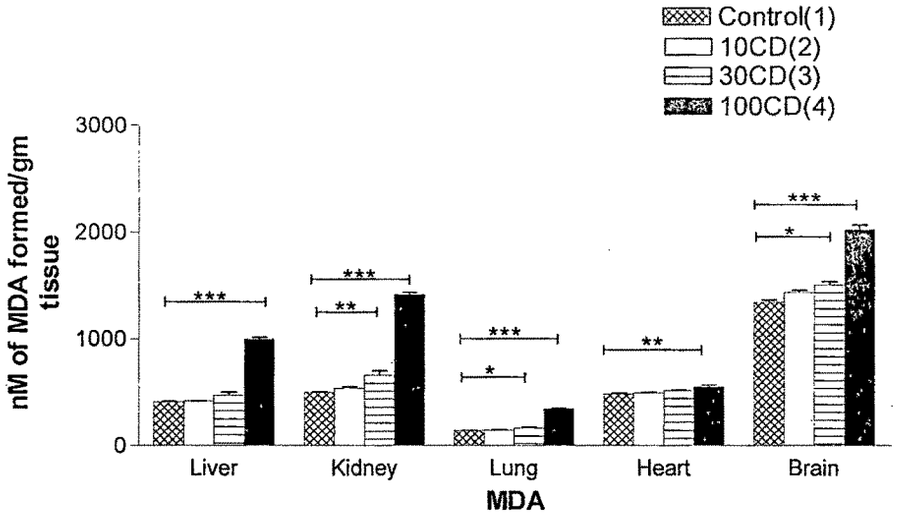


Fig: 4.2. Effect of cadmium chloride (CD-10, 30,100ppm) exposure for 30 days on the levels of malondialdehyde in liver, kidney, lung, heart and brain of rat

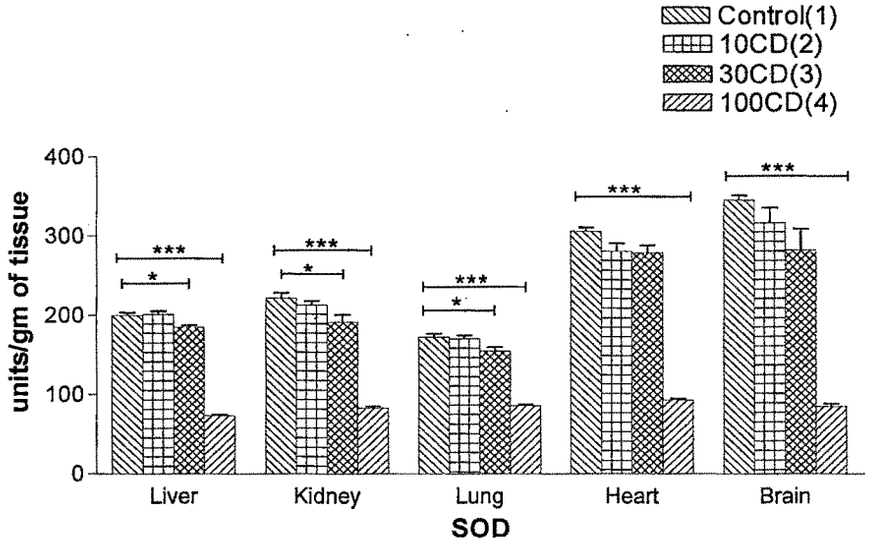


Fig: 4.3. Effect of cadmium chloride (CD-10, 30,100ppm) exposure for 30 days on the levels of superoxide dismutase in liver, kidney, lung, heart and brain of rats.

Values are expressed as mean ± SEM for six animals in each group.
Group 2, 3, 4 compared with group 1.
$^{*}p<0.05$, $^{**}p<0.01$, $^{***}p<0.001$.

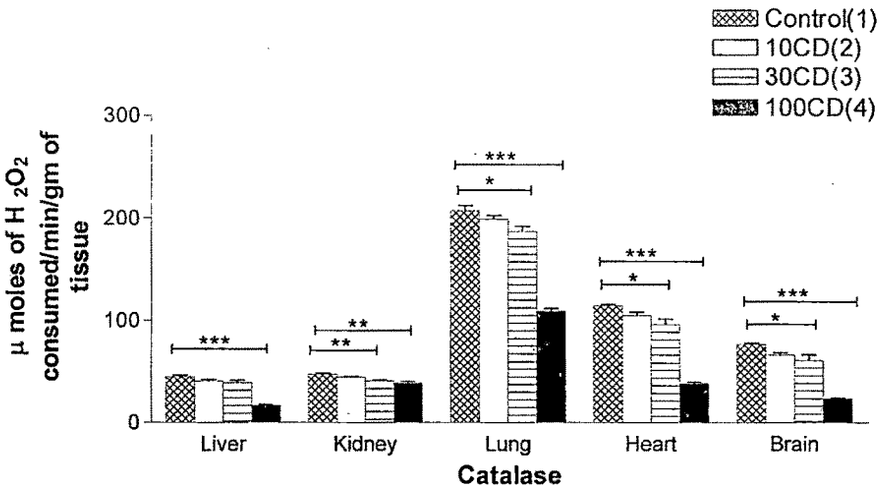


Fig: 4.4. Effect of cadmium chloride (CD-10, 30,100ppm) exposure for 30 days on the levels of catalase in liver, kidney, lung, heart and brain of rats.

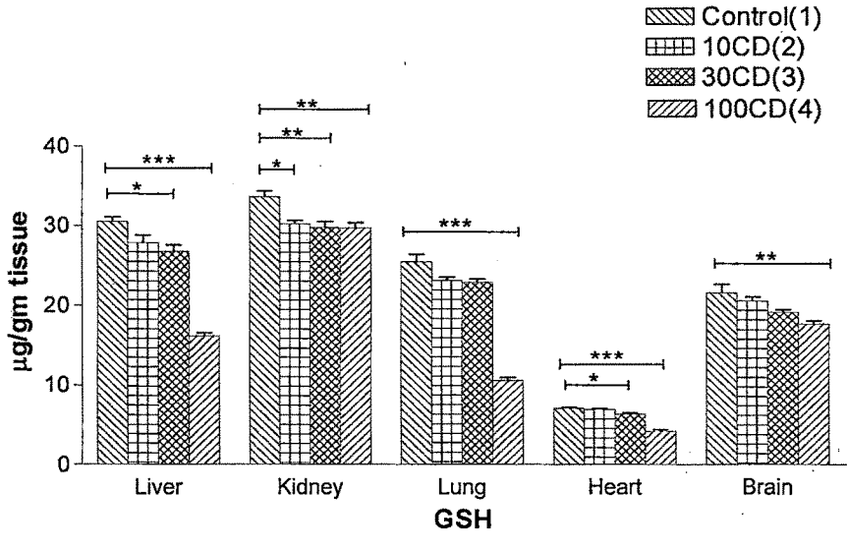


Fig: 4.5. Effect of cadmium chloride (CD-10, 30,100ppm) exposure for 30 days on the levels of reduced glutathione in liver, kidney, lung, heart and brain of rats.

Values are expressed as mean ± SEM for six animals in each group.
Group 2, 3, 4 compared with group 1.
$^{*}p<0.05$, $^{**}p<0.01$, $^{***}p<0.001$.

4.1.3 SERUM INVESTIGATIONS

4.1.3.1 Changes in the levels of Serum Glutamate Oxaloacetate Transaminases (GOT) and Glutamate Pyruvate Transaminases (GPT)

There was a significant ($p<0.001$) increase in the levels of serum GOT in the rats of group 4 (100CD) as compared to group 1 (control). There was no significant increase in the levels in group 2 (10CD) or group 3 (30CD) as compared to group 1 (control) **(Fig 4.6)**.

There was a significant ($p<0.001$) increase in the levels of serum GPT in the rats of group 4 (100CD) as compared to group 1 (control). There was also a significant increase ($p<0.05$) in the levels of serum GPT in the rats of group 3 (30CD) as compared to group 1 (control). No significant increase was found in the group 2 (10CD) as compared to group 1 (control) **(Fig 4.7)**.

4.1.3.2 Changes in the levels of Alkaline phosphatase (Alkp)

There was a significant ($p<0.001$) increase in the levels of serum Alkp in the rats of group 4 (100 CD) as compared to group 1 (control). No significant increase was found in the groups 2 (10CD) and 3 (30CD) as compared to group 1 (control) **(Fig 4.8)**.

4.1.3.3 Changes in the levels of Lactate Dehydrogenase (LDH)

There was a significant ($p<0.001$) increase in the levels of serum LDH in group 4 (100CD) as compared to group 1 (control). There was also a significant ($p<0.05$) increase in the group 3 (30CD) as compared to group 1 (control). No significant increase was found in the group 2 (10CD) as compared to group1 (control) **(Fig 4.9)**.

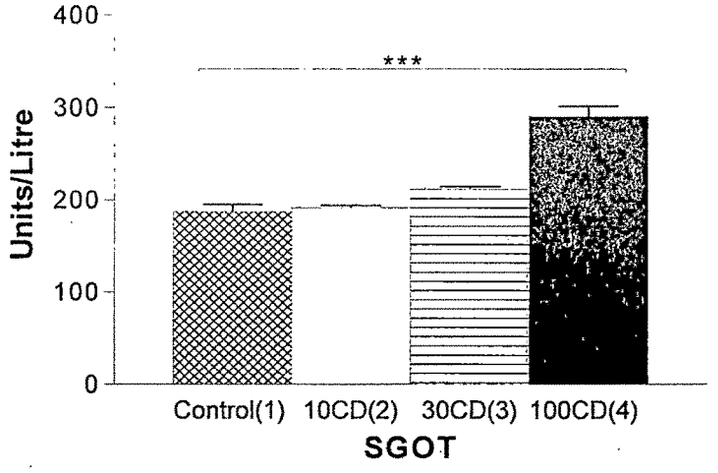


Fig: 4.6. **Effect of cadmium chloride (CD-10, 30,100ppm) exposure for 30 days on the levels of serum glutamate oxaloacetate transaminase of rats.**

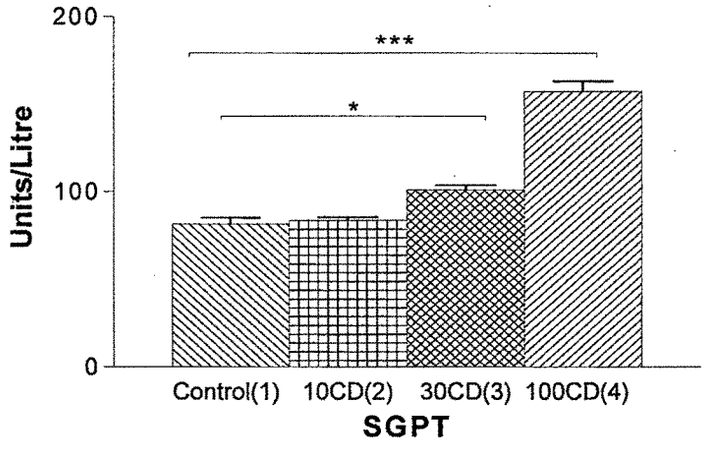


Fig: 4.7. **Effect of cadmium chloride (CD-10, 30,100ppm) exposure for 30 days on the levels of serum glutamate pyruvate transaminase of rats.**

Values are expressed as mean ± SEM for six animals in each group.
Group 2, 3, 4 compared with group 1.
$^{*}p<0.05$, $^{**}p<0.01$, $^{***}p<0.001$.

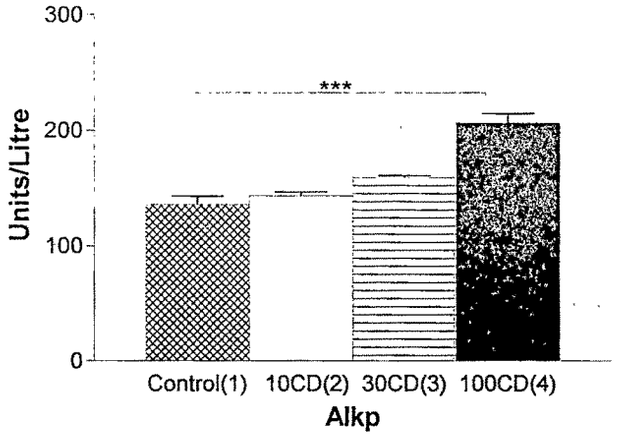


Fig: 4.8. **Effect of cadmium chloride (CD-10, 30,100ppm) exposure for 30 days on the levels of alkaline phosphatase in serum of rats.**

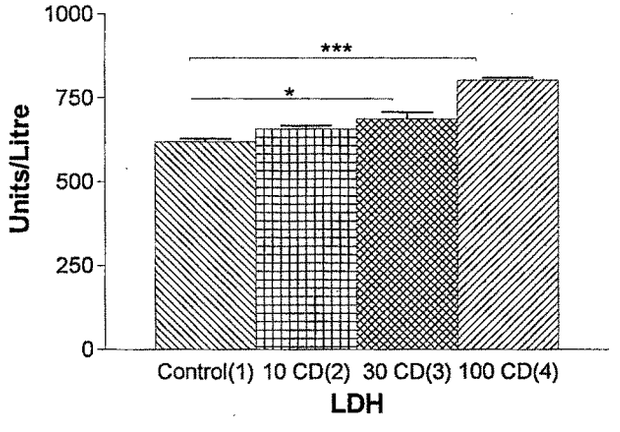


Fig: 4.9. **Effect of cadmium chloride (CD-10, 30,100ppm) exposure for 30 days on the levels of lactate dehydrogenase in serum of rats.**

Values are expressed as mean ± SEM for six animals in each group.
Group 2, 3, 4 compared with group 1.
$^{*}p<0.05$, $^{**}p<0.01$, $^{***}p<0.001$.

4.2 PHARMACOLOGICAL INVESTIGATIONS

Pilot study carried out on 10ppm, 30ppm and 100ppm cadmium showed that most of the changes in the various enzymes and cellular components have occurred in animals exposed to 100ppm of cadmium chloride. Hence further studies were carried out with 100 ppm of cadmium chloride alone and in combination with alpha lipoic acid, selenium and coenzyme Q10.

4.2.1 GENERAL OBSERVATIONS

4.2.1.1 Changes in Body and Organ Weight

There was a significant decrease ($p<0.001$) in the body weight of animals of group 2 (100CD) as compared to group 1 (control). There was no significant increase in the weight of animals of group 3 (ALA) as compared to group 1 (control). The weight was significantly increased ($p<0.01$) in group 4 (100CD + ALA) as compared to group 2 (100CD). There was no significant increase in the weight of animals of group 5 (Se) as compared to group 1 (control). The weight was significantly increased ($p<0.05$) in group 6 (100CD + Se) as compared to group 2 (100CD). There was no significant increase in the weight of animals of group 7 (CoQ10) as compared to group 1 (control). The weight was significantly increased ($p<0.01$) in group 8 (100CD + CoQ10) as compared to group 2 (100CD) **(Fig 4.10)**.

There was a significant increase in the weight of liver ($p<0.001$), kidney ($p<0.001$), heart ($p<0.001$) and lung ($p<0.01$) in group 2 (100CD) as compared to group 1 (control). But there was no significant change in the weight of brain in group 2 (100CD) as compared to group 1 (control). There was no significant change in weight of liver, kidney, lung, heart and brain of animals in group 3 (ALA), group 5 (Se) and group 7 (COQ10) as compared to group 1 (control). There was a significant decrease in the weight of kidney ($p<0.001$), liver ($p<0.01$), heart ($p<0.01$) and lung ($p<0.05$) in group 4 (100CD + ALA) as compared to group 2 (100CD). There was no significant change in the weight of brain in group 4 (100CD + ALA) as compared to that of group 2 (100CD). There was a significant decrease in the weight of kidney ($p<0.01$), liver ($p<0.01$), heart ($p<0.05$) and lung ($p<0.05$) in group 6 (100CD + Se) as compared to group 2 (100CD). There was no significant change in the weight of brain in group 6 (100CD + Se) as compared to that of group 2 (100CD). There was a significant

decrease in the weight of kidney ($p<0.05$), liver ($p<0.05$), heart ($p<0.05$) and lung ($p<0.05$) in group 8 (100CD + CoQ10) as compared to group 2 (100CD). There was no significant change in the weight of brain in group 8 (100CD+CoQ10) as compared to that of group 2 (100CD) **(Table 4.1)**.

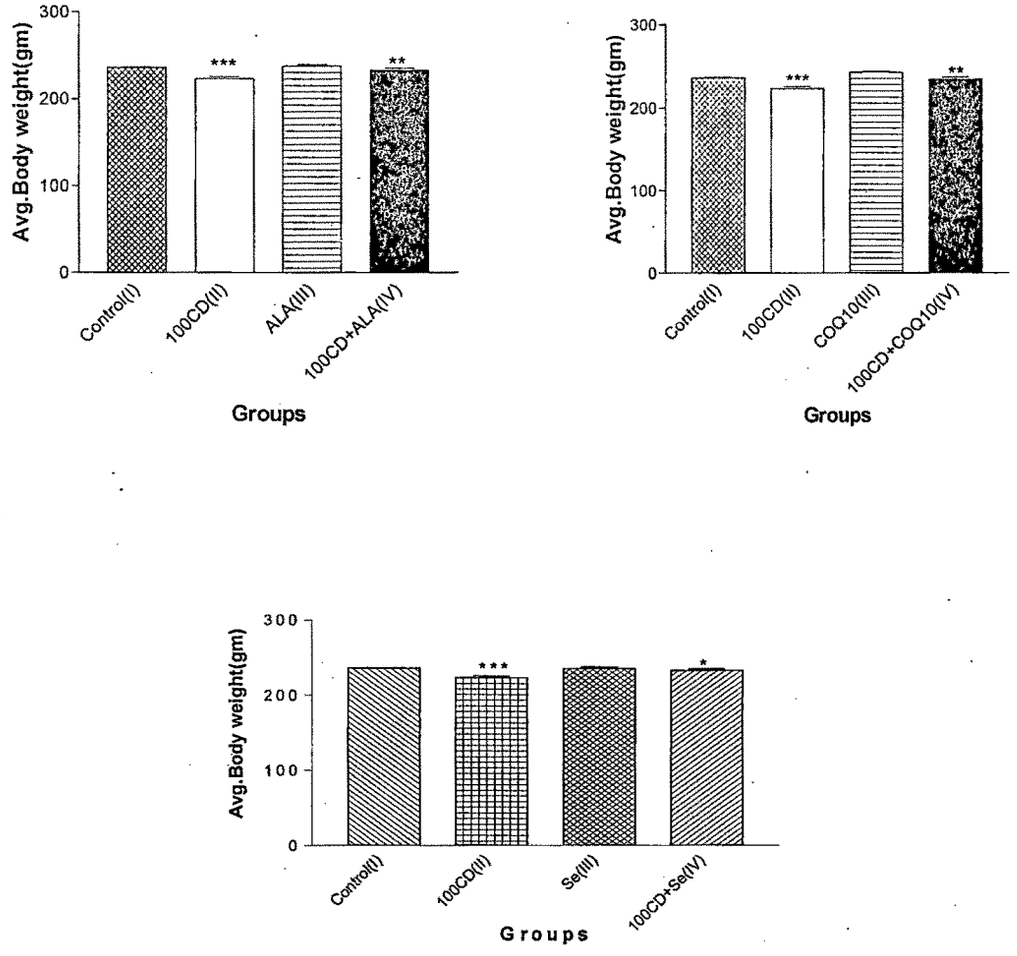


Fig: 4.10. Effect of 100 ppm of cadmium chloride (100CD) exposure for 30 days alone and in combination with antioxidants i.e. Alpha lipoic acid, Selenium or Coenzyme Q10 (ALA, Se or COQ10) on body weight of rats during 30 days of experiment.

Values expressed as mean ± SEM (n=6) for each observation.
Group II and Group III compared to control group.
Group IV compared to cadmium treated group.
$^{*}p<0.05$, $^{**}p<0.01$, $^{***}p<0.001$.

Table-4.1. Effect of 100 ppm of cadmium chloride exposure for 30 days alone and in combination with antioxidants i.e. Alpha lipoic acid, Selenium or CoenzymeQ10 (ALA, Se or COQ10) on organ weights of rats. (gm)

GROUP	ORGAN WEIGHT				
	Liver	**Kidney**	**Lung**	**Heart**	**Brain**
1.Control	6.190 ± 0.09869	1.34 ± 0.02236	1.550 ± 0.04147	0.5260 ± 0.01939	2.074 ± 0.04665
2.100Cd	7.154 ± 0.1675 ^{***b}	1.81 ± 0.03082 ^{***b}	1.746 ± 0.02926 ^{**b}	0.7680 ± 0.02871 ^{***b}	1.928 ± 0.01828 ^{ns}
3.ALA	6.218 ± 0.08015	1.320 ± 0.02569	1.514 ± 0.01778	0.5440 ± 0.02315	2.058 ± 0.04432
4.Cd+ALA	6.426 ± 0.1628 ^{**a}	1.434 ± 0.04864 ^{***a}	1.608 ± 0.03597 ^{*a}	0.6080 ± 0.02267 ^{**a}	1.972 ± 0.03382 ^{ns}
5.Se	6.126 ± 0.05528	1.360 ± 0.04111	1.534 ± 0.02821	0.5320 ± 0.03262	2.024 ± 0.03970
6.Cd+Se	6.492 ± 0.09851 ^{**a}	1.648 ± 0.01020 ^{**a}	1.608 ± 0.02267 ^{*a}	0.6468 ± 0.01650 ^{*a}	1.902 ± 0.05122 ^{ns}
7.COQ10	6.212 ± 0.07088	1.356 ± 0.02713	1.518 ± 0.02939	0.5480 ± 0.02417	2.060 ± 0.03899
8.Cd+COQ10	6.518 ± 0.1590 ^{*a}	1.686 ± 0.01913 ^{*a}	1.596 ± 0.01364 ^{*a}	0.6440 ± 0.03076 ^{*a}	1.936 ± 0.02786 ^{ns}

Values are expressed as mean ± SEM.
a: Group 4, 6 and 8 as compared to group 2.
b: Group 2, 3,5 and 7 as compared to group 1.
$p<0.05$, $^{**}p<0.01$, $^{***}p<0.001$.

4.2.2 ELECTROCARDIOGRAM and HAEMODYNAMIC MEASUREMENTS

4.2.2.1 Changes in the heart rate

The heart rate of the animals of group 2 (100CD) was significantly increased ($p<0.001$) compared to group 1 (control). The heart rate significantly decreased ($p<0.001$) in the animals of group 4 (100CD + ALA) compared to group 2 (100CD). This decrease was also significantly ($p<0.01$) found in the animals of group 6 (100CD + Se) compared to that of group 2 (100CD). In group 8 (100CD + CoQ10) too the decrease in the heart rate was significant ($p<0.001$) compared to group 2 (100CD) **(Fig: 4.11)**.

4.2.2.2 Changes in the systolic blood pressure

No significant increase in the systolic blood pressure was noted in the animals of group 2 (100CD) compared to group 1 (control) in the first two weeks. However there was a significant increase noted in the 3rd week ($p<0.05$), 4th week ($p<0.001$) and 5th week ($p<0.001$) in the animals of group 2 (100CD) compared to that of group 1 (control). There was no significant decrease in the systolic blood pressure of animals of group 4 (100CD + ALA) compared to group 2 (100CD) in the first three weeks. However a significant decrease ($p<0.001$) was noted in the next two weeks in the systolic blood pressure of animals of group 4 (100CD +ALA) **(Fig: 4.12)**compared to group 2 (100CD). There was no significant decrease in the systolic blood pressure of animals of group 6 (100CD + Se) **(Fig: 4.13)** compared to group 2 (100CD) in the first three weeks. However a significant decrease ($p<0.001$) was noted in the next two weeks in the systolic blood pressure of animals of group 6 (100CD + Se) compared to group 2 (100CD). There was no significant decrease in the systolic blood pressure of animals of group 8 (100CD + CoQ10) **(Fig: 4.14)** compared to group 2 (100CD) in the first four weeks. However a significant decrease ($p<0.001$) was noted in the 5th week in the systolic blood pressure of animals of group 8 (100CD +CoQ10) compared to group 2 (100CD).

4.2.2.3 Changes in the diastolic blood pressure

There was no significant increase in the diastolic blood pressure of animals of group 2 (100CD) compared to that of group 1 (control) for the first week. However the increase was

significant in the 2nd week ($p<0.05$), 3rd week ($p<0.05$), 4th week ($p<0.001$) and 5th week ($p<0.001$) in the animals of group 2 (100CD) compared with the animals of group 1 (control). There was no significant decrease in the diastolic blood pressure of animals of group 4 (100CD + ALA) compared with that of group 2 (100CD) in the first 3 weeks. However the decrease of diastolic blood pressure was significant in the 4th week ($p<0.05$) and the 5th week ($p<0.001$) in the animals of group 4 (100CD + ALA) **(Fig: 4.12)** compared to that of group 2 (100CD). There was no significant decrease in the diastolic blood pressure of animals of group 6 (100CD + Se) compared with that of group 2 (100CD) in the first 3 weeks. However the decrease of diastolic blood pressure was significant in the 4th week ($p<0.05$) and the 5th week ($p<0.001$) in the animals of group 6 (100CD + Se) **(Fig: 4.13)** compared to that of group 2 (100CD). There was no significant decrease in the diastolic blood pressure of animals of group 8 (100CD + CoQ10) compared with that of group 2 (100CD) in the first 3 weeks. However the decrease of diastolic blood pressure was significant in the 4th week ($p<0.05$) and the 5th week ($p<0.001$) in the animals of group 8 (100CD + CoQ10) **(Fig: 4.14)** compared to that of group 2 (100CD).

4.2.2.4 Changes in the mean blood pressure

The mean blood pressure was not significantly increased in group 2 (100CD) compared to group 1 (control) in the first week. There was a significant increase in the mean blood pressure in the 2nd wk ($p<0.05$), 3rd wk ($p<0.05$), 4th wk ($p<0.001$) and 5th wk ($p<0.001$) in animals of group 2 (100CD) compared to those of group 1 (control). The decrease in mean blood pressure was not significant in the animals of group 4 (100CD + ALA) **(Fig: 4.12)** in the first 3 wks, but the decrease was significant in the 4th week ($p<0.01$) and in the 5th week ($p<0.001$) in group 4 (100CD + ALA) compared to group 2 (100CD). The decrease in mean blood pressure was not significant in the animals of group 6 (100CD + Se) **(Fig: 4.13)** in the first 3 wks, but the decrease was significant in the 4th week ($p<0.01$) and in the 5th week ($p<0.001$) compared to group 2 (100CD). The decrease in mean blood pressure was not significant in the animals of group 8 (100CD + CoQ10) **(Fig: 4.14)** in the first 3 weeks, but the decrease was significant in the 4th week ($p<0.05$) and in the 5th week ($p<0.001$) compared to group 2 (100CD).

4.2.2.5 Changes in the vascular reactivity to various drugs

4.2.2.5.1 Changes in the pressor and depressor response to adrenaline

There was a significant increase ($p<0.01$) in the pressor response to adrenaline 1μg/kg in group 2 (100CD) compared to group 1 (control). There was also a significant increase ($p<0.05$) in the pressor response to adrenaline 2 μg/kg in group 2(100CD) compared to group 1(control). There was no significant increase in the depressor response to adrenaline in group 2 (100CD) compared to group 1 (control). The pressor response was significantly reduced when adrenaline 1μg/kg and 2 μg/kg were administered, ($p<0.05$) in group 4 (100CD + ALA) **(Fig: 4.15)** ($p<0.05$) in group 6 (100CD + Se) **(Fig: 4.18)** and ($p<0.05$) in group 8 (100CD + CoQ10) **(Fig: 4.21)** compared to group 2 (100CD).

4.2.2.5.2 Changes in the pressor response to noradrenaline

There was a significant increase ($p<0.01$) in the pressor response to noradrenaline 1μg/kg in group 2 (100CD) compared to group 1 (control). There was also a significant increase ($p<0.01$) in the pressor response to noradrenaline 2 μg/kg in group 2(100CD) compared to group 1(control). The pressor response was significantly reduced ($p<0.05$) in group 4 (100CD + ALA) **(Fig: 4.16)** ($p<0.01$) in group 6 (100CD + Se) **(Fig 4.19)** when 1μg/kg noradrenaline was given and ($p<0.05$) when 2 μg/kg noradrenaline was given and ($p<0.05$) in group 8 (100CD + CoQ10) **(Fig: 4.22)** when 1μg/kg of noradrenaline was given and ($p<0.01$) when 2μg/kg of noradrenaline was given compared to group 2 (100CD).

4.2.2.5.3 Changes in the depressor response to isoprenaline

There was a significant increase ($p<0.01$) in the depressor response to isoprenaline 1μg/kg in group 2 (100CD) compared to group 1 (control). There was also a significant increase ($p<0.05$) in the depressor response to isoprenaline 2 μg/kg in group 2(100CD) compared to group 1(control). The depressor response was significantly reduced ($p<0.05$) in group 4 (100CD + ALA) **(Fig: 4.17)**, ($p<0.05$) in group 6 (100CD + Se) **(Fig: 4.20)** and ($p<0.05$) in group 8 (100CD + CoQ10) **(Fig: 4.23)** compared to group 2 (100CD).

4.2.2.6 **Electrocardiographic Changes:**

The electrocardiogram of the rats who were administered cadmium chloride (100 ppm) for 30 days showed changes that were suggestive of damage to the myocardium in the form of S-T segment elevation which is suggestive of ischemia, T wave inversion which is suggestive of injury to myocardium and Q wave inversion which is suggestive of infarction. When the animals administered cadmium chloride (100 ppm) were supplemented with alpha lipoic acid, selenium or coenzyme Q10 these changes were not observed and the electrocardiogram was normal. **(Figs: 4.24, 4.25, 4.26)**

MEASUREMENT OF HEART RATE

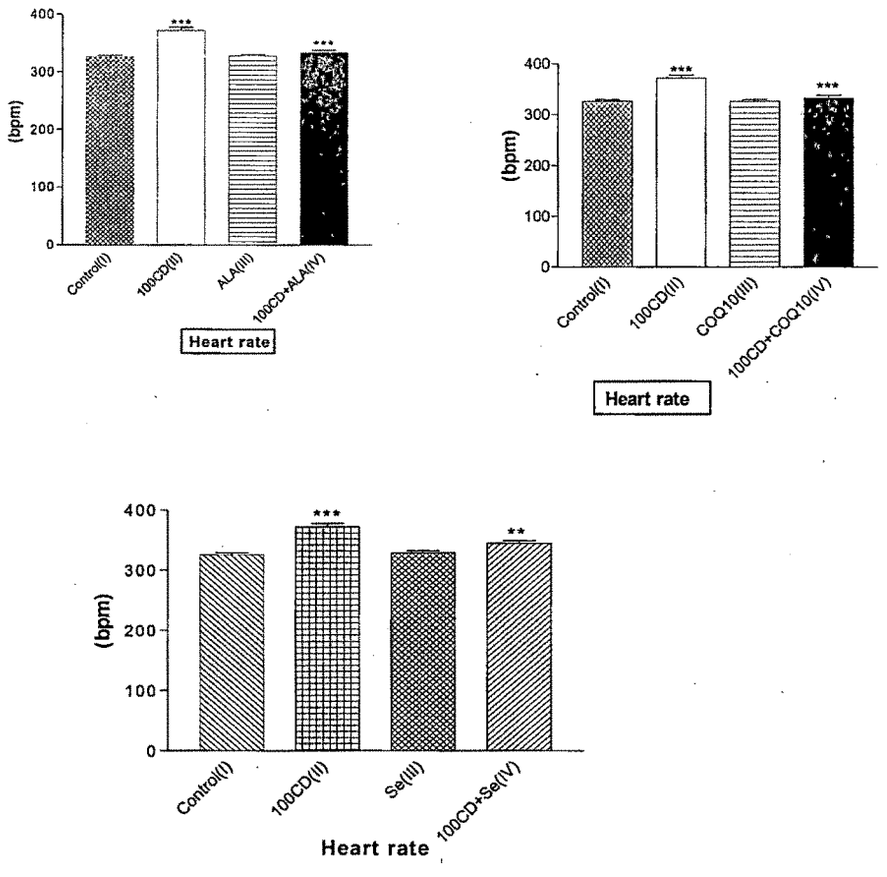


Fig: 4.11. Effect of 100 ppm of cadmium chloride (100CD) exposure for 30 days alone and in combination with antioxidants i.e. Alpha lipoic acid, Coenzyme Q10 or Selenium (ALA, COQ10 or Se) on the Heart Rate of rats.

Values expressed as mean ± SEM (n=6) for each observation.
Group II compared to control group.
Group IV compared to cadmium treated group.
$^{*}p<0.05$, $^{**}p<0.01$, $^{***}p<0.001$.

MEASUREMENT OF BLOOD PRESSURE BY NON INVASIVE METHOD

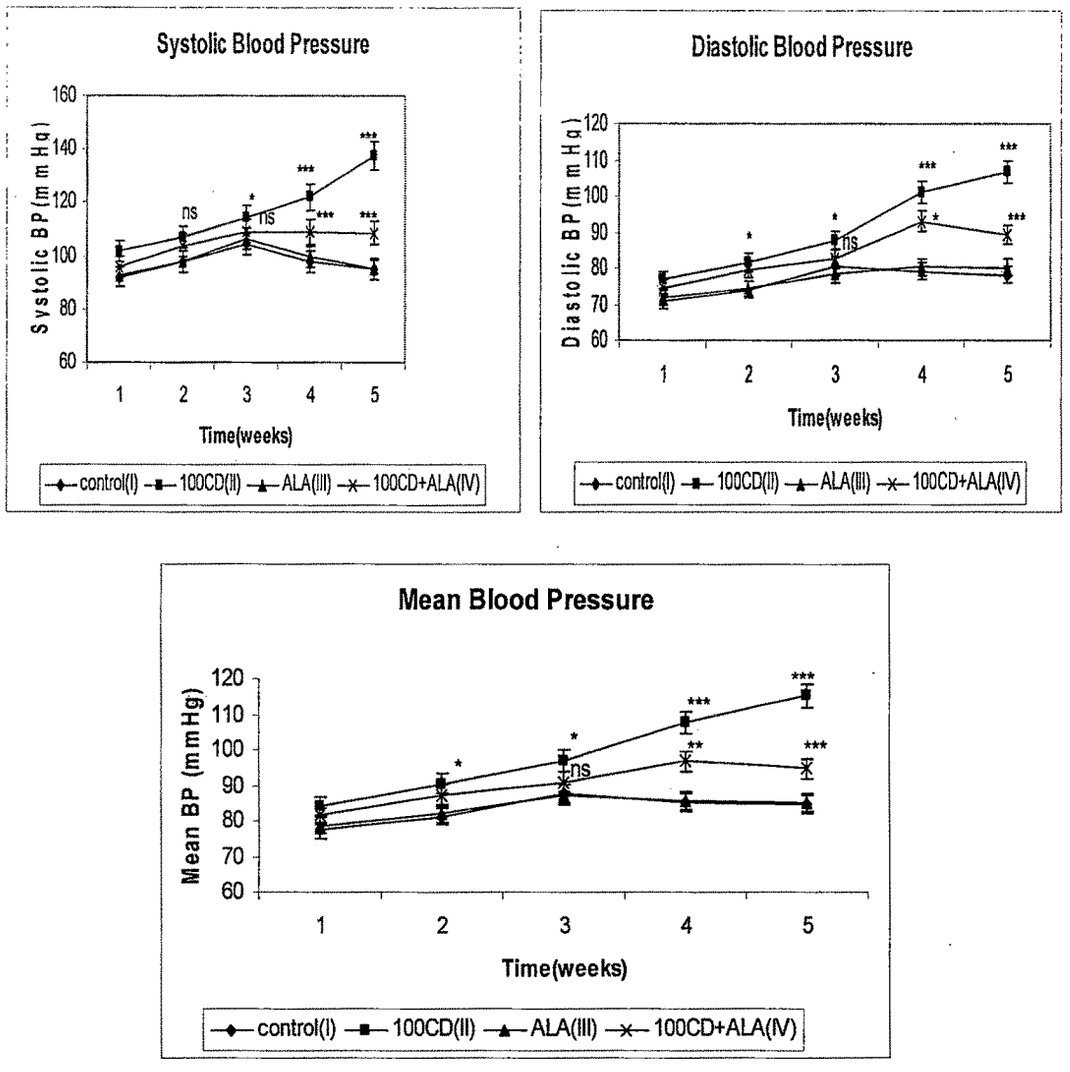


Fig: 4.12. Effect of 100 ppm cadmium chloride (100CD) exposure alone and in combination with antioxidant i.e. Alpha lipoic acid on Blood pressure (Systolic, Diastolic and Mean Blood pressure) by Non invasive method during 30days of treatment.

Values expressed as mean ± SEM (n=6) for each observation.
Group II compared to control group.
Group IV compared to cadmium treated group.
$^{*}p<0.05$, $^{**}p<0.01$, $^{***}p<0.001$.

MEASUREMENT OF BLOOD PRESSURE BY NON INVASIVE METHOD

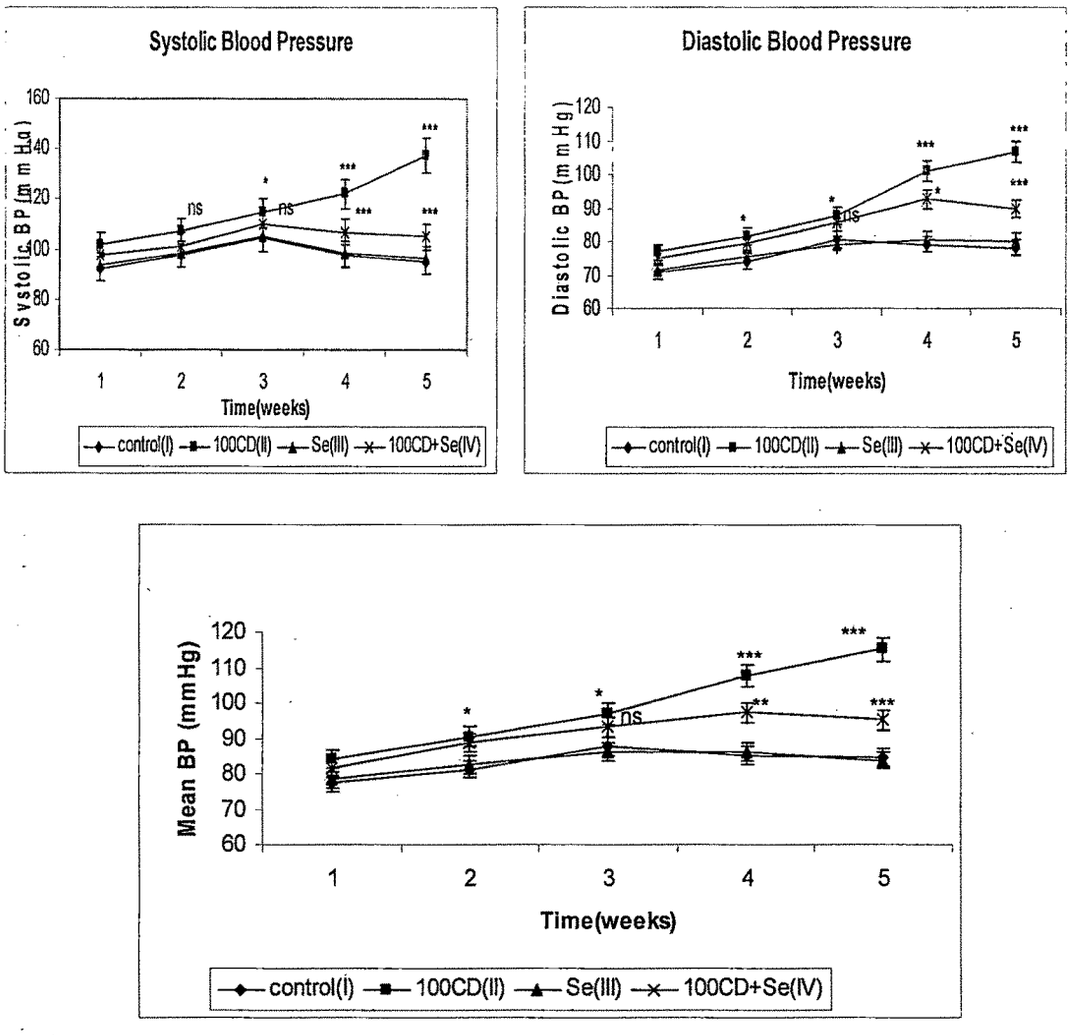


Fig: 4.13. Effect of 100 ppm cadmium chloride (100CD) exposure alone and in combination with antioxidant i.e. Selenium on Blood pressure (Systolic, Diastolic and Mean Blood pressure) by Non invasive method during 30 days of treatment.

Values expressed as mean ± SEM (n=6) for each observation.
Group II compared to control group.
Group IV compared to cadmium treated group.
$^{*}p<0.05$, $^{**}p<0.01$, $^{***}p<0.001$.

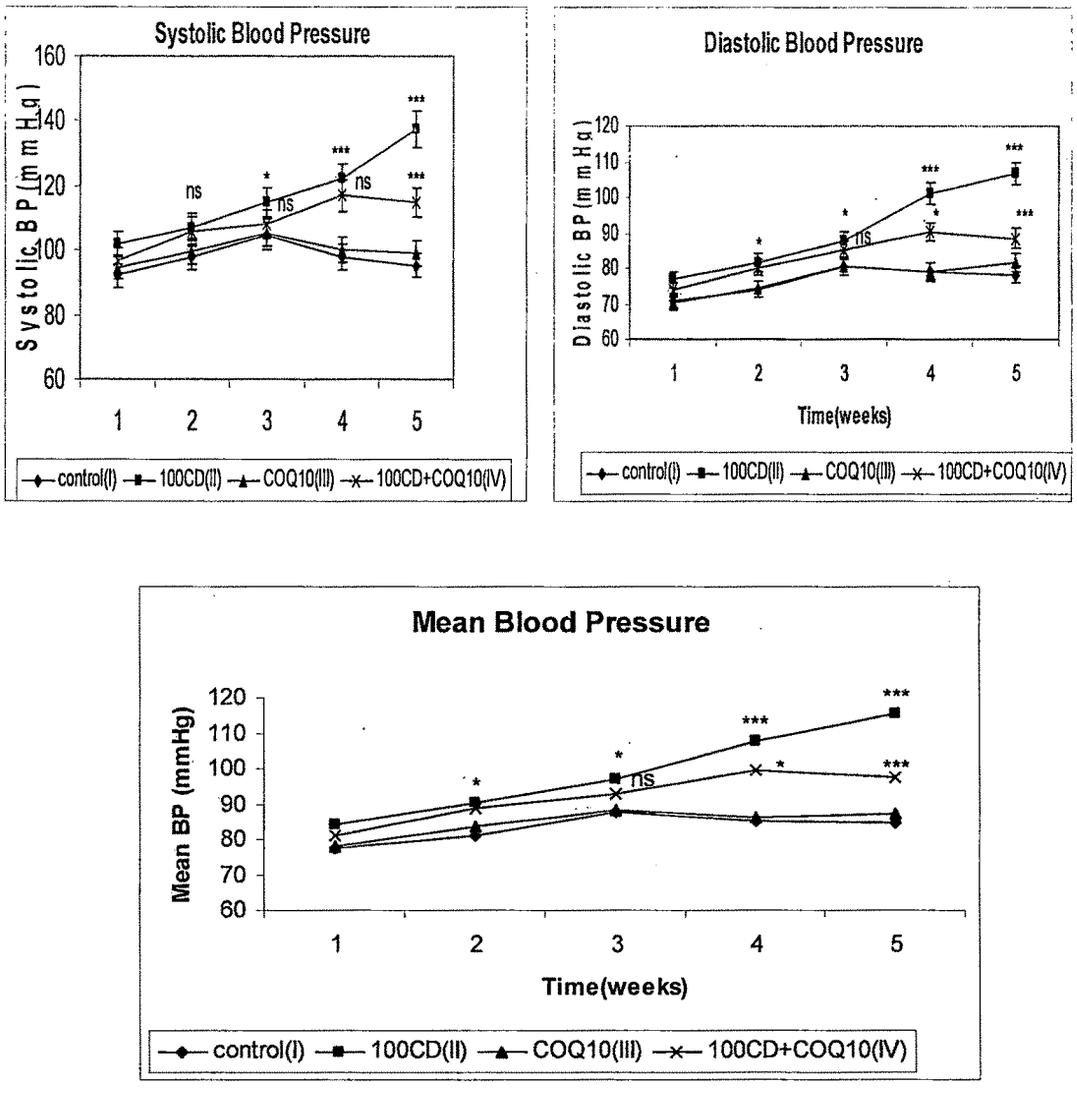


Fig: 4.14. Effect of 100 ppm cadmium chloride (100CD) exposure alone and in combination with antioxidant i.e. Coenzyme Q10 on Blood pressure (Systolic, Diastolic and Mean Blood pressure) by Non invasive method during 30days of treatment.

Values expressed as mean ± SEM (n=6) for each observation.
Group II compared to control group.
Group IV compared to cadmium treated group.
$^{*}p<0.05$, $^{**}p<0.01$, $^{***}p<0.001$.

Mean change in blood pressure after administration of Adrenaline-Alpha lipoic acid

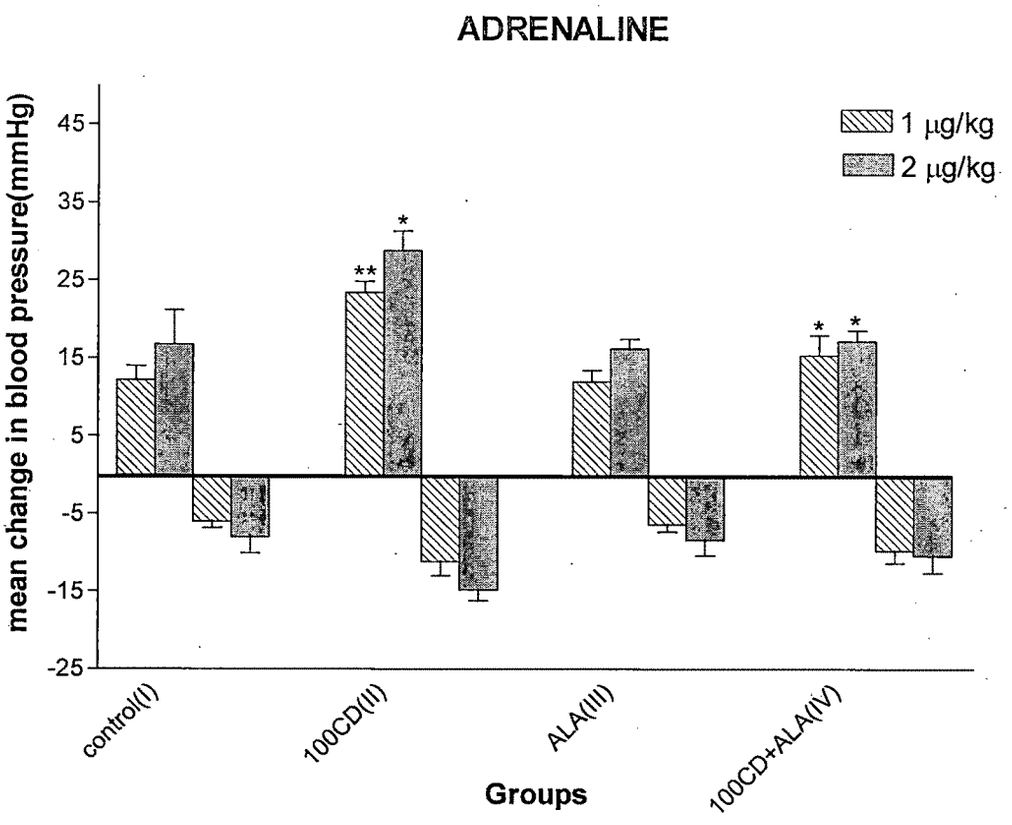


Fig: 4.15. Effect of 100 ppm cadmium chloride (100CD) exposure alone and in combination with antioxidant i.e. Alpha lipoic acid on mean change in Blood pressure after administration of Adrenaline.

Values expressed as mean ± SEM (n=6) for each observation.
Group II compared to control group.
Group IV compared to cadmium treated group.
$^{*}p<0.05$, $^{**}p<0.01$, $^{***}p<0.001$.

Mean change in blood pressure after administration of Noradrenaline-Alpha lipoic acid

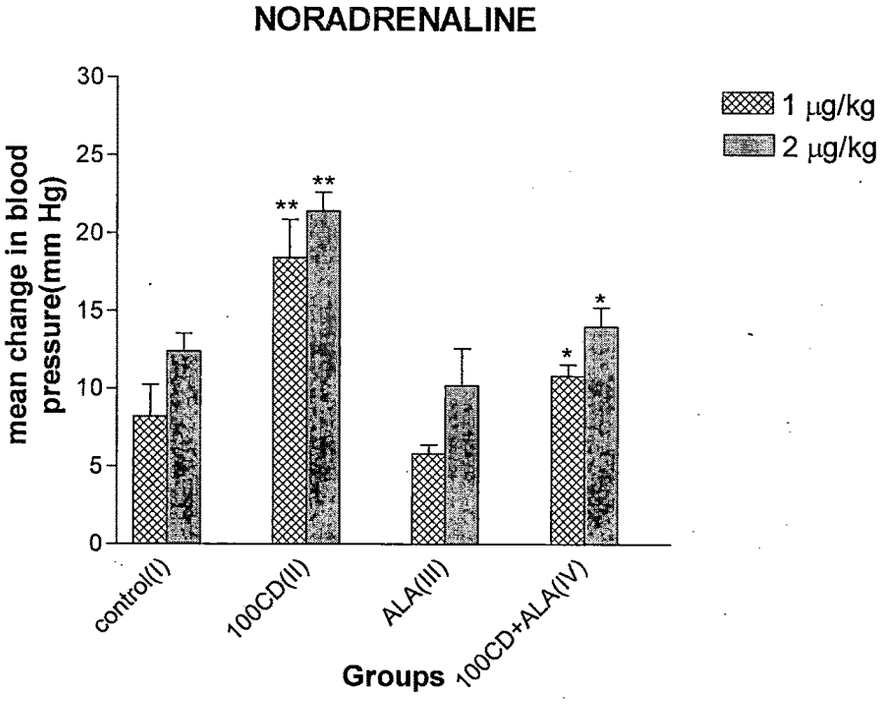


Fig: 4.16. Effect of 100 ppm cadmium chloride (100CD) exposure alone and in combination with antioxidant i.e. Alpha lipoic acid on mean change in Blood pressure after administration of Noradrenaline.

Values expressed as mean ± SEM (n=6) for each observation.
Group II compared to control group.
Group IV compared to cadmium treated group.
$^{*}p<0.05$, $^{**}p<0.01$, $^{***}p<0.001$.

Mean change in blood pressure after administration of Isoprenaline-Alpha lipoic acid

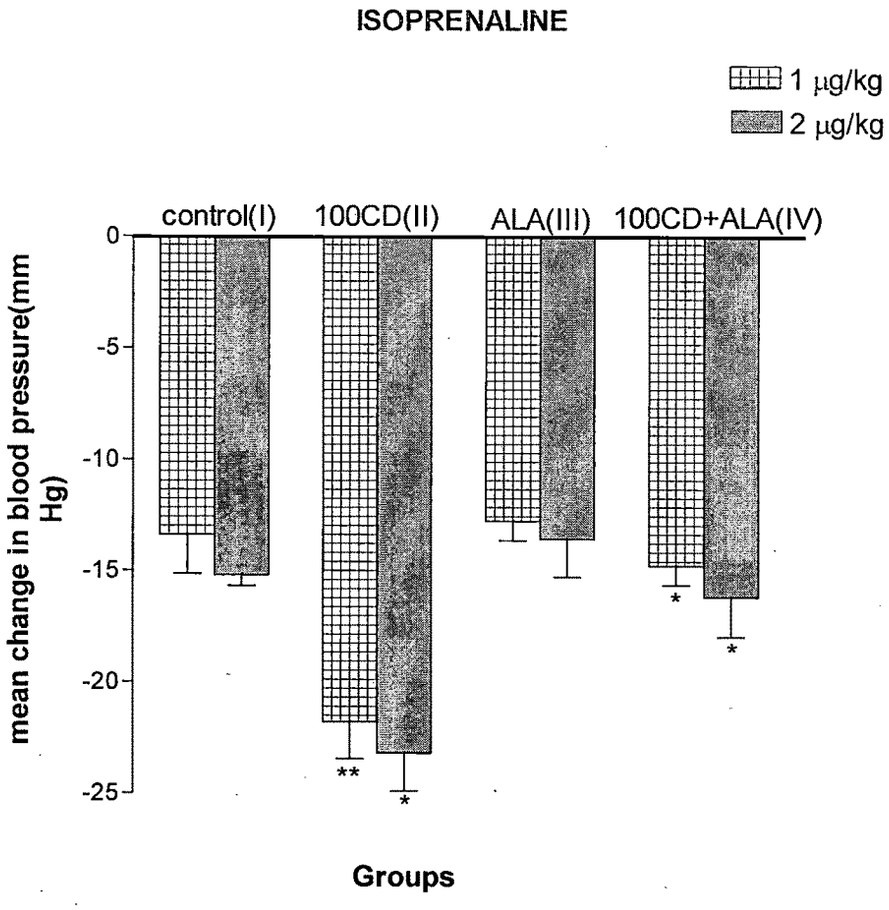


Fig: 4.17. Effect of 100 ppm cadmium chloride (100CD) exposure alone and in combination with antioxidant i.e. Alpha lipoic acid on mean change in Blood pressure after administration of Isoprenaline.

Values expressed as mean ± SEM (n=6) for each observation.
Group II compared to control group.
Group IV compared to cadmium treated group.
$^{*}p<0.05$, $^{**}p<0.01$, $^{***}p<0.001$.

Mean change in blood pressure after administration of Adrenaline-Selenium

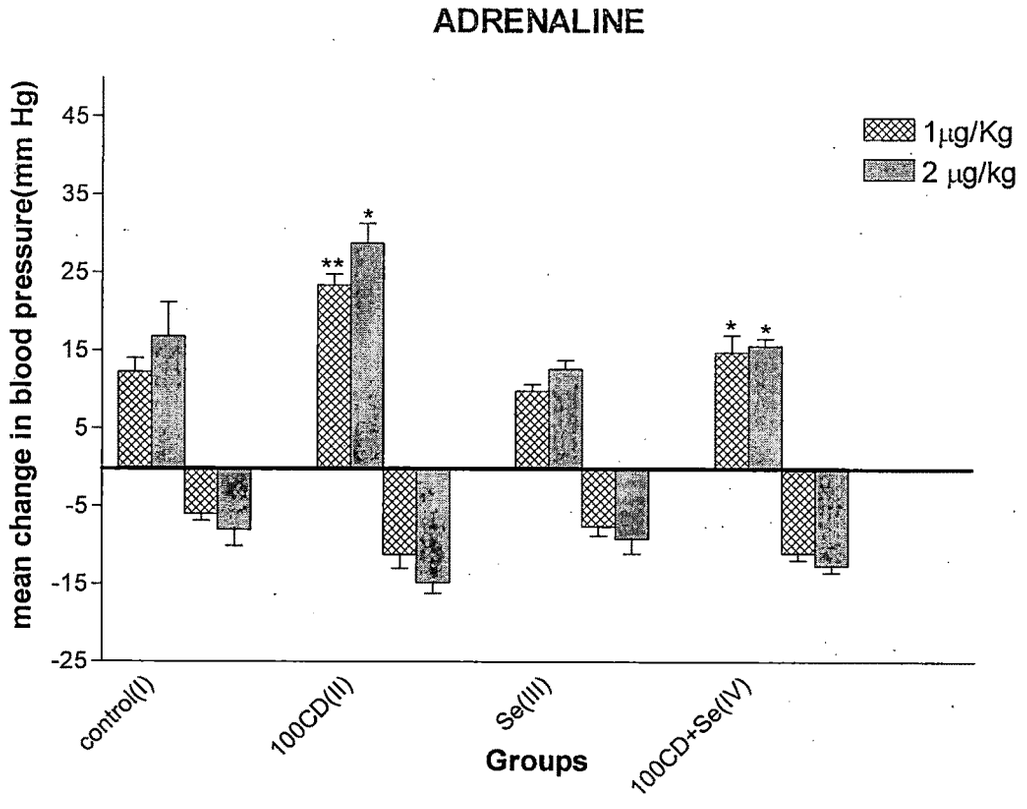


Fig: 4.18. Effect of 100 ppm cadmium chloride (100CD) exposure alone and in combination with antioxidant i.e. Selenium on mean change in Blood pressure after administration of Adrenaline.

Values expressed as mean ± SEM (n=6) for each observation.
Group II compared to control group.
Group IV compared to cadmium treated group.
$^{*}p<0.05$, $^{**}p<0.01$, $^{***}p<0.001$.

Mean change in blood pressure after administration of Noradrenaline-Selenium

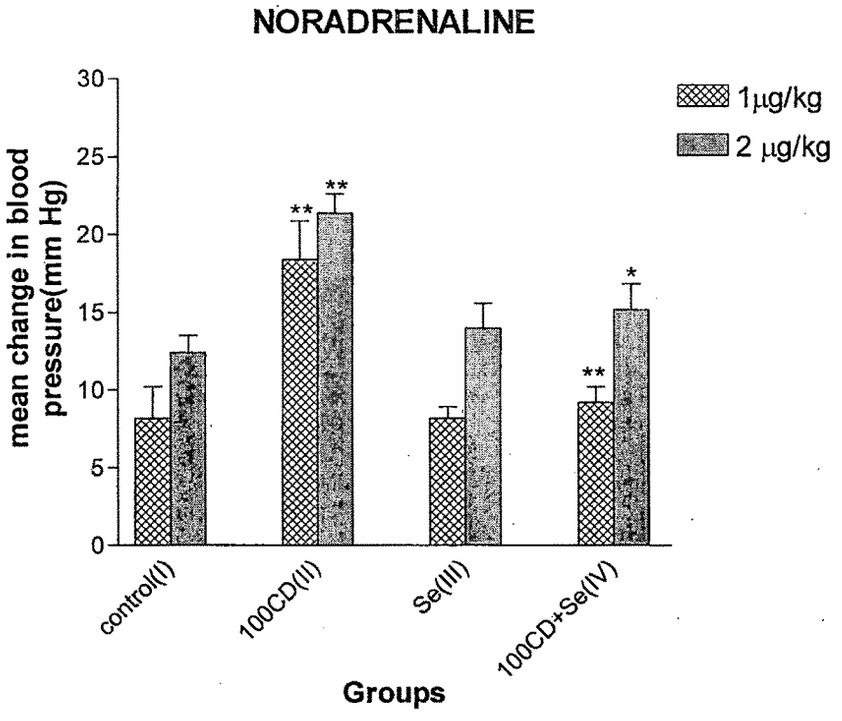


Fig: 4.19. Effect of 100 ppm cadmium chloride (100CD) exposure alone and in combination with antioxidant i.e. Selenium on mean change in Blood pressure after administration of Noradrenaline.

Values expressed as mean ± SEM (n=6) for each observation.
Group II compared to control group.
Group IV compared to cadmium treated group.
$^{*}p<0.05$, $^{**}p<0.01$, $^{***}p<0.001$.

Mean change in blood pressure after administration of Isoprenaline-Selenium

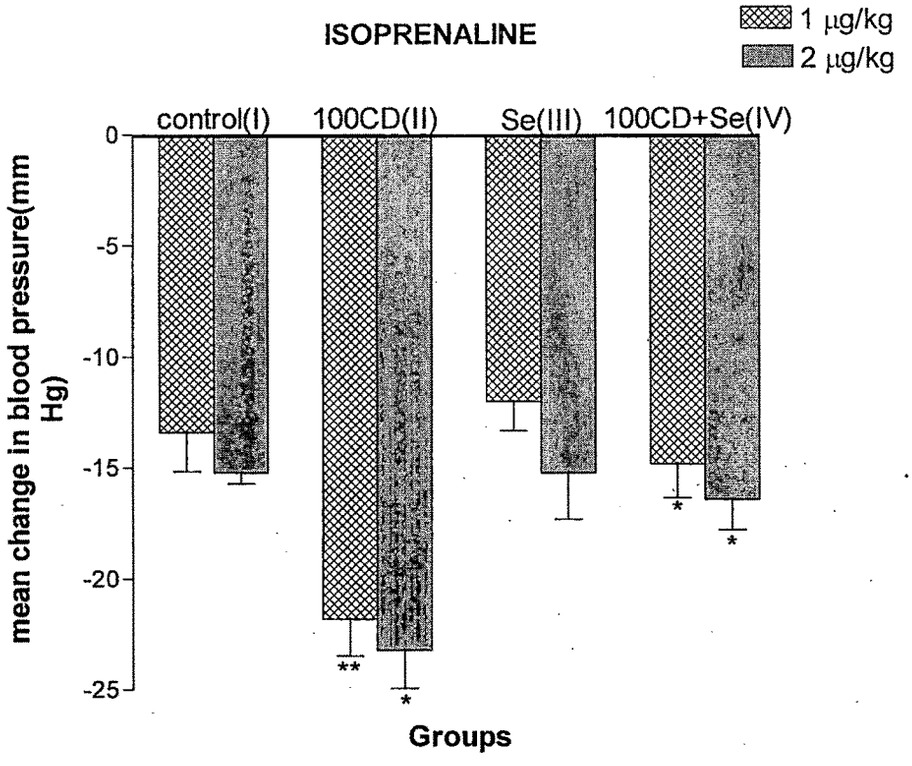


Fig: 4.20. Effect of 100 ppm cadmium chloride (100CD) exposure alone and in combination with antioxidant i.e. Selenium on mean change in Blood pressure after administration of Isoprenaline.

Values expressed as mean ± SEM (n=6) for each observation.
Group II compared to control group.
Group IV compared to cadmium treated group.
$^{*}p<0.05$, $^{**}p<0.01$, $^{***}p<0.001$.

Mean change in blood pressure after administration of Adrenaline-Coenzyme Q10

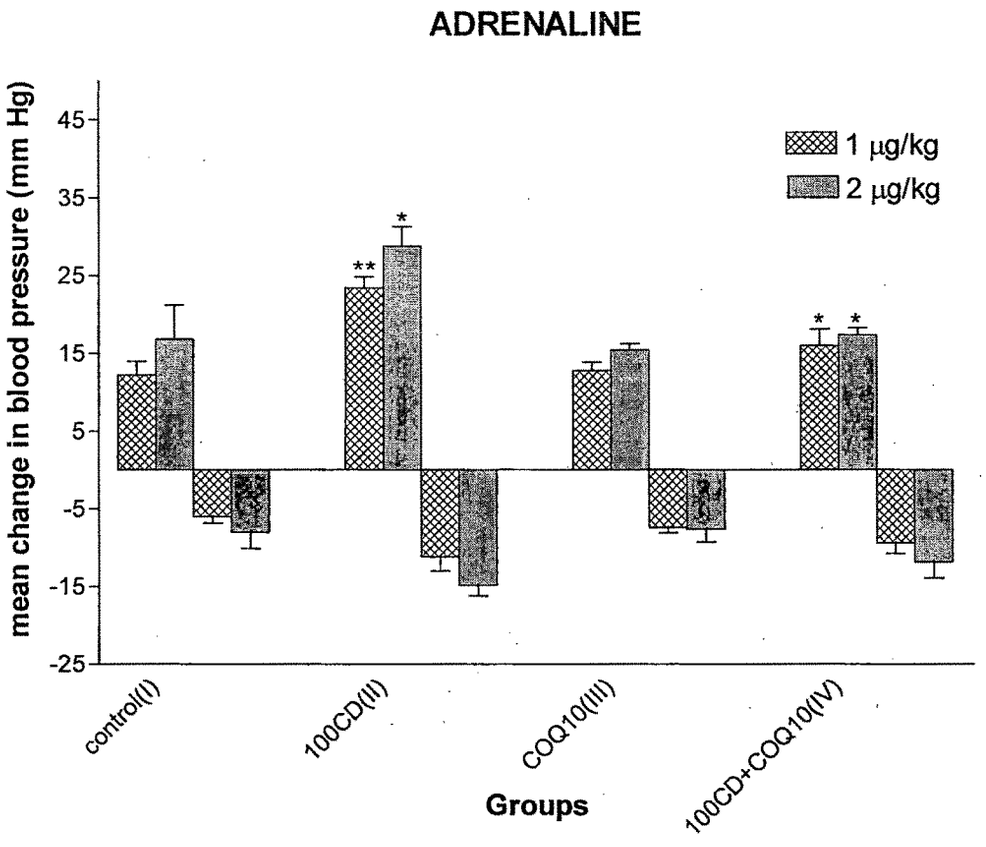


Fig: 4.21. Effect of 100 ppm cadmium chloride (100CD) exposure alone and in combination with antioxidant i.e. Coenzyme Q10 on mean change in Blood pressure after administration of Adrenaline.

Values expressed as mean ± SEM (n=6) for each observation.
Group II compared to control group.
Group IV compared to cadmium treated group.
$^{*}p<0.05$, $^{**}p<0.01$, $^{***}p<0.001$.

Mean change in blood pressure after administration of Noradrenaline-Coenzyme Q10

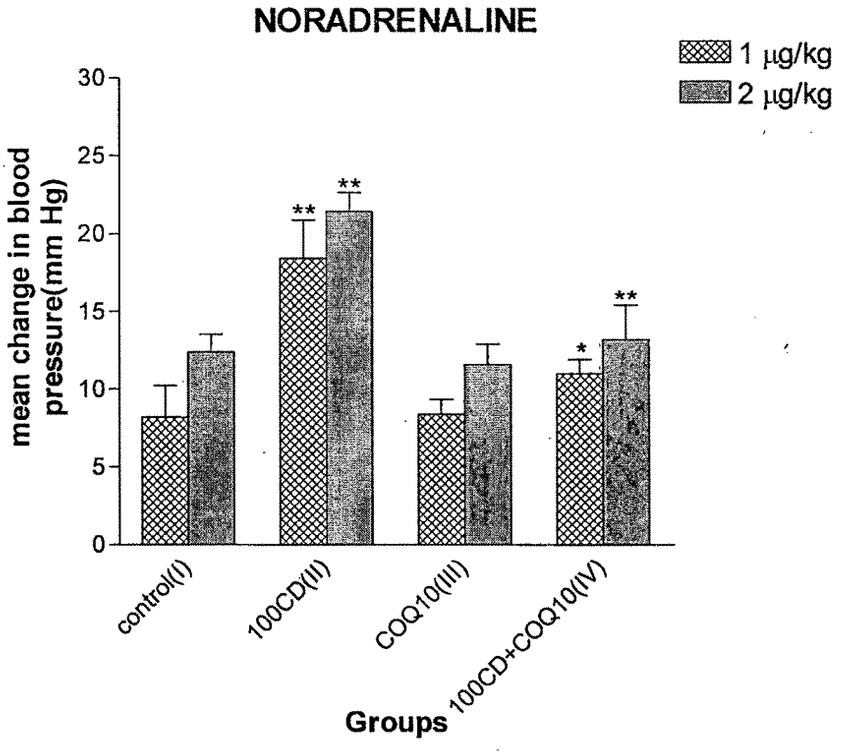


Fig: 4.22. Effect of 100 ppm cadmium chloride (100CD) exposure alone and in combination with antioxidant i.e. Coenzyme Q10 on mean change in Blood pressure after administration of Noradrenaline.

Values expressed as mean ± SEM (n=6) for each observation.
Group II compared to control group.
Group IV compared to cadmium treated group.
$^{*}p<0.05$, $^{**}p<0.01$, $^{***}p<0.001$.

Mean change in blood pressure after administration of Isoprenaline-Coenzyme Q10

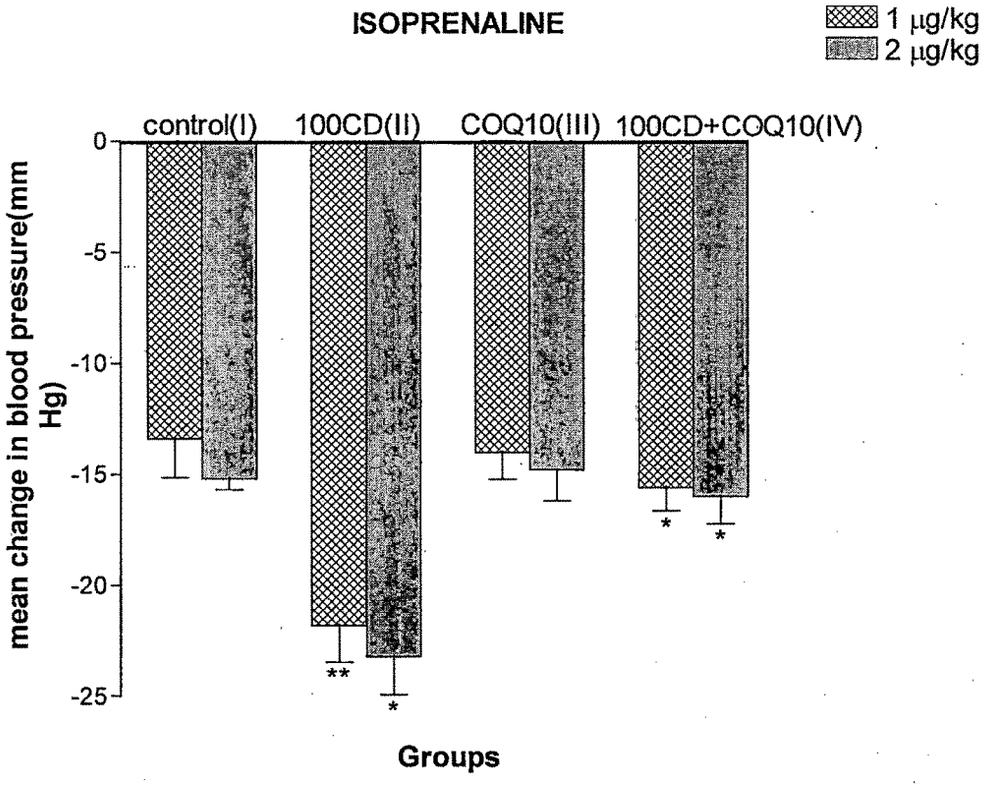
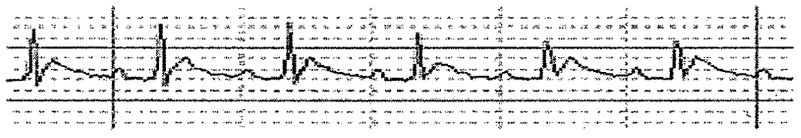


Fig: 4.23. Effect of 100 ppm cadmium chloride (100CD) exposure alone and in combination with antioxidant i.e. Coenzyme Q10 on mean change in Blood pressure after administration of Isoprenaline.

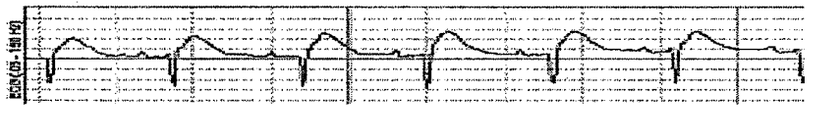
Values expressed as mean ± SEM (n=6) for each observation.
Group II compared to control group.
Group IV compared to cadmium treated group.
$^{*}p<0.05$, $^{**}p<0.01$, $^{***}p<0.001$.

Fig: 4.24. Recordings showing changes in the Electrocardiogram-Alpha lipoic acid

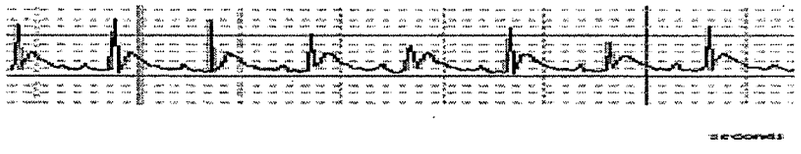
Control



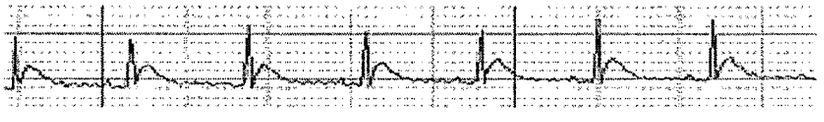
Cadmium



Cadmium 100ppm + Alpha lipoic acid



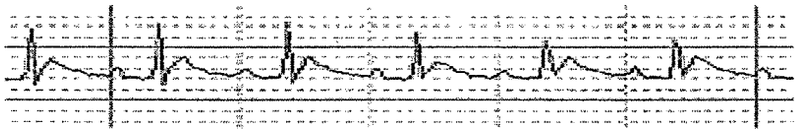
Alpha lipoic acid



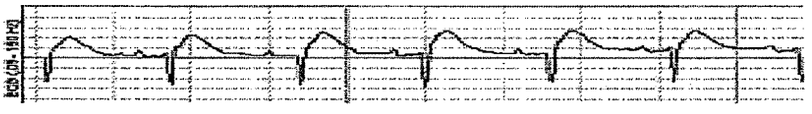
CADMIUM INDUCED CARDIOTOXICITY

Fig: 4.25. Recordings showing changes in the Electrocardiogram-Selenium

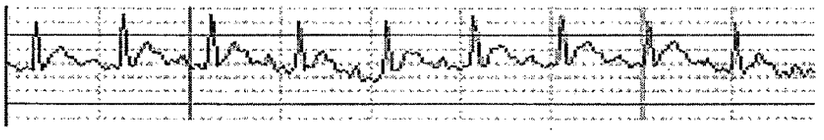
Control



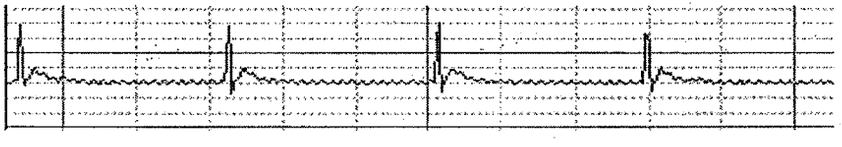
Cadmium



Cadmium 100ppm + Selenium



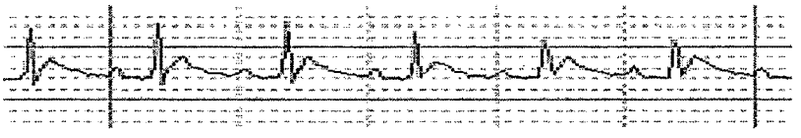
Selenium



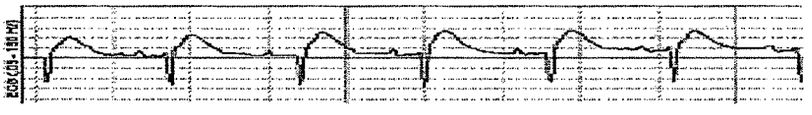
CADMIUM INDUCED CARDIOTOXICITY

Fig: 4.26. Recordings showing changes in the Electrocardiogram-Coenzyme Q10

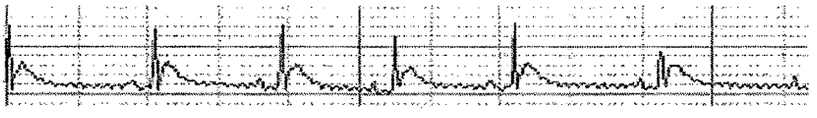
Control



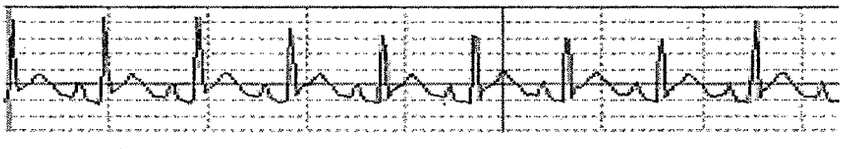
Cadmium



Cadmium 100ppm + Coenzyme Q10



Coenzyme Q10



4.2.3 TISSUE ESTIMATIONS

4.2.3.1 Changes in the Levels of Malondialdehyde (MDA)

The Malondialdehyde (MDA) levels in liver, lung, kidney and brain were increased significantly ($p<0.001$) in group 2 (100 CD) as compared to group 1 (control). In heart it was increased significantly ($p<0.01$) in group 2 (100CD) compared to group 1 (control). However in all the tissues it was decreased highly significantly ($p<0.001$) in group 4 (100CD + ALA) compared to group 2 (100CD). In group 6 (100CD + Se) it was significantly decreased in all tissues, kidney ($p<0.001$), liver ($p<0.01$), brain ($p<0.01$), lung ($p<0.05$) and heart ($p<0.05$) compared to group 2 (100CD) **(Fig 4.27)**. In group 8 (100CD + CoQ10) it was significantly decreased in all tissues, liver, kidney and brain ($p<0.001$), lung ($p<0.01$), heart ($p<0.05$) compared to group 2 (100CD) **(Fig 4.28)**.

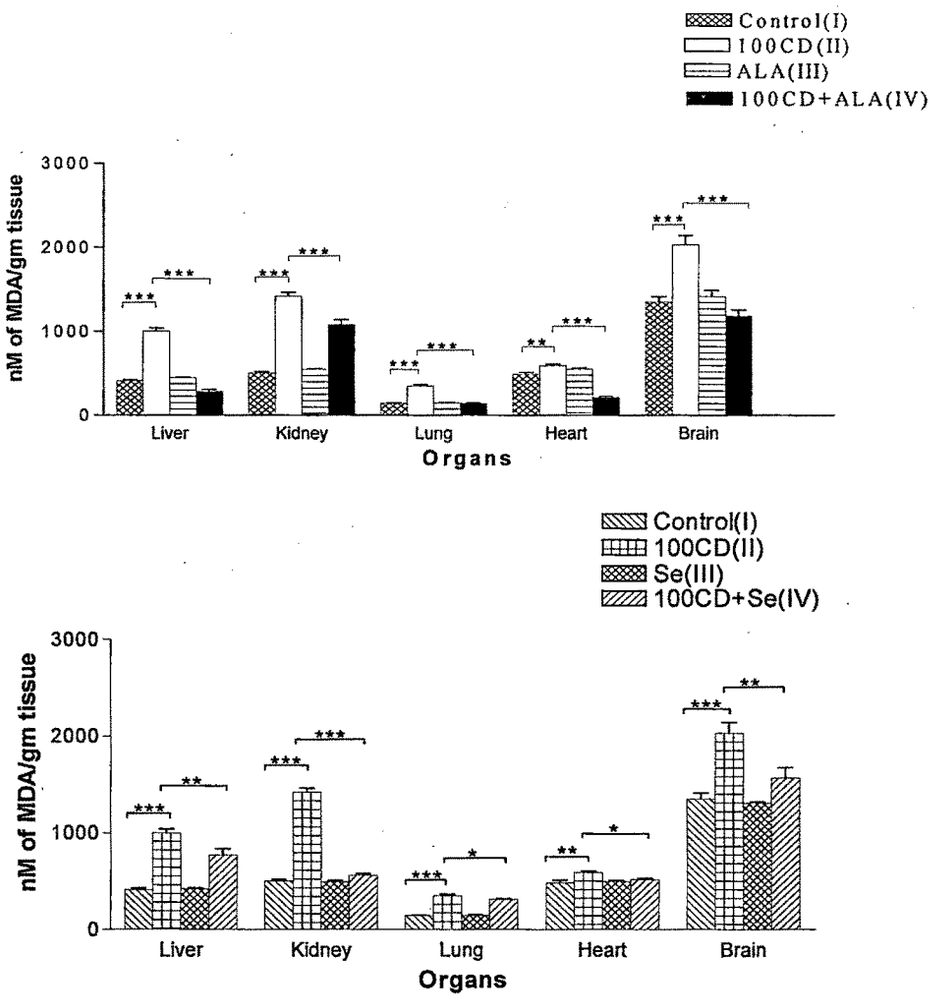


Fig: 4.27. Effect of 100 ppm of cadmium chloride (100CD) exposure for 30 days alone and in combination with antioxidants i.e. Alpha lipoic acid or Selenium (ALA or Se) on the formation of malondialdehyde in liver, kidney, lung, heart and brain of rats.

Values expressed as mean ± SEM (n=6) for each observation.
Group II compared to control group.
Group IV compared to cadmium treated group.
$^{*}p<0.05$, $^{**}p<0.01$, $^{***}p<0.001$.

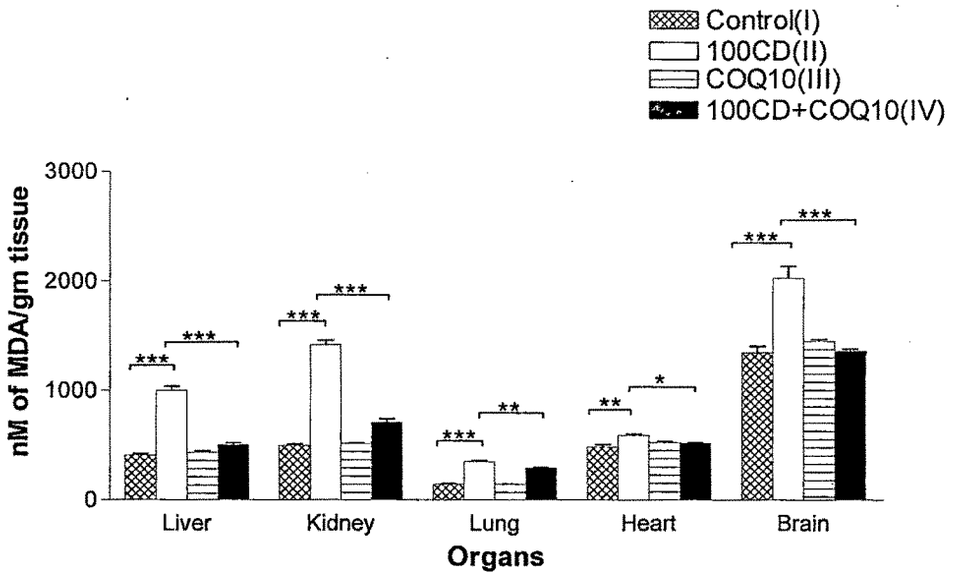


Fig: 4.28. Effect of 100 ppm of cadmium chloride (100CD) exposure for 30 days alone and in combination with antioxidant i.e. Coenzyme Q10(COQ10) on the formation of malondialdehyde in liver, kidney, lung, heart and brain of rats.

Values expressed as mean ± SEM (n=6) for each observation.
Group II compared to control group.
Group IV compared to cadmium treated group.
$^{*}p<0.05$, $^{**}p<0.01$, $^{***}p<0.001$.

4.2.3.2. Changes in the levels of Endogenous Antioxidants

4.2.3.2.1 Changes in the Levels of Superoxide dismutase (SOD)

The Superoxide dismutase (SOD) levels in liver, kidney, lung, heart and brain were decreased significantly ($p<0.001$) in group 2 (100 CD) as compared to group 1 (control). However in all the tissues it was increased significantly ($p<0.001$) in group 4 (100CD + ALA) compared to group 2 (100CD). In group 6 (100CD + Se) the increase was significant in all tissues kidney $p<0.001$), lung ($p<0.01$), heart ($p<0.01$) and brain ($p<0.05$) except liver where the increase was insignificant compared to group 2 (100CD) **(Fig 4.29).** In group 8 (100CD + CoQ10) it was significantly increased in all tissues kidney ($p<0.001$), heart ($p<0.001$), brain ($p<0.01$) liver ($p<0.01$), and lung ($p<0.05$) compared to group 2 (100CD) **(Fig 4.30).**

4.2.3.2.2 Changes in the Levels of Catalase (CAT)

The Catalase levels in liver, lung, heart, and brain were decreased significantly ($p<0.001$) in group 2 (100 CD) as compared to group 1 (control). In kidney it was decreased significantly ($p<0.01$) in group 2 (100CD) compared to group 1 (control). However in all the tissues except kidney and lung it was increased significantly ($p<0.001$) in group 4 (100CD + ALA) compared to group 2 (100CD). In kidney the increase was significant ($p<0.01$) in group 4 (100CD + ALA) compared to group 2 (100CD). In lung the increase was not significant in group 4 (100CD + ALA) compared to group 2 (100CD). In group 6 (100CD + Se) the increase was significant in all tissues except lung and brain compared to group 2 (100CD). The increase was significant in liver ($p<0.01$), heart ($p<0.05$) and kidney ($p<0.05$) in group 6 (100CD + Se) compared to group 2 (100CD) **(Fig 4.31).** In group 8 (100CD + CoQ10) it was significantly increased in all tissues, brain ($p<0.001$), liver and lung ($p<0.01$), heart ($p<0.05$) except kidney where the increase was not significant compared to group 2 (100CD) **(Fig 4.32).**

4.2.3.2.3 Changes in the Levels of Reduced Glutathione (GSH)

The Reduced glutathione (GSH) levels in liver, heart and lung were decreased significantly ($p<0.001$) in group 2 (100 CD) as compared to group 1 (control). In kidney and brain it was decreased significantly ($p<0.01$) in group 2 (100CD) compared to group 1 (control). However in all the tissues except brain it was increased significantly ($p<0.001$) in group 4

(100CD + ALA) compared to group 2 (100CD). In brain the increase was significant ($p<0.01$) in group 4 (100CD + ALA) compared to group 2 (100CD). In group 6 the increase was significant in lung ($p<0.001$), kidney ($p<0.01$), liver ($p<0.01$), heart ($p<0.05$) and brain ($p<0.05$) in group 6 (100CD + Se) compared to the animals of group 2 (100CD) **(Fig 4.33)**. In group 8 (100CD + CoQ10) it was significantly increased in all tissues, liver, kidney and lung ($p<0.001$), heart ($p<0.05$) except brain where the increase was not significant compared to group 2 (100CD) **(Fig 4.34)**.

4.2.3.3. Changes in the levels of Membrane Bound Enzymes

4.2.3.3.1 Changes in levels of Sodium Potassium dependent ATPase (Na^+-K^+-ATPase)

The Na^{++}- K^+- ATPase levels in liver, kidney, lung and brain were decreased significantly ($p<0.001$) in group 2 (100 CD) as compared to group 1 (control). In heart it was significantly ($p<0.01$) decreased in group 2 (100CD) compared to group 1 (control). However in all the tissues except lung it was increased significantly ($p<0.001$) in group 4 (100CD + ALA) compared to group 2 (100CD). In lung the increase was not significant in group 4 (100CD + ALA) compared to group 2 (100CD). It was significantly increased in all tissues in group 6 (100CD + Se) in liver ($p<0.01$), lung ($p<0.01$), kidney ($p<0.05$) and brain ($p<0.05$) except heart where the increase was insignificant compared to group 2 (100CD) **(Fig 4.35)**. It was significantly increased in all tissues in group 8 (100CD + CoQ10) except heart. The levels were significantly increased in brain ($p<0.001$), in kidney and lung ($p<0.01$) and in liver ($p<0.05$) compared to group 2 (100CD) **(Fig 4.36)**.

4.2.3.3.2 Changes in levels of Calcium dependent ATPase (Ca^+-ATPase)

The Ca^{++}- ATPase levels in liver and kidney were decreased significantly ($p<0.001$) in group 2 (100 CD) as compared to group 1 (control). In lung and brain it was decreased significantly ($p<0.01$) in group 2 (100CD) compared to group 1 (control). In heart it was significantly ($p<0.05$) decreased in group 2 (100CD) compared to group 1 (control). However in all the tissues except brain it was increased significantly ($p<0.001$) in group 4 (100CD + ALA) compared to group 2 (100CD). In brain the increase was significant ($p<0.01$) in group 4 (100CD + ALA) compared to group 2 (100CD).). In group 6 (100CD + Se) the increase was significant in all tissues except lung. The increase was significant in kidney ($p<0.001$), liver ($p<0.01$), brain ($p<0.01$) and heart ($p<0.05$) in group 6 (100CD + Se) compared to group 2

(100CD) **(Fig 4.37).** In group 8 (100CD + CoQ10) significantly increased in all tissues liver and kidney ($p<0.01$), lung and brain ($p<0.05$) except heart where the increase was not significant compared to group 2 (100CD) **(Fig 4.38).**

4.2.3.3.3 Changes in levels of Magnessium dependent ATPase (Mg^{++}ATPase)

The Mg^{++}- ATPase levels in liver, kidney, heart and brain were decreased significantly ($p<0.01$) in group 2 (100 CD) as compared to group 1 (control). In lung it was significantly ($p<0.001$) decreased in group 2 (100CD) compared to group 1 (control). However in all the tissues except kidney it was increased significantly ($p<0.001$) in group 4 (100CD + ALA). In kidney the increase was not significant in group 4 (100CD + ALA) compared to group 2 (100CD). In group 6 (100CD + Se) it was significantly increased in all tissues lung ($p<0.01$), heart ($p<0.01$), liver ($p<0.05$), kidney ($p<0.05$) except brain where the increase was insignificant compared to group 2 (100CD) **(Fig 4.39).** In group 8 (100CD + CoQ10) it was significantly increased in all tissues except heart compared to group 2 (100CD). The increase was significant in liver, lung and brain ($p<0.01$) and in kidney ($p<0.05$) compared to group 2 (100CD) **(Fig 4.40).**

4.2.3.4. Changes in the levels of Tissue Lipids

4.2.3.4.1 Changes in levels of Cholesterol

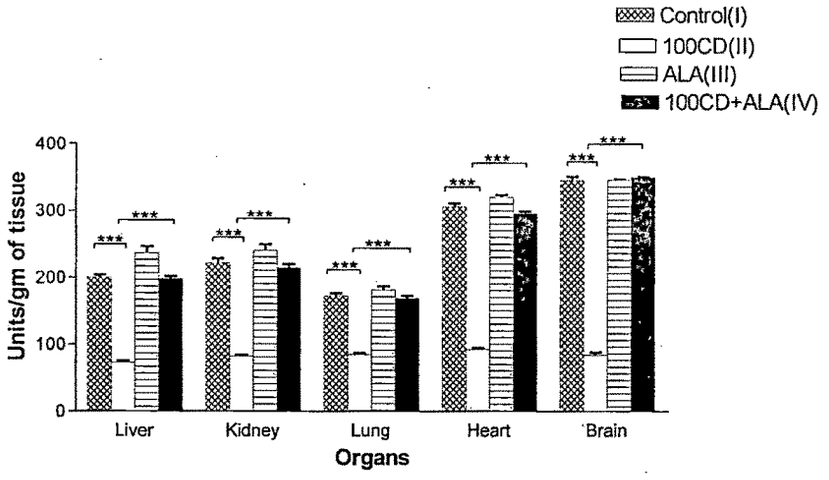
There was a significant increase in the level of cholesterol in all the tissues in group 2 (100CD) lung ($p<0.001$), liver ($p<0.001$), kidney ($p<0.001$), brain ($p<0.001$) and heart ($p<0.001$) compared to group 1 (control). There was a significant decrease in the level of cholesterol in group 4 (100CD + ALA) in all the tissues liver ($p<0.001$), kidney ($p<0.001$), heart ($p<0.01$), lung ($p<0.05$) and brain ($p<0.05$) compared to group 2 (100CD). There was a significant decrease in the level of cholesterol in group 6 (100CD + Se) in all the tissues liver ($p<0.01$), kidney ($p<0.01$), lung ($p<0.01$), brain ($p<0.01$) and heart ($p<0.05$) compared to group 2 (100CD) **(Fig 4.41).**In group 8 (100CD + CoQ10) there was a significant decrease in the level of cholesterol in liver ($p<0.001$), lung ($p<0.001$), kidney ($p<0.01$) and heart ($p<0.05$) except brain where the decrease was not significant compared to group 2 (100CD) **(Fig 4.42).**

4.2.3.4.2 Changes in levels of Triglyceride

There was a significant increase in the level of triglyceride in all the tissues in group 2 (100CD) lung ($p<0.001$), liver ($p<0.001$), kidney ($p<0.001$), brain ($p<0.001$) and heart ($p<0.001$) compared to group 1 (control). There was a significant decrease in the level of triglyceride in group 4 (100CD + ALA) in all the tissues brain ($p<0.01$), liver ($p<0.05$), heart ($p<0.05$) and lung ($p<0.05$) except kidney where the difference was insignificant compared to group 2 (100CD). There was a significant decrease in the level of triglyceride in group 6 (100CD + Se) in all the tissues brain ($p<0.05$), liver ($p<0.05$), kidney ($p<0.05$) and lung ($p<0.05$) except heart where the difference was insignificant compared to group 2 (100CD) **(Fig 4.43)**. There was a significant decrease in the level of triglycerides in all tissues liver ($p<0.01$), lung ($p<0.01$), heart ($p<0.01$), kidney ($p<0.01$) and brain ($p<0.05$) in group 8 (100CD + CoQ10) compared to group 2 (100CD) **(Fig 4.44)**.

4.2.3.4.3 Changes in levels of Phospholipid

There was a significant increase in the level of phospholipid in all the tissues in group 2 (100CD) lung ($p<0.001$), liver ($p<0.001$), kidney ($p<0.01$), brain ($p<0.01$) and heart ($p<0.05$) compared to group 1 (control). In liver ($p<0.01$), lung ($p<0.05$) and heart ($p<0.05$) there was a significant decrease in the level of phospholipid in group 4 (100CD + ALA) compared to group 2 (100CD). On comparison of the same groups no significant increase was found in the levels of phospholipid in brain and kidney. There was a significant decrease in the level of phospholipids of all the tissues liver ($p<0.01$), kidney ($p<0.01$), heart ($p<0.05$), brain ($p<0.05$) in group 6 (100CD + Se) except lung where the difference was insignificant compared to group 2 (100CD) **(Fig 4.45)**.There was a significant decrease in the level of phospholipids of all the tissues lung ($p<0.01$), heart ($p<0.01$), kidney ($p<0.05$), liver ($p<0.05$) and brain ($p<0.05$) in group 8 (100CD + CoQ10) compared to group 2 (100CD) **(Fig 4.46)**.



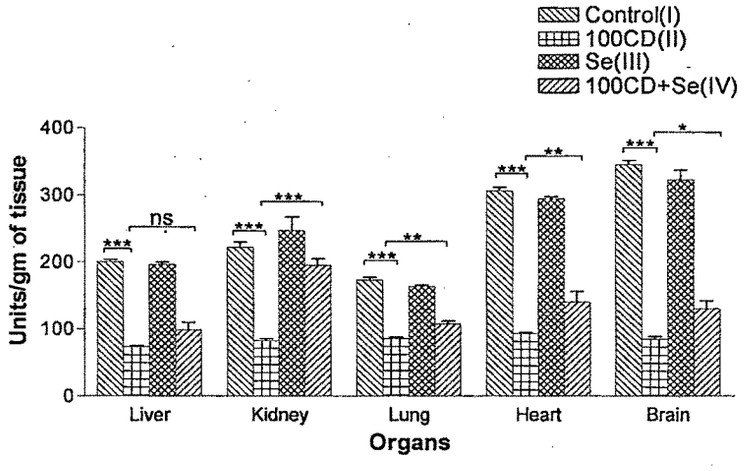


Fig: 4.29. Effect of 100 ppm of cadmium chloride (100CD) exposure alone and in combination with antioxidants i.e. Alpha lipoic acid or Selenium (ALA or Se) on the levels of superoxide dismutase in liver, kidney, lung, heart and brain of rats during 30 days of experiment.

Values expressed as mean ± SEM (n=6) for each observation.
Group II compared to control group.
Group IV compared to cadmium treated group.
$^{*}p<0.05$, $^{**}p<0.01$, $^{***}p<0.001$.

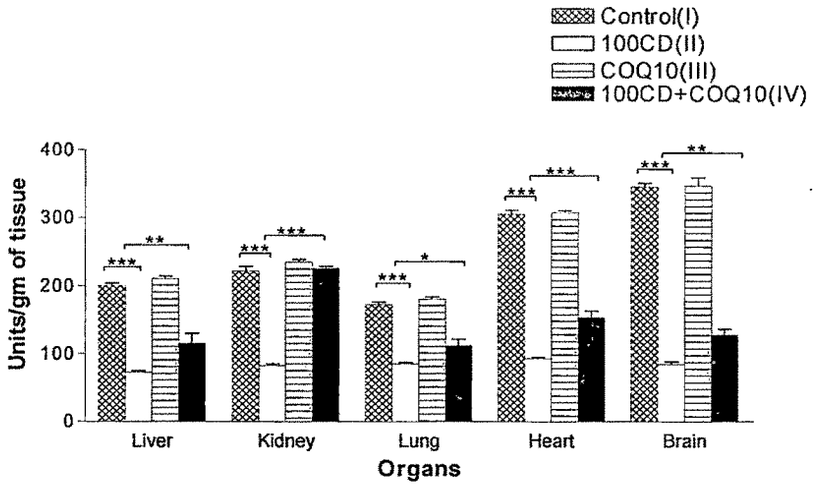


Fig: 4.30. Effect of 100 ppm of cadmium chloride (100CD) exposure alone and in combination with antioxidant i.e. Coenzyme Q10 (COQ10) on the levels of superoxide dismutase in liver, kidney, lung, heart and brain of rats during 30 days of experiment.

Values expressed as mean ± SEM (n=6) for each observation.
Group II compared to control group.
Group IV compared to cadmium treated group.
$^{*}p<0.05$, $^{**}p<0.01$, $^{***}p<0.001$.

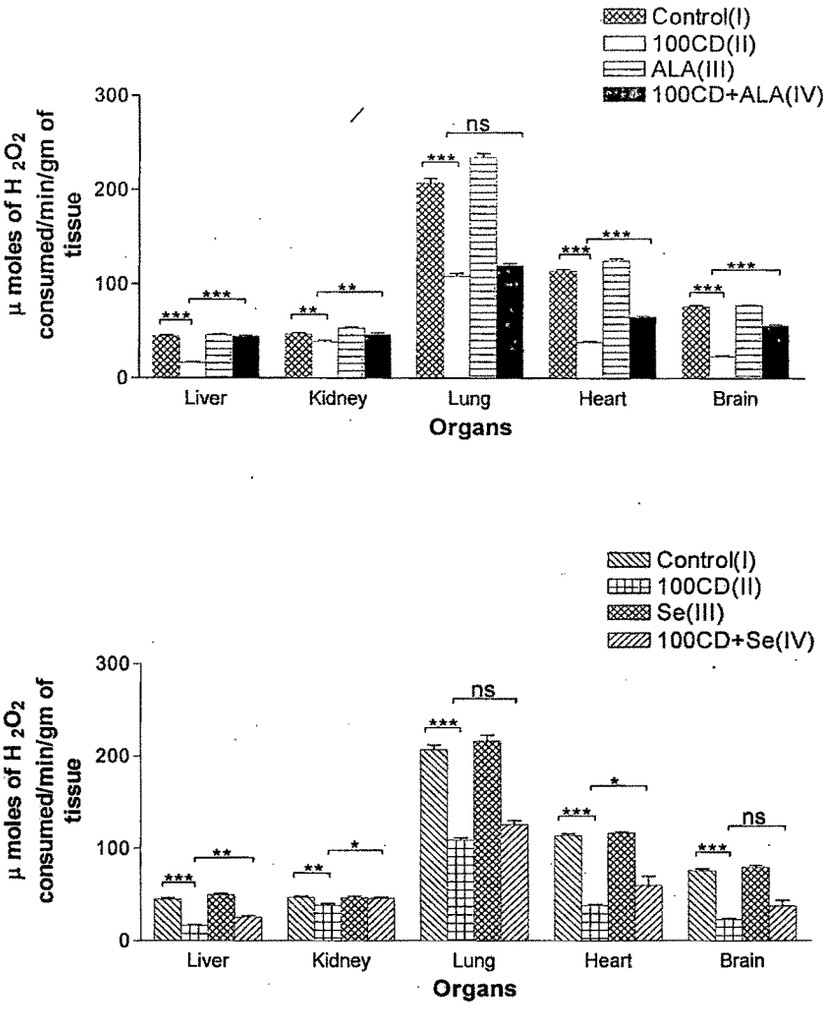


Fig: 4.31. Effect of 100 ppm of cadmium chloride (100CD) exposure for 30 days alone and in combination with antioxidants i.e. Alpha lipoic acid or Selenium (ALA or Se) on the levels of catalase in liver, kidney, lung, heart and brain of rats.

Values expressed as mean ± SEM (n=6) for each observation.
Group II compared to control group.
Group IV compared to cadmium treated group.
$^{*}p<0.05$, $^{**}p<0.01$, $^{***}p<0.001$.

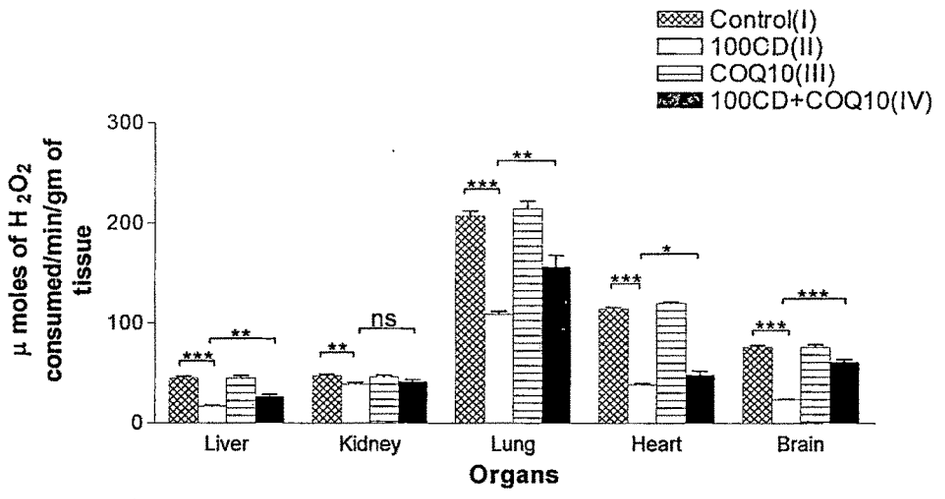


Fig: 4.32. Effect of 100 ppm of cadmium chloride (100CD) exposure for 30 days alone and in combination with antioxidant i.e. Coenzyme Q10 (COQ10) on the levels of catalase in liver, kidney, lung, heart and brain of rats.

Values expressed as mean ± SEM (n=6) for each observation.
Group II compared to control group.
Group IV compared to cadmium treated group.
$^{*}p<0.05$, $^{**}p<0.01$, $^{***}p<0.001$.

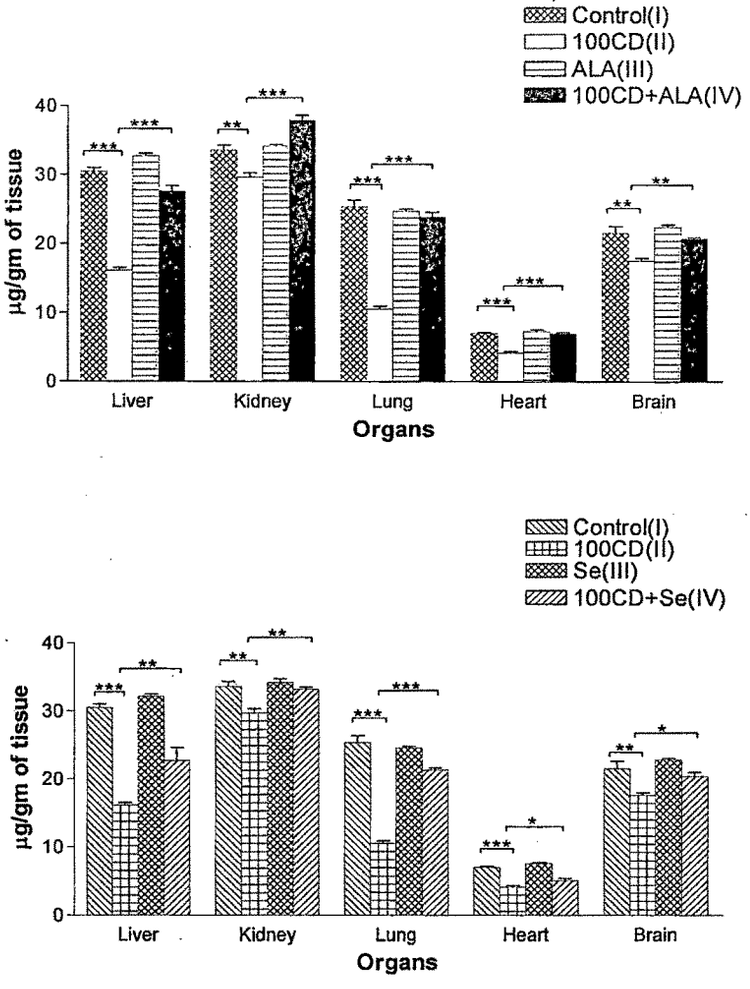


Fig: 4.33. Effect of 100 ppm of cadmium chloride (100CD) exposure alone and in combination with antioxidants i.e. Alpha lipoic acid or Selenium (ALA or Se) on the levels of reduced glutathione in liver, kidney, lung, heart and brain of rats during 30 days of experiment.

Values expressed as mean ± SEM (n=6) for each observation.
Group II compared to control group.
Group IV compared to cadmium treated group.
$^{*}p<0.05$, $^{**}p<0.01$, $^{***}p<0.001$.

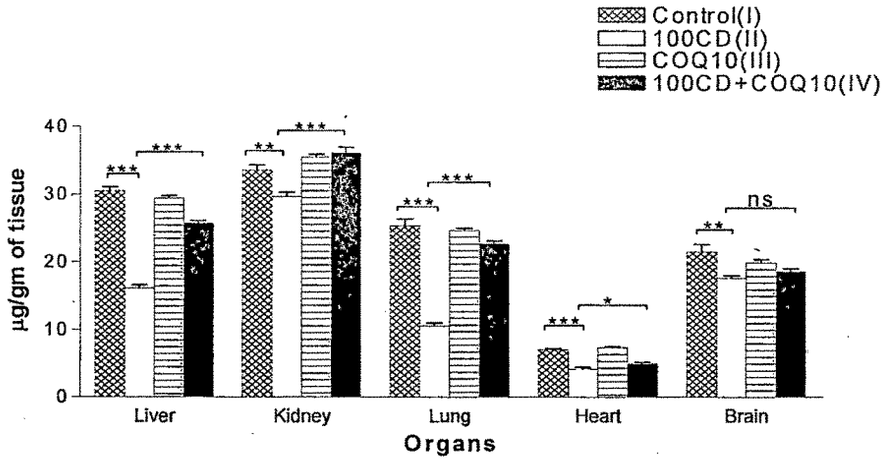


Fig: 4.34. Effect of 100 ppm of cadmium chloride (100CD) exposure alone and in combination with antioxidant i.e. Coenzyme Q10 (COQ10) on the levels of reduced glutathione in liver, kidney, lung, heart and brain of rats during 30 days of experiment.

Values expressed as mean ± SEM (n=6) for each observation.
Group II compared to control group.
Group IV compared to cadmium treated group.
$^{*}p<0.05$, $^{**}p<0.01$, $^{***}p<0.001$.

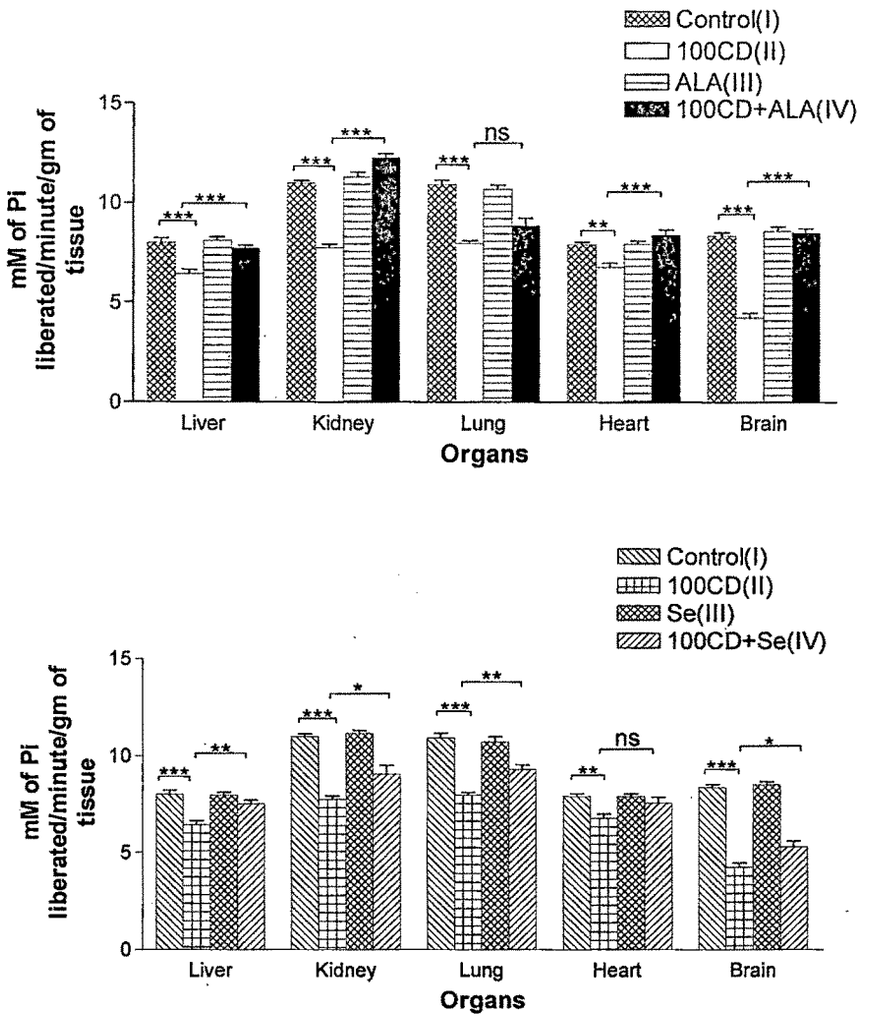


Fig: 4.35.Effect of 100 ppm of cadmium chloride (100CD) exposure for 30 days alone and in combination with antioxidants i.e. Alpha lipoic acid or Selenium (ALA or Se) on the levels of sodium potassium dependent ATPase in liver, kidney, lung, heart and brain of rats.

Values expressed as mean ± SEM (n=6) for each observation.
Group II compared to control group.
Group IV compared to cadmium treated group.
$^{*}p<0.05$, $^{**}p<0.01$, $^{***}p<0.001$.

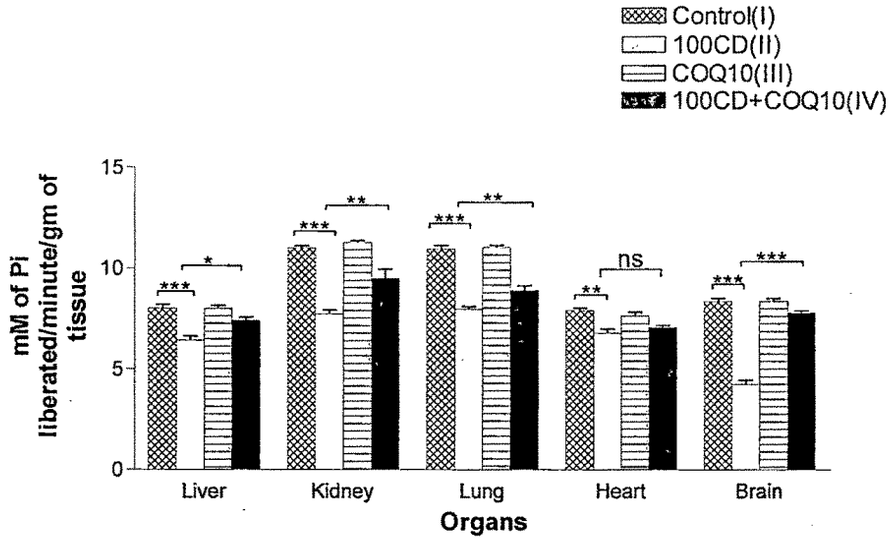


Fig: 4.36. Effect of 100 ppm of cadmium chloride (100CD) exposure for 30 days alone and in combination with antioxidant i.e. Coenzyme Q10(COQ10)on the levels of sodium potassium dependent ATPase in liver, kidney, lung, heart and brain of rats.

Values expressed as mean ± SEM (n=6) for each observation.
Group II compared to control group.
Group IV compared to cadmium treated group.
$^{*}p<0.05$, $^{**}p<0.01$, $^{***}p<0.001$.

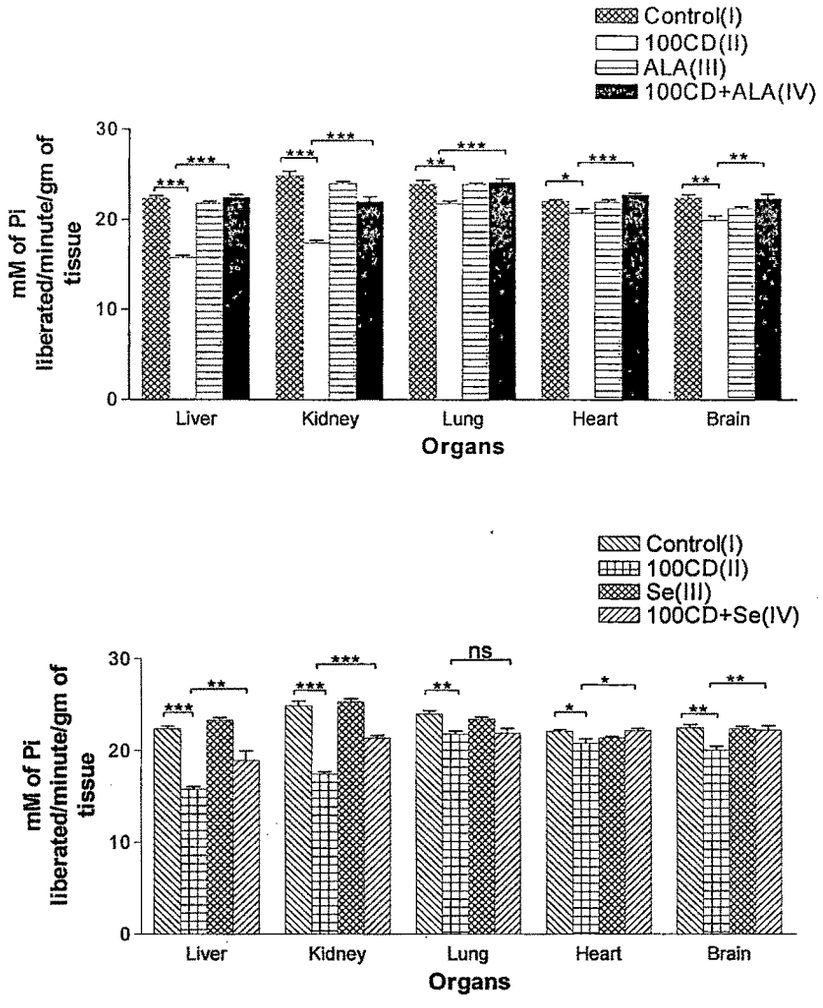


Fig: 4.37. Effect of 100 ppm of cadmium chloride (100CD) exposure for 30 days alone and in combination with antioxidants i.e. Alpha lipoic acid or Selenium (ALA or Se) on the levels of calcium dependent ATPase in liver, kidney, lung, heart and brain of rats.

Values expressed as mean ± SEM (n=6) for each observation.
Group II compared to control group.
Group IV compared to cadmium treated group.
$^{*}p<0.05$, $^{**}p<0.01$, $^{***}p<0.001$.

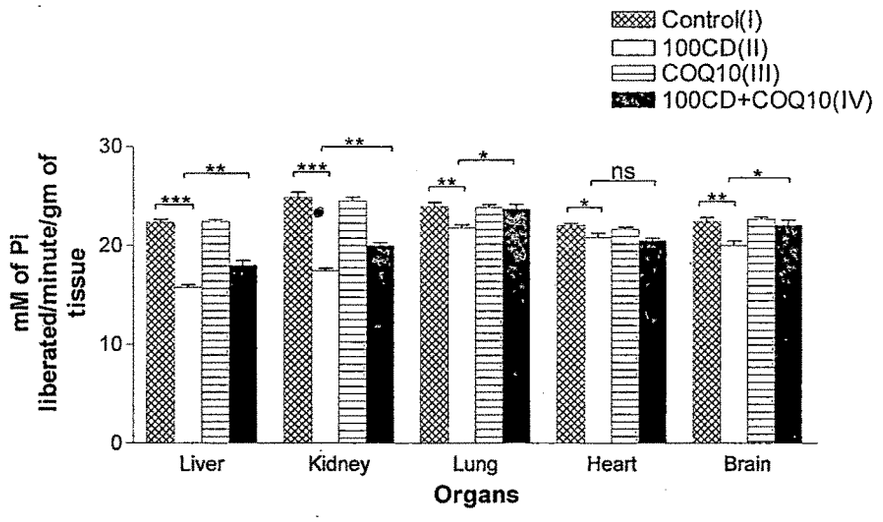


Fig: 4.38. Effect of 100 ppm of cadmium chloride (100CD) exposure for 30 days alone and in combination with antioxidant i.e. Coenzyme Q10 (COQ10)on the levels of calcium dependent ATPase in liver, kidney, lung, heart and brain of rats.

Values expressed as mean ± SEM (n=6) for each observation.
Group II compared to control group.
Group IV compared to cadmium treated group.
$^{*}p<0.05$, $^{**}p<0.01$, $^{***}p<0.001$.

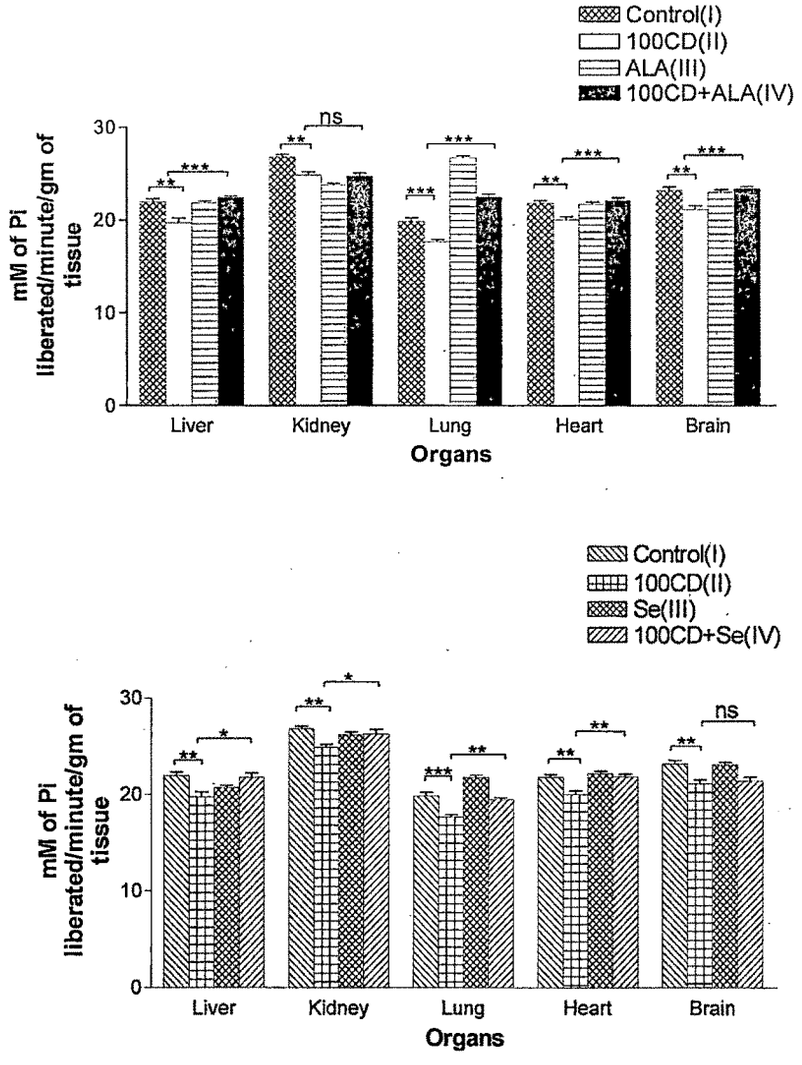


Fig: 4.39. Effect of 100 ppm of cadmium chloride (100CD) exposure for 30 days alone and in combination with antioxidants i.e. Alpha lipoic acid or Selenium (ALA or Se) on the levels of magnesium dependent ATPase in liver, kidney, lung, heart and brain of rats.

Values expressed as mean ± SEM (n=6) for each observation.
Group II compared to control group.
Group IV compared to cadmium treated group.
$^{*}p<0.05$, $^{**}p<0.01$, $^{***}p<0.001$.

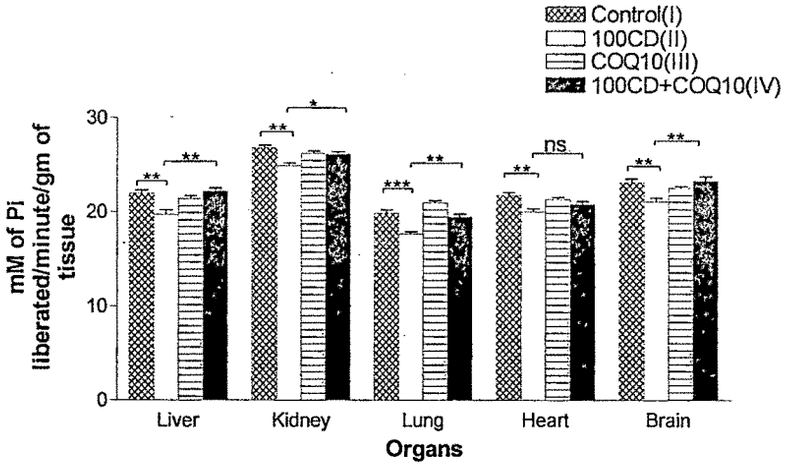
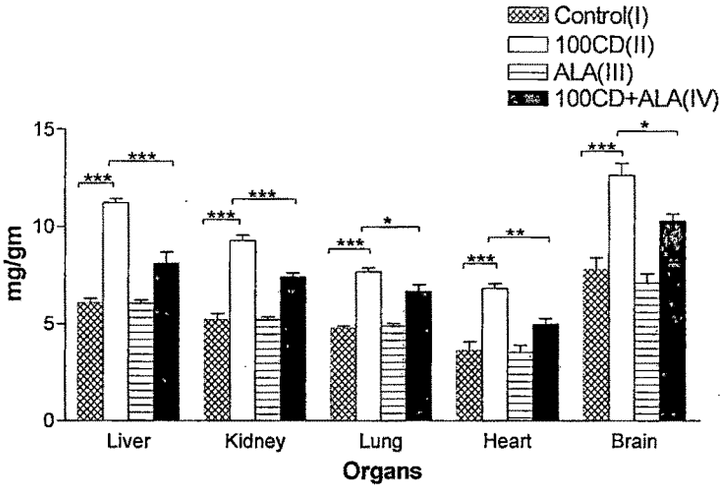


Fig: 4.40. Effect of 100 ppm of cadmium chloride (100CD) exposure for 30 days alone and in combination with antioxidant i.e. Coenzyme Q10 (COQ10)on the levels of magnesium dependent ATPase in liver, kidney, lung, heart and brain of rats.

Values expressed as mean ± SEM (n=6) for each observation.
Group II compared to control group.
Group IV compared to cadmium treated group.
$^{*}p<0.05$, $^{**}p<0.01$, $^{***}p<0.001$.



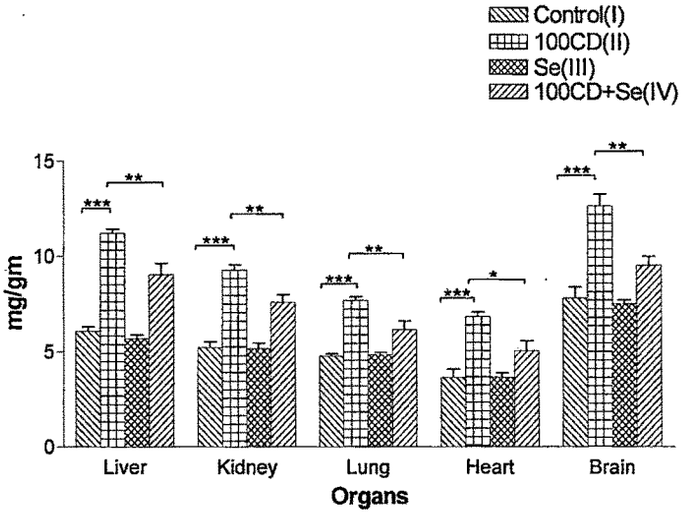


Fig: 4.41. Effect of 100 ppm of cadmium chloride (100CD) exposure for 30 days alone and in combination with antioxidants i.e. Alpha lipoic acid or Selenium (ALA or Se) on the levels of cholesterol in liver, kidney, lung, heart and brain of rats.

Values expressed as mean ± SEM (n=6) for each observation.
Group II compared to control group.
Group IV compared to cadmium treated group.
$^{*}p<0.05$, $^{**}p<0.01$, $^{***}p<0.001$.

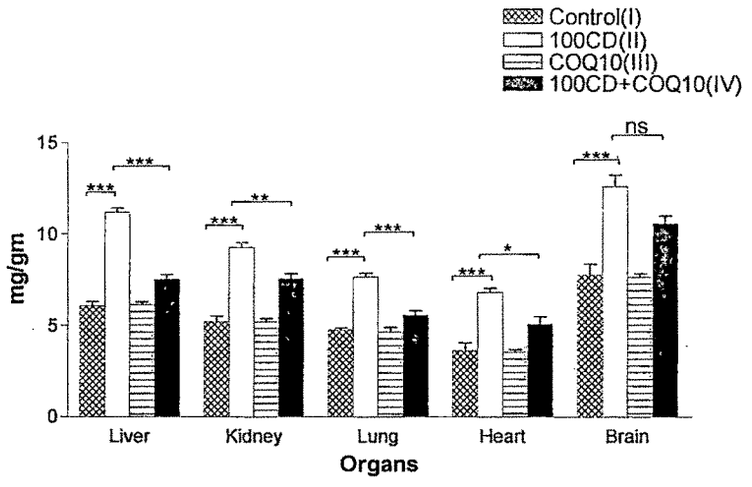


Fig: 4.42. Effect of 100 ppm of cadmium chloride (100CD) exposure for 30 days alone and in combination with antioxidant i.e. Coenzyme Q10 (COQ10) on the levels of cholesterol in liver, kidney, lung, heart and brain of rats.

Values expressed as mean ± SEM (n=6) for each observation.
Group II compared to control group.
Group IV compared to cadmium treated group.
$^{*}p<0.05$, $^{**}p<0.01$, $^{***}p<0.001$.

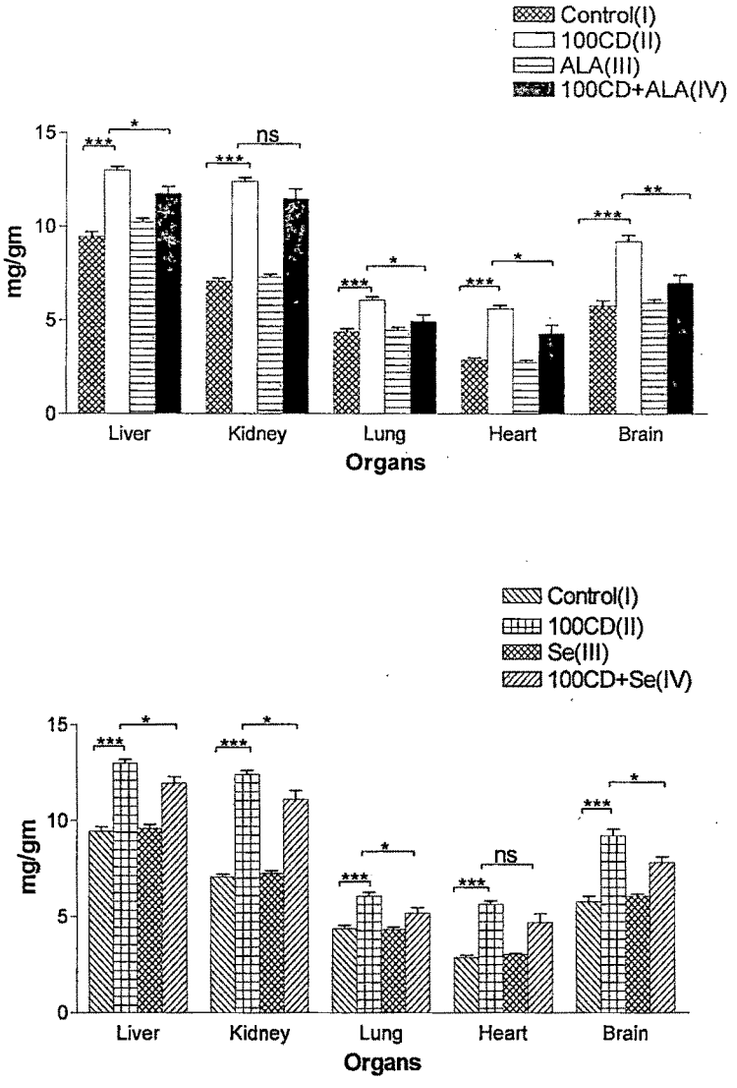


Fig: 4.43. Effect of 100 ppm of cadmium chloride (100CD) exposure for 30 days alone and in combination with antioxidants i.e. Alpha lipoic acid or Selenium (ALA or Se) on the levels of triglyceride in liver, kidney, lung, heart and brain of rats.

Values expressed as mean ± SEM (n=6) for each observation.
Group II compared to control group.
Group IV compared to cadmium treated group.
$^{*}p<0.05$, $^{**}p<0.01$, $^{***}p<0.001$.

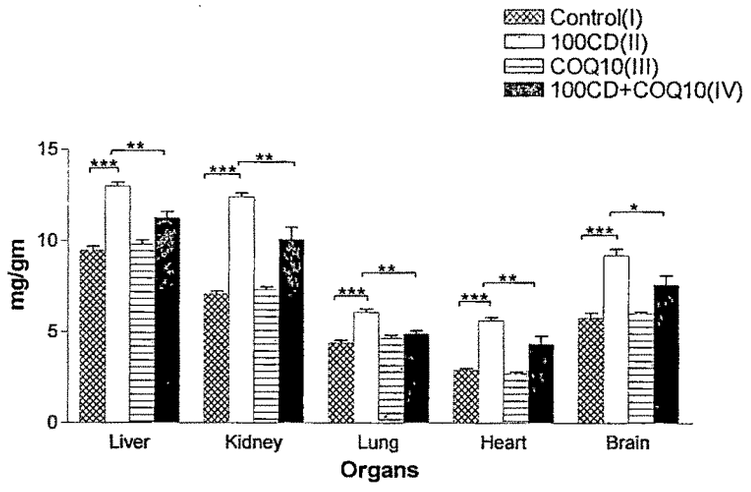


Fig:4.44. Effect of 100 ppm of cadmium chloride (100CD) exposure for 30 days alone and in combination with antioxidant i.e. Coenzyme Q10(COQ10) on the levels of triglyceride in liver, kidney, lung, heart and brain of rats.

Values expressed as mean ± SEM (n=6) for each observation.
Group II compared to control group.
Group IV compared to cadmium treated group.
$^{*}p<0.05$, $^{**}p<0.01$, $^{***}p<0.001$.

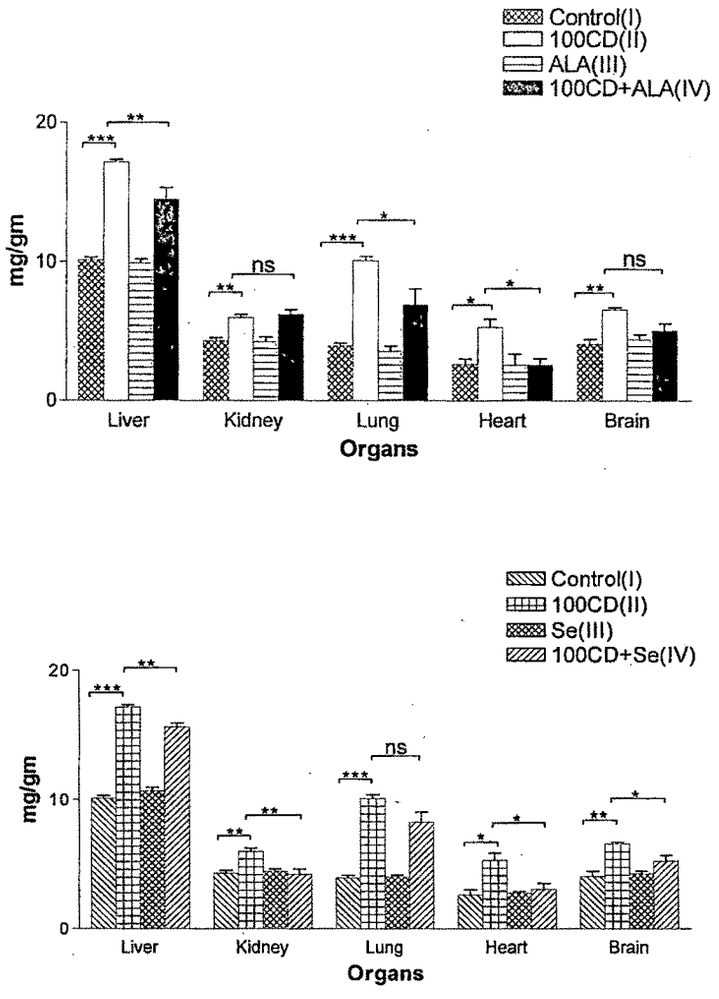


Fig: 4.45. Effect of 100 ppm of cadmium chloride (100CD) exposure for 30 days alone and in combination with antioxidants i.e. Alpha lipoic acid or Selenium (ALA or Se) on the levels of phospholipid in liver, kidney, lung, heart and brain of rats.

Values expressed as mean ± SEM (n=6) for each observation.
Group II compared to control group.
Group IV compared to cadmium treated group.
$^{*}p<0.05$, $^{**}p<0.01$, $^{***}p<0.001$.

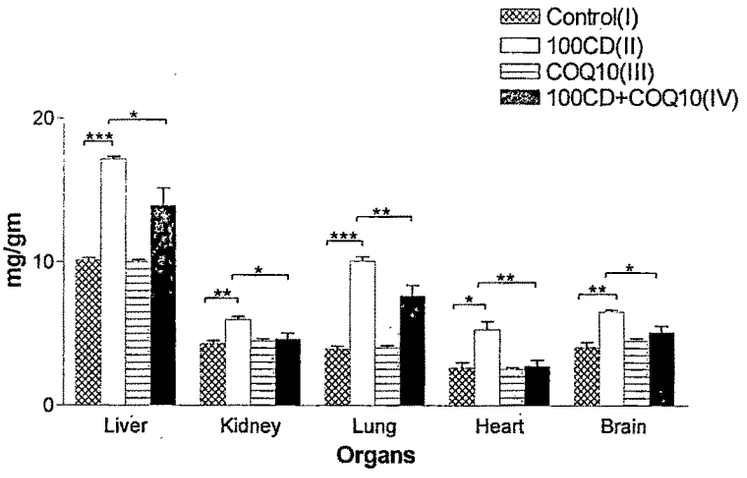


Fig: 4.46. Effect of 100 ppm of cadmium chloride (100CD) exposure for 30 days alone and in combination with antioxidant i.e. Coenzyme Q10(COQ10) on the levels of phospholipid in liver, kidney, lung, heart and brain of rats.

Values expressed as mean ± SEM (n=6) for each observation.
Group II compared to control group.
Group IV compared to cadmium treated group.
$^{*}p<0.05$, $^{**}p<0.01$, $^{***}p<0.001$.

4.2.4. SERUM ESTIMATIONS

4.2.4.1 Changes in the levels of Serum Glutamate Oxaloacetate Transaminases (GOT) and Glutamate Pyruvate Transaminases (GPT)

There was a significant ($p<0.001$) increase in the level of serum GOT in group 2 (100 CD) as compared to group 1 (control). This increase significantly decreased ($p<0.05$) in group 4 (100CD + ALA), ($p<0.01$) in group 6 (100CD + Se), ($p<0.001$) in group 8 (100CD + CoQ10) **(Fig 4.47).**

There was a significant ($p<0.001$) increase in the level of serum GPT in group 2(100 CD) as compared to group 1 (control). This increase significantly decreased ($p<0.001$) in group 4 (100CD + ALA), ($p<0.01$) in group 6 (100CD + Se) and ($p<0.01$) in group 8 (100CD + CoQ10) **(Fig 4.48).**

4.2.4.2 Changes in the levels of Serum Alkaline Phosphatase (Alkp)

There was a significant ($p<0.001$) increase in the level of serum alkaline phosphatase in group 2 (100 CD) as compared to group 1 (control). This increase significantly decreased ($p<0.001$) in group 4 (100CD + ALA), ($p<0.01$) in group 6 (100CD + Se) and also ($p<0.001$) in group 8 (100CD + CoQ10) **(Fig 4.49).**

4.2.4.3 Changes in the levels of Serum Lactate Dehydrogenase

There was a significant ($p<0.001$) increase in the level of serum lactate dehydrogenase in group 2 (100 CD) as compared to group 1 (control). This increase significantly decreased ($p<0.001$) in group 4 (100CD + ALA), ($p<0.01$) in group 6(100CD + Se), ($p<0.001$) in group 8 (100CD + CoQ10) **(Fig 4.50).**

4.2.4.4 Changes in the levels of Serum Total Bilirubin (TBil) and Total Protein (protein)

There was a significant ($p<0.001$) increase in the level of serum bilirubin in group 2 (100 CD) as compared to group 1 (control). This increase significantly decreased ($p<0.001$) in group 4 (100CD + ALA), ($p<0.001$) in group 6 (100CD + Se) and ($p<0.05$) in group 8 (100CD + CoQ10) **(Fig 4.51).**

There was a significant ($p<0.01$) decrease in the level of serum total protein in group 2 (100CD) as compared to group 1 (control). This decrease significantly increased ($p<0.05$) in group 4 (100CD + ALA), ($p<0.01$) in group 6 (100CD + Se) and ($p<0.01$) in group 8 (100CD + CoQ10) **(Fig 4.52)**.

4.2.4.5 Changes in the levels of Serum Cholesterol and Triglyceride.

There was a significant ($p<0.01$) decrease in the level of serum cholesterol in group 2 (100 CD) as compared to group 1 (control). This decrease significantly increased ($p<0.01$) in group 4 (100CD + ALA), ($p<0.05$) in group 6 (100CD + Se), ($p<0.05$) in group 8 (100CD + CoQ10) **(Fig 4.53)**.

There was a significant ($p<0.01$) increase in the level of serum triglycerides in group 2 (100CD) as compared to group 1 (control). There was a significant decrease in the levels of triglycerides in group 4 (100CD + ALA) ($p<0.001$), group 6 (100CD + Se) ($p<0.05$) and group 8 (100CD + CoQ10) ($p<0.05$) as compared to that of group 2 (100CD) **(Fig 4.54)**.

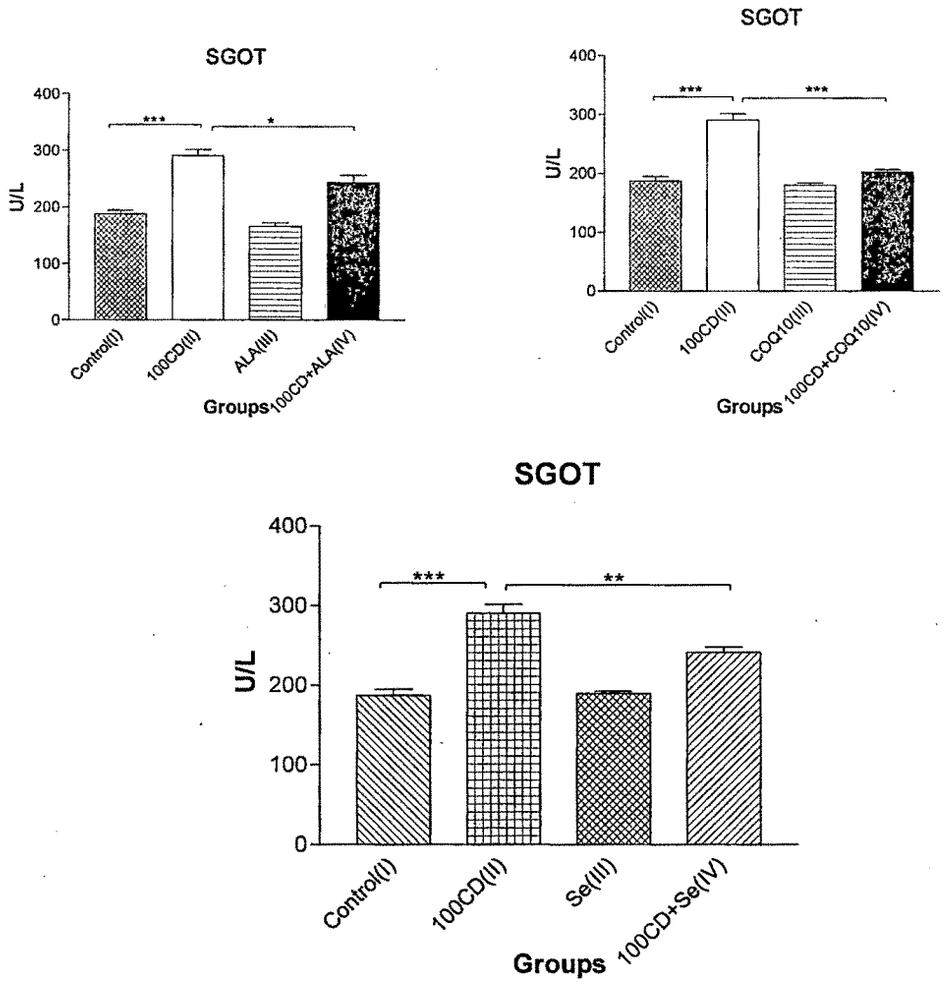


Fig: 4.47. Effect of 100 ppm of cadmium chloride (100CD) exposure for 30 days alone and in combination with antioxidants i.e. Alpha lipoic acid, Coenzyme Q10 or Selenium (ALA, COQ10 or Se) on the levels of serum glutamate oxaloacetate transaminases.

Values expressed as mean ± SEM (n=6) for each observation.
Group II compared to control group.
Group IV compared to cadmium treated group.
$^{*}p<0.05$, $^{**}p<0.01$, $^{***}p<0.001$.

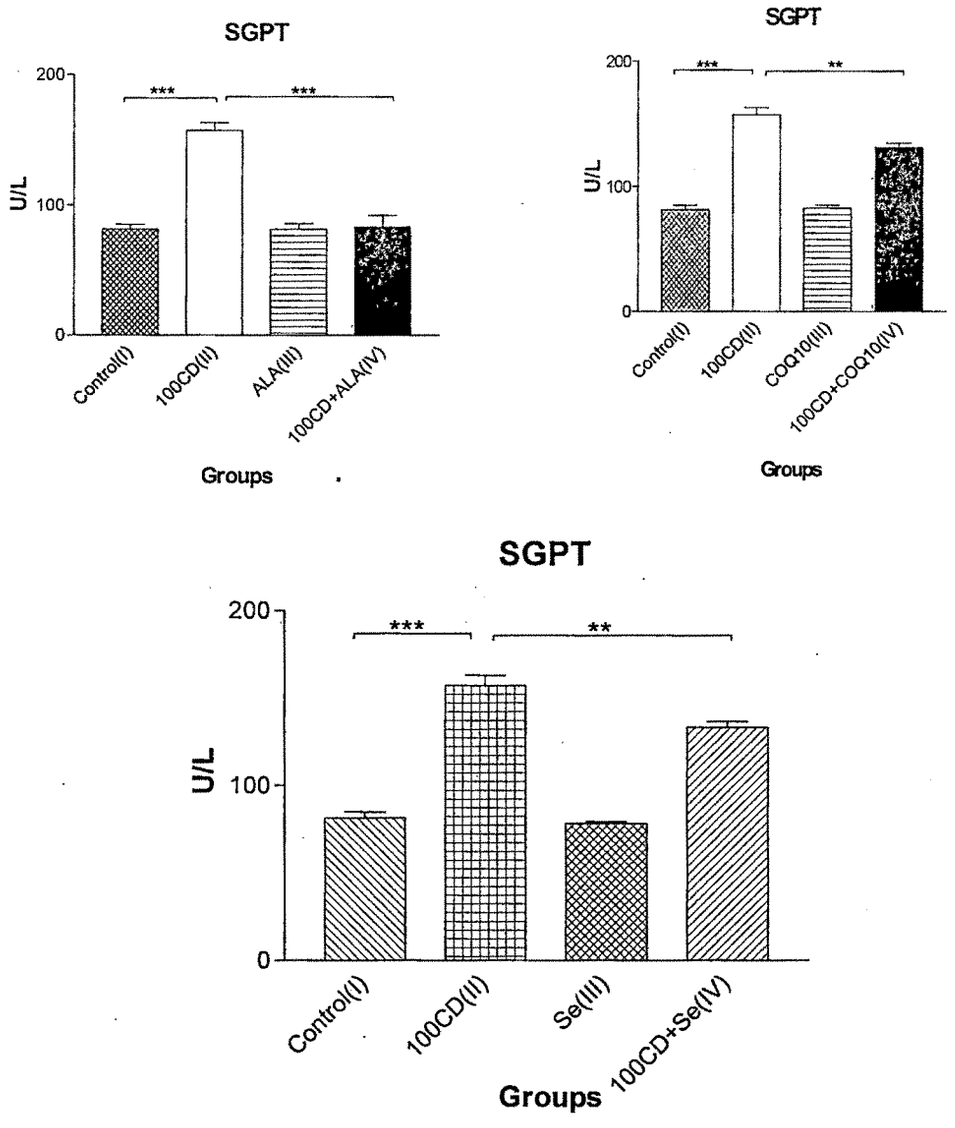


Fig: 4.48. Effect of 100 ppm of cadmium chloride (100CD) exposure for 30 days alone and in combination with antioxidants i.e. Alpha lipoic acid, Coenzyme Q10 or Selenium (ALA, COQ10 or Se) on the levels of serum glutamate pyruvate transaminases.

Values expressed as mean ± SEM (n=6) for each observation.
Group II compared to control group.
Group IV compared to cadmium treated group.
$^{*}p<0.05$, $^{**}p<0.01$, $^{***}p<0.001$.

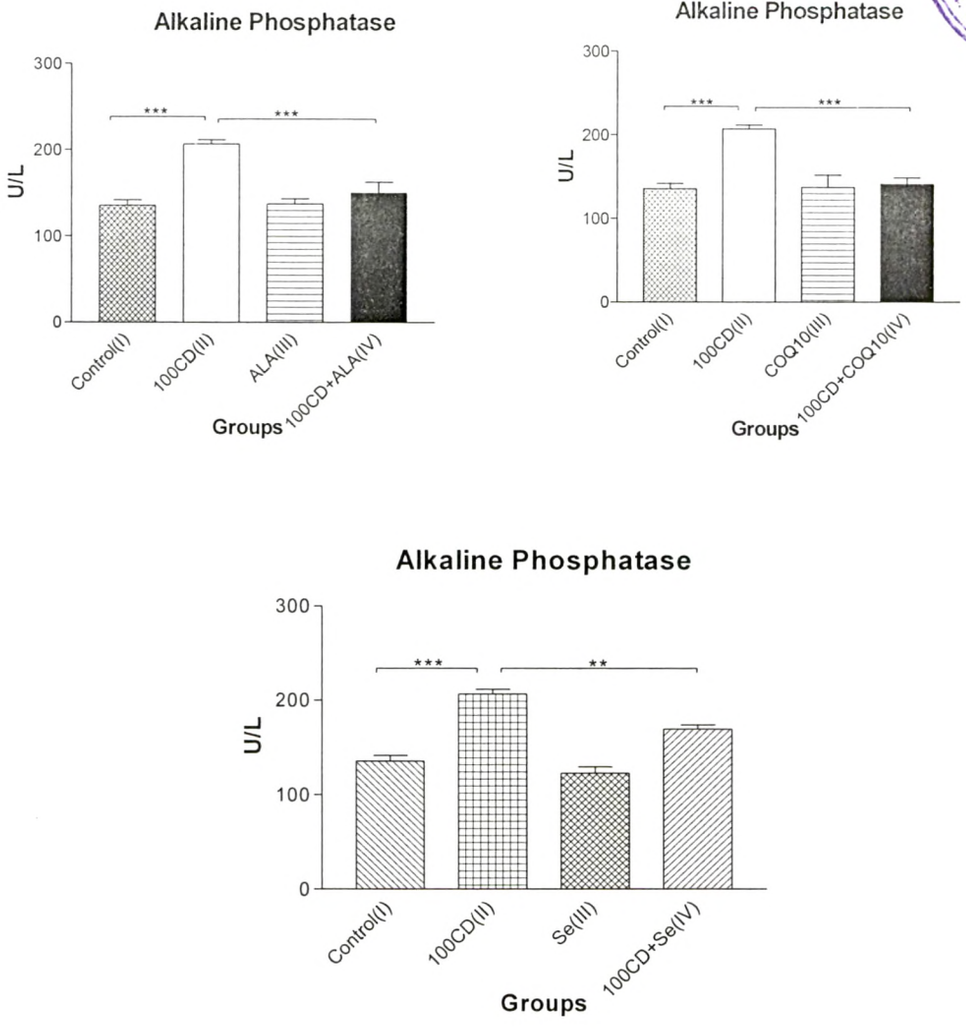


Fig: 4.49. Effect of 100 ppm of cadmium chloride (100CD) exposure for 30 days alone and in combination with antioxidants i.e. Alpha lipoic acid, Coenzyme Q10 or Selenium (ALA, COQ10 or Se) on the levels of alkaline phosphatase in serum of rats.

Values expressed as mean ± SEM (n=6) for each observation.
Group II compared to control group.
Group IV compared to cadmium treated group.
$^{*}p<0.05$, $^{**}p<0.01$, $^{***}p<0.001$.

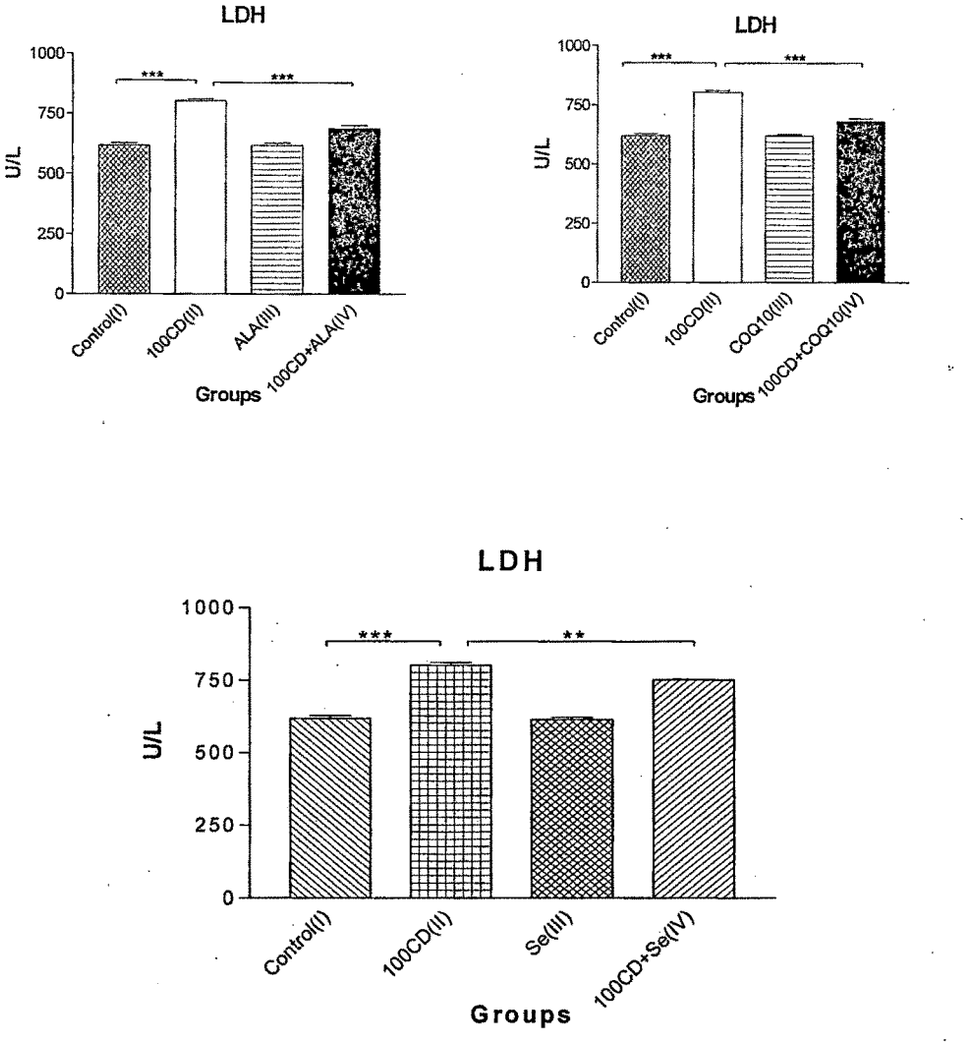


Fig: 4.50. Effect of 100 ppm of cadmium chloride (100CD) exposure for 30 days alone and in combination with antioxidants i.e. Alpha lipoic acid, Coenzyme Q10 or Selenium (ALA, COQ10 or Se) on the levels of lactate dehydrogenase in serum of rats.

Values expressed as mean ± SEM (n=6) for each observation.
Group II compared to control group.
Group IV compared to cadmium treated group.
$^{*}p<0.05$, $^{**}p<0.01$, $^{***}p<0.001$.

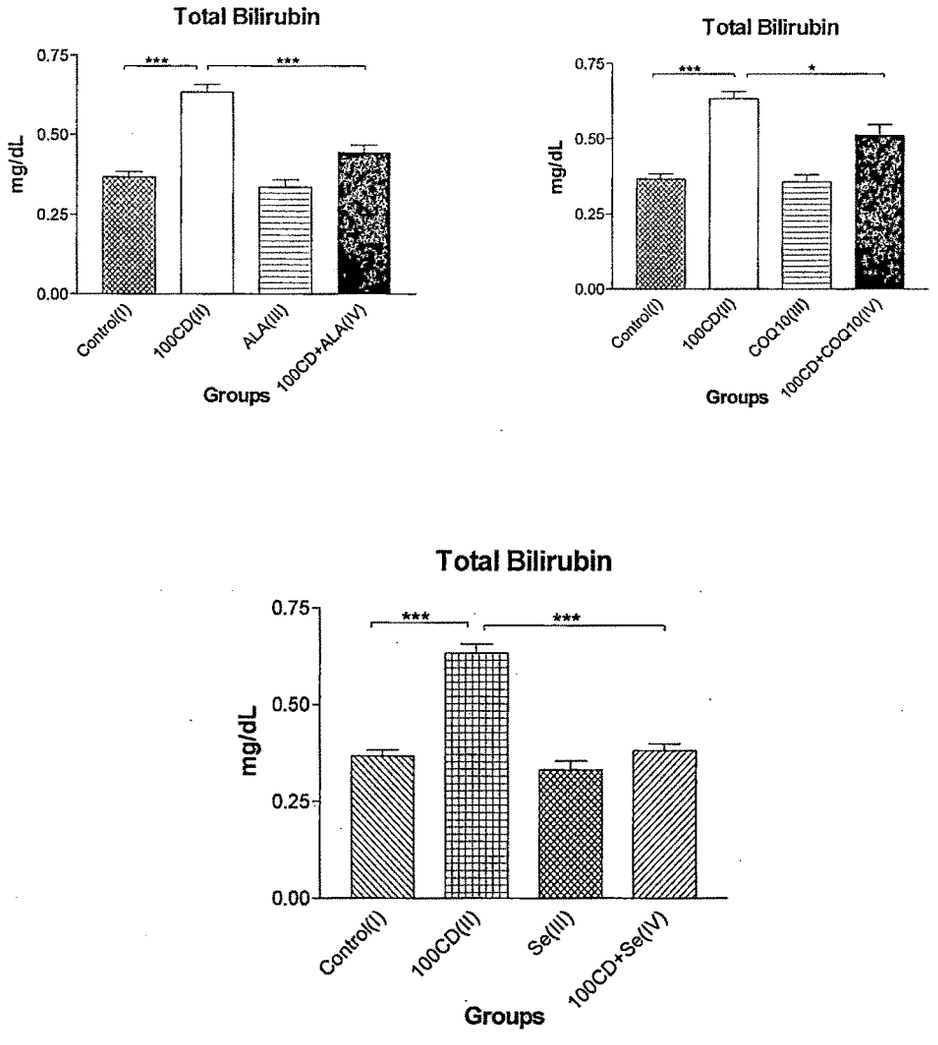


Fig: 4.51. Effect of 100 ppm of cadmium chloride (100CD) exposure for 30 days alone and in combination with antioxidants i.e. Alpha lipoic acid, Coenzyme Q10 or Selenium (ALA, COQ10 or Se) on the levels of total bilirubin in serum of rats.

Values expressed as mean ± SEM (n=6) for each observation.
Group II compared to control group.
Group IV compared to cadmium treated group.
$^{*}p<0.05$, $^{**}p<0.01$, $^{***}p<0.001$.

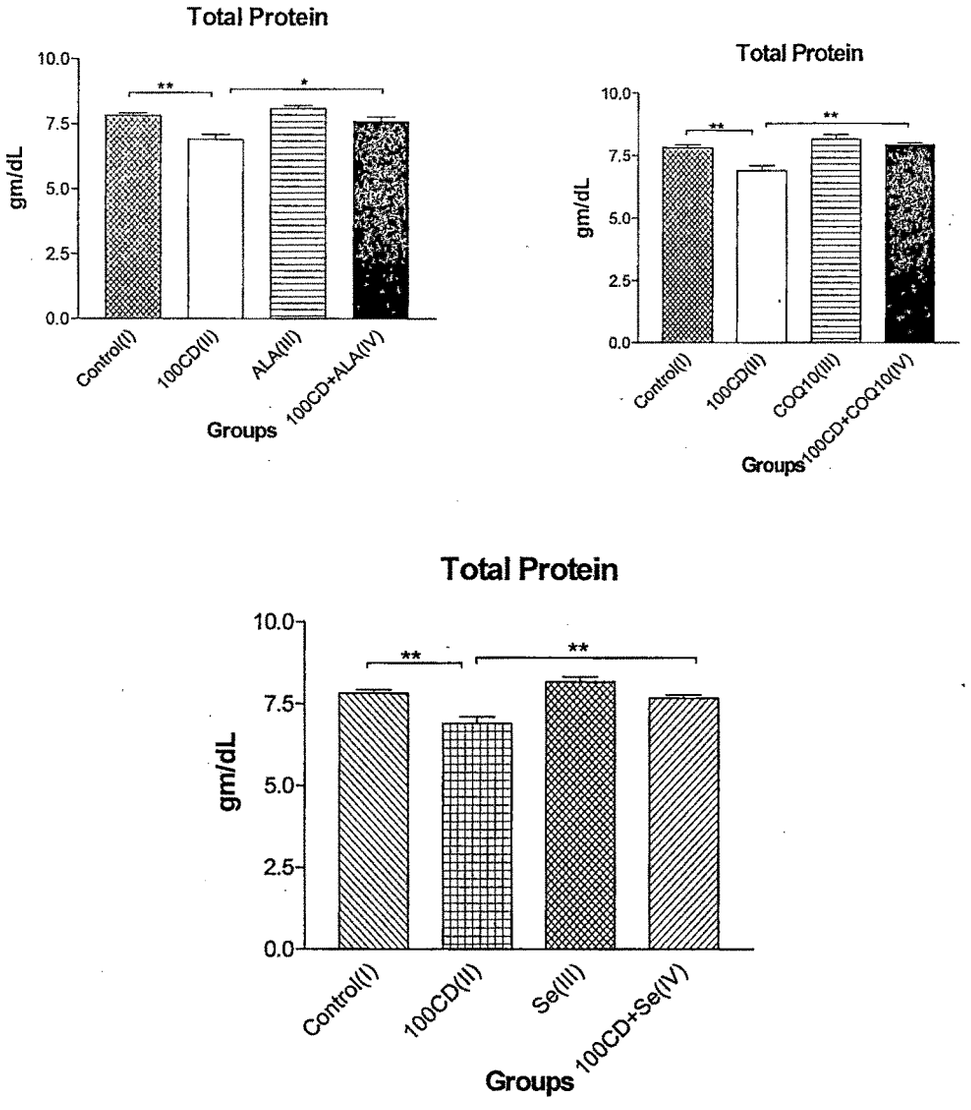


Fig: 4.52. Effect of 100 ppm of cadmium chloride (100CD) exposure for 30 days alone and in combination with antioxidants i.e. Alpha lipoic acid, Coenzyme Q10 or Selenium (ALA, COQ10 or Se) on the levels of total protein in serum of rats.

Values expressed as mean ± SEM (n=6) for each observation.
Group II compared to control group.
Group IV compared to cadmium treated group.
$^{*}p<0.05$, $^{**}p<0.01$, $^{***}p<0.001$.

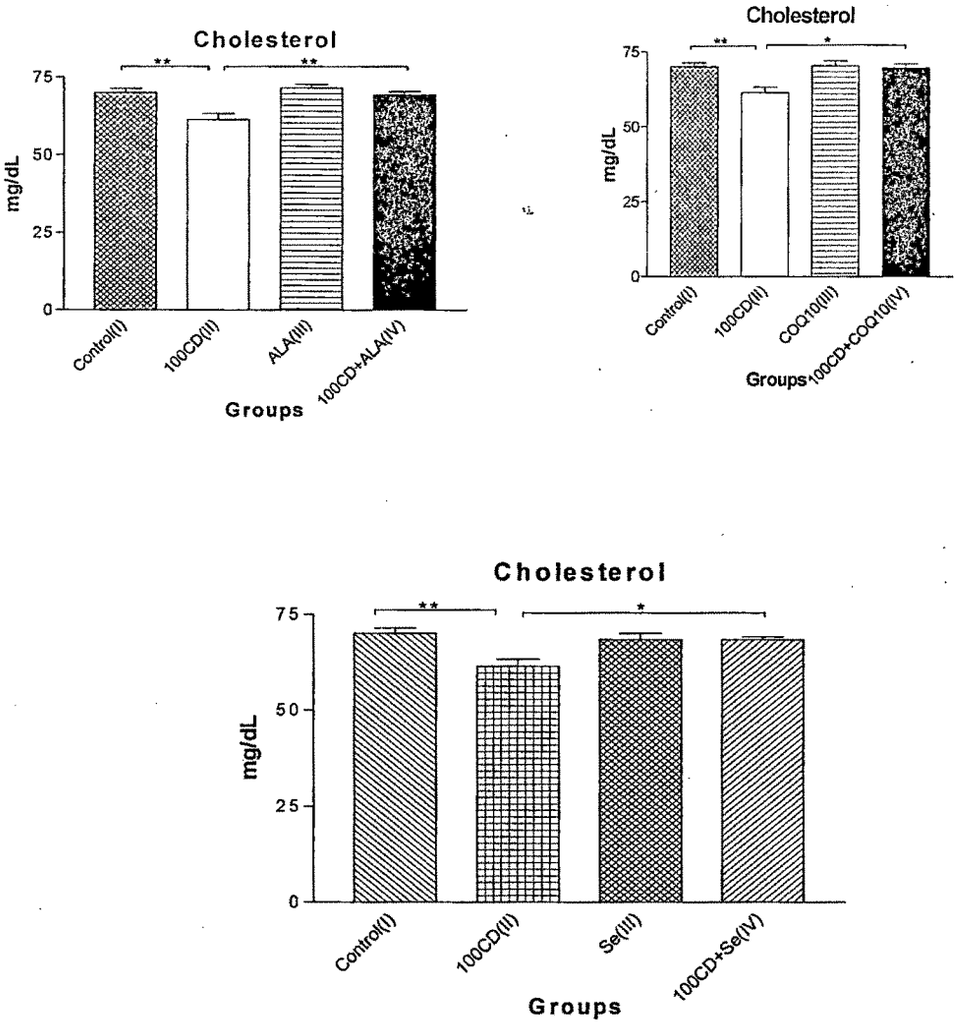


Fig: 4.53. Effect of 100 ppm of cadmium chloride (100CD) exposure for 30 days alone and in combination with antioxidants i.e. Alpha lipoic acid, Coenzyme Q10 or Selenium (ALA, COQ10 or Se) on the levels of cholesterol in serum of rats.

Values expressed as mean ± SEM (n=6) for each observation.
Group II compared to control group.
Group IV compared to cadmium treated group.
$^{*}p<0.05$, $^{**}p<0.01$, $^{***}p<0.001$.

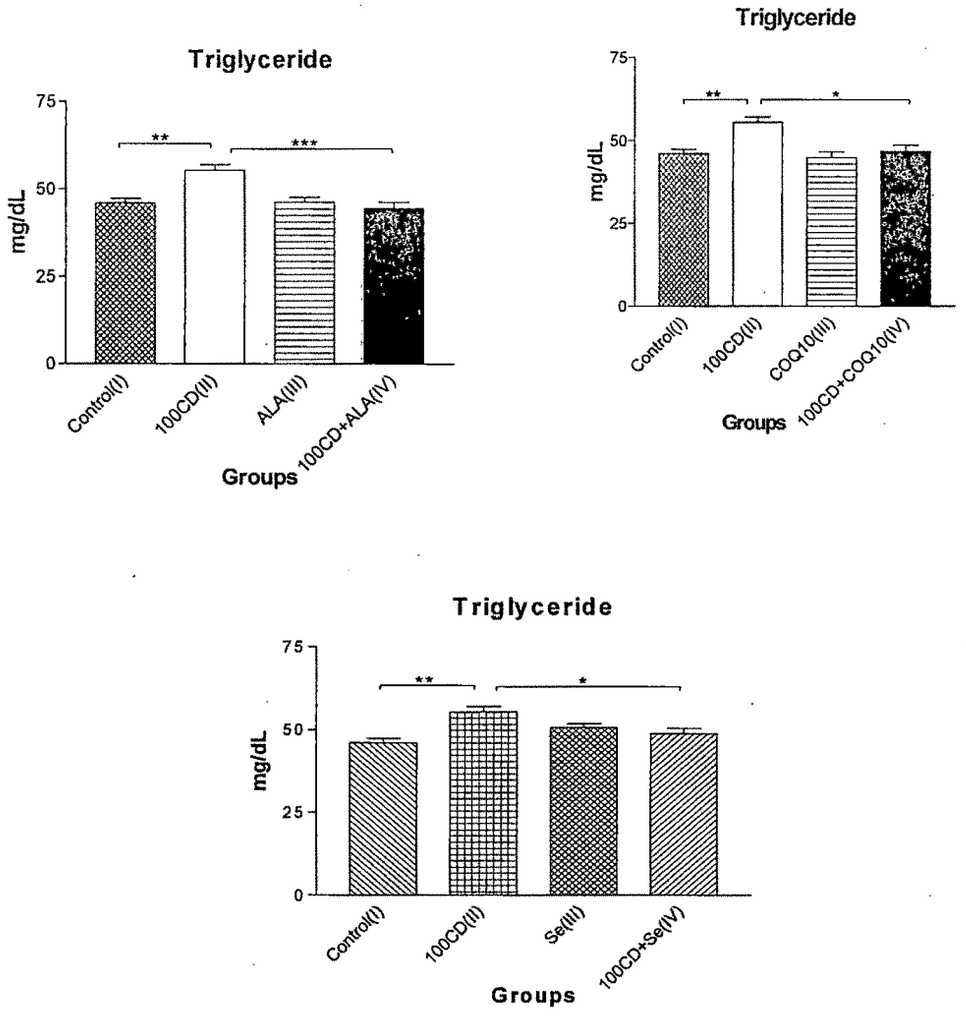


Fig: 4.54. Effect of 100 ppm of cadmium chloride (100CD) exposure for 30 days alone and in combination with antioxidants i.e. Alpha lipoic acid, Coenzyme Q10 or Selenium (ALA, COQ10 or Se) on the levels of Triglyceride in serum of rats.

Values expressed as mean ± SEM (n=6) for each observation.
Group II compared to control group.
Group IV compared to cadmium treated group.
$^{*}p<0.05$, $^{**}p<0.01$, $^{***}p<0.001$.

4.3 TOXICOLOGICAL INVESTIGATIONS

4.3.1 Changes in the levels of Cadmium in tissues

After thirty days of exposure to cadmium chloride the levels of this metal was significantly ($p<0.001$) increased in all the organs in group 2 (100CD) compared to group 1 (control). The levels of cadmium was decreased significantly ($p<0.001$) in all the organs in group 4 (100CD + ALA) compared to group 2 (100CD). The levels of cadmium was also decreased significantly in brain ($p<0.001$), kidney ($p<0.001$), lung ($p<0.001$), heart ($p<0.01$) and liver ($p<0.01$) in group 6 (100CD + Se) compared to group 2 (100CD). In group 8 (100CD + CoQ10) also there was a significant decrease in the level of cadmium in brain ($p<0.001$), heart ($p<0.01$), lung ($p<0.01$), kidney ($p<0.01$) and liver ($p<0.01$) compared to group 2 (100CD) **(Table: 4.2).**

4.5.2 HISTOPATHOLOGICAL CHANGES:

Histopathological examination of liver, kidney, lung, heart and brain showed pathological changes in these organs after thirty days of administration of Cadmium Chloride and there were significant changes in the organs on administration of 100ppm of the drug.

Liver: The overall changes in the liver due to administration of cadmium chloride 100ppm was that of **fatty liver (Fig: 4.55.)**. These include early changes like dilatation of rough endoplasmic reticulum, increase in perichromatic granules, loss of membrane associated ribosomes and generalized hydropic changes (swelling) with loss of cristae, pyknotic nuclei and clumps of coagulated chromatin. There was a significant decrease in size of the nucleolus and nucleus, in addition to the nuclei being pyknotic. This along with the increase in the cytoplasm gave an appearance of empty cell.

There was a fatty infiltration in the hepatic cells in form of vacuoles along with hydropic changes (swelling). The cytoplasmic material was pushed towards the periphery of the cell due to fatty infiltration into the cells. All this lead to complete disruption of the cell architecture.

These hydropic changes along with fatty infiltration lead to the increase in the weight of the organ. Sometimes when the damage was excessive it lead to the rupture of the cells and coalescence of adjacent expanded cells which together gave the picture of a fatty cyst.

Inflammatory cells in form of polymorphonuclear neutrophils and lymphocytes were seen infiltrating the portal tracts with spillover to the adjacent parenchyma in most of the places.

Alpha lipoic acid, selenium and coenzyme Q10 administration along with cadmium gave a protective effect and there was no significant damage either to the portal tracts or parenchyma except fatty infiltration at some places.

Kidney: The kidneys of the animals exposed to cadmium chloride in the strength of 100ppm showed a marked cystic dilatation of the proximal convoluted tubules. There was marked inflammation of the renal cells with infiltration of inflammatory cells in form of neutrophils and lymphocytes. Granular debris was seen in the tubular lumen along with fatty infiltration. All these changes were markedly reduced in animals where supplementation of alpha lipoic acid, selenium and coenzyme Q10 was given along with Cadmium **(Fig: 4.56.)**.

Lung: The organs of animals exposed to cadmium chloride in strength of 100ppm showed hyperemia along with interstitial inflammation. There was breakage and widening of the alveolar septa. The inflammatory cells infiltrating the peribronchial tissue were mainly lymphocytes. Supplementation of alpha lipoic acid, selenium and coenzyme Q10 conferred a protection to these tissues from the fore mentioned damage **(Fig: 4.57.)**.

Heart: The changes seen in the heart of the animals exposed to cadmium chloride in the strength of 100ppm was in form of cellular swelling and disruption along with some inflammatory invasion of cells in form of neutrophils and lymphocytes. When alpha lipoic acid, selenium and coenzyme Q10 were administered simultaneously with cadmium it had a protective effect. There was no cellular swelling and disruption only a minimal infiltration of inflammatory cells **(Fig: 4.58.)**.

Brain: The organ of the animals exposed to cadmium chloride in the strength of 100ppm showed infiltration of inflammatory cells in clumps and hydropic changes at places along

with cell disruption. The antioxidants ie alpha lipoic acid, selenium and coenzyme Q10 when given along with cadmium offered a protective effect and the organs of these animals did not show any pathological changes **(Fig: 4.59.)**.

Fig 4.2: Effect of 100 ppm of cadmium chloride (100CD) exposure (30 days) alone and in Combination with antioxidants i.e. Alpha lipoic acid, Coenzyme Q10 or Selenium (ALA, COQ10 or Se) on the levels of cadmium in liver.kidney, lung, heart and brain of rats.
(µg/gm)

GROUP	ORGANS				
	Liver	**Kidney**	**Lung**	**Heart**	**Brain**
1.Control	0.09120 ± 0.001855	0.08840 ± 0.001965	0.08314 ± 0.003375	0.0918 ± 0.005660	0.0488 ± 0.001855
2.100 CD	2.108 ± 0.04622^{***b}	3.058 ± 0.07552^{***b}	0.1636 ± 0.006735^{***b}	0.2734 ± 0.01814^{***b}	0.1764 ± 0.006524^{***b}
3.ALA	0.09946 ± 0.003146	0.0992 ± 0.003601	0.09768 ± 0.001806	0.1056 ± 0.005307	0.0498 ± 0.002709
4.ALA+100CD	0.6174 ± 0.02185^{***a}	1.747 ± 0.02602^{***a}	0.03402 ± 0.002500^{***a}	0.1208 ± 0.01092^{***a}	0.0516 ± 0.003311^{***a}
5.Se	0.09931± 0.004337	0.09781± 0.004415	0.1018± 0.003216	0.1158± 0.004858	0.05006± 0.002368
6.Se+100CD	1.663± 0.1213^{**a}	1.826± 0.03622^{***a}	0.1220± 0.008626^{***a}	0.1970± 0.01814^{**a}	0.06892± 0.004712^{***a}
7.COQ10	0.09346 ± 0.002115	0.09344 ± 0.001604	0.0980 ± 0.002500	0.1100 ± 0.0007359	0.04844 ± 0.001800
8.COQ10+100CD	1.433 ± 0.2201^{**a}	2.356 ± 0.2369^{**a}	0.1390 ± 0.002984^{**a}	0.2029 ± 0.008861^{**a}	0.06552 ± 0.005057^{***a}

Values expressed as mean ± SEM.
a: Group 4, 6 and 8 when compared with group 2.
b: Group 2, 3, 5 and 7when compared with group 1.
$^{*}p<0.05$, $^{**}p<0.01$, $^{***}p<0.001$.

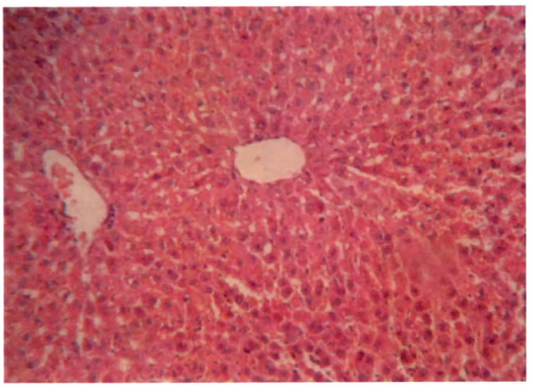
Fig: 4.55. PHOTOMICROGRAPHS SHOWING LIVER OF RATS AFTER FOLLOWING TREATMENTS
(MAGNIFICATION 40 X)

A. CONTROL
B. 100 ppm Cadmium
C. Alpha lipoic acid + 100 ppm Cadmium
D. Selenium + 100 ppm Cadmium
E. Coenzyme Q10 + 100 ppm Cadmium

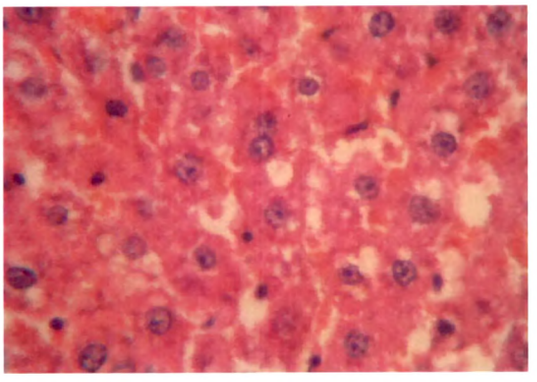
⇨ Pyknotic nuclei

→ fatty infiltration

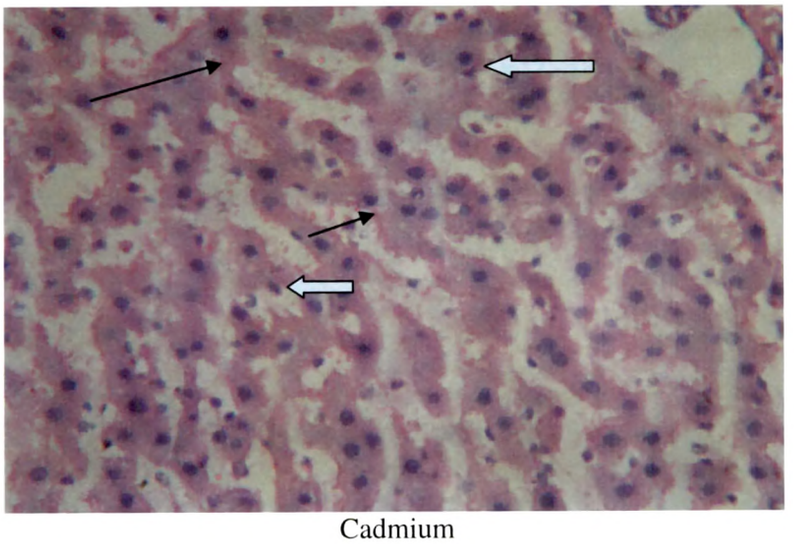
Fig: 4.55.



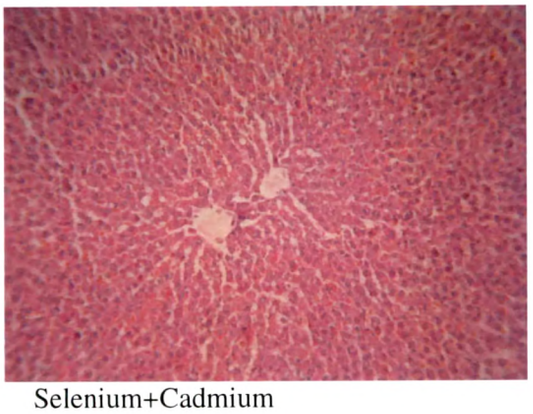
Control



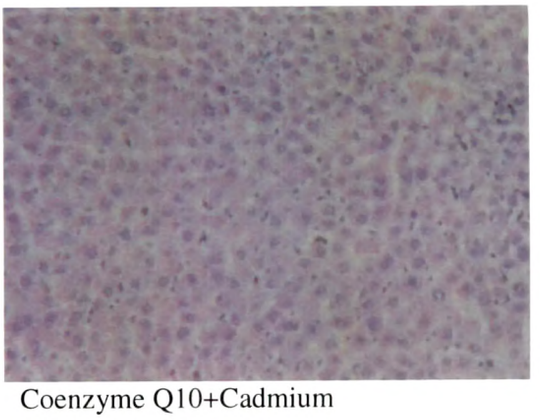
Alpha lipoic acid+Cadmium



Cadmium



Selenium+Cadmium



Coenzyme Q10+Cadmium

Fig: 4.56. PHOTOMICROGRAPHS SHOWING KIDNEY OF RATS AFTER FOLLOWING TREATMENTS (MAGNIFICATION 40 X)

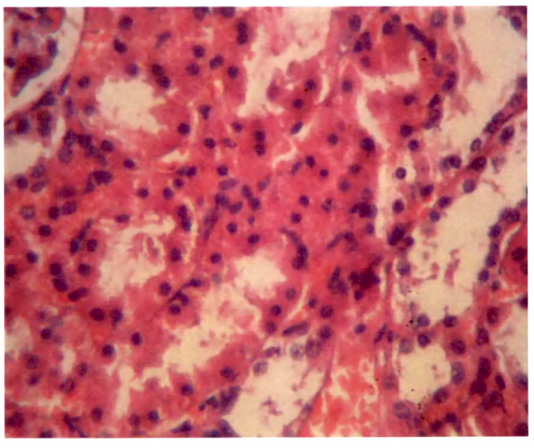
A. Control
B. 100 ppm Cadmium
C. Alpha lipoic acid+ 100 ppm Cadmium
D. Selenium + 100 ppm Cadmium
E. Coenzyme Q10 + 100 ppm Cadmium

⇨ fatty infiltration

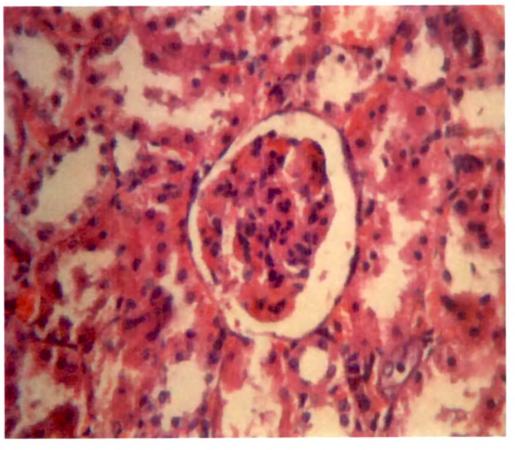
→ dilated proximal tubule

haemorrage & necrosis

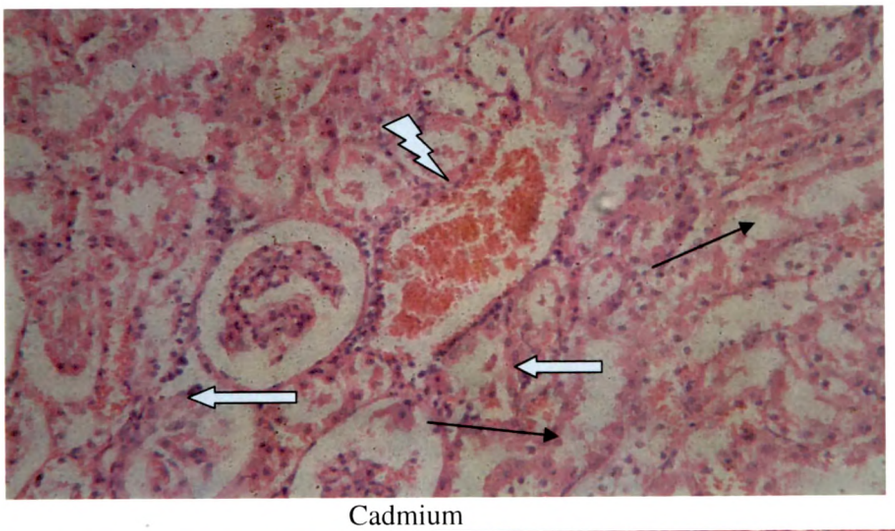
Fig: 4.56.



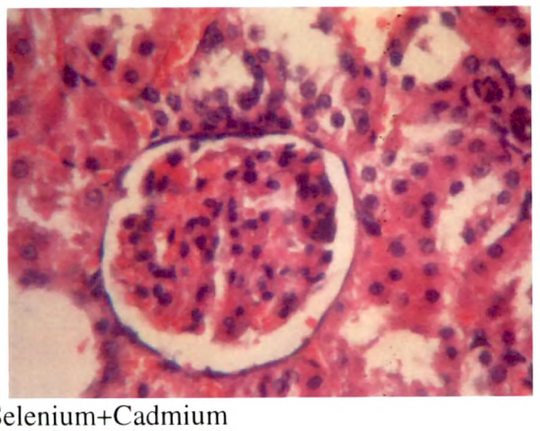
Control



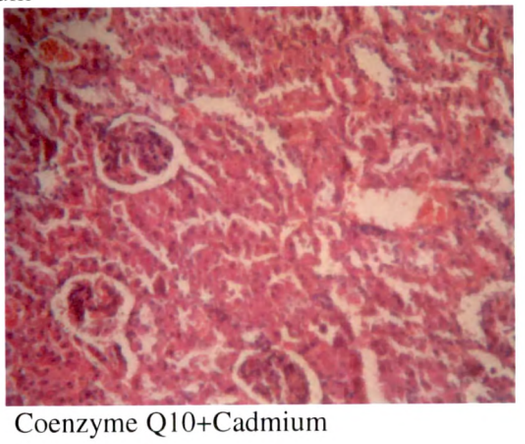
Alpha lipoic acid+Cadmium



Cadmium



Selenium+Cadmium

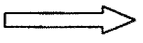


Coenzyme Q10+Cadmium

Fig: 4.57. PHOTOMICROGRAPHS SHOWING LUNG OF RATS AFTER FOLLOWING TREATMENTS (MAGNIFICATION 40 X)

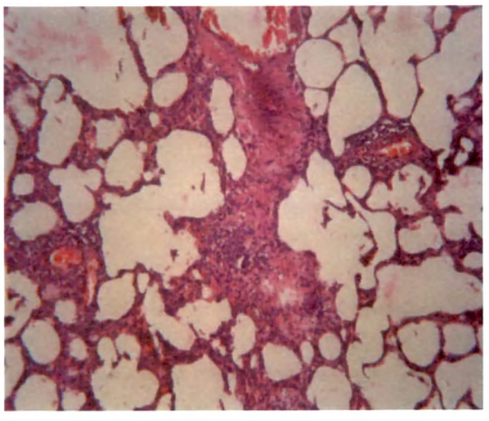
A. Control
B. 100 ppm Cadmium
C. Alpha lipoic acid + 100 ppm Cadmium
D. Selenium + 100 ppm Cadmium
E. Coenzyme Q10 + 100 ppm Cadmium

Widened alveolar septa

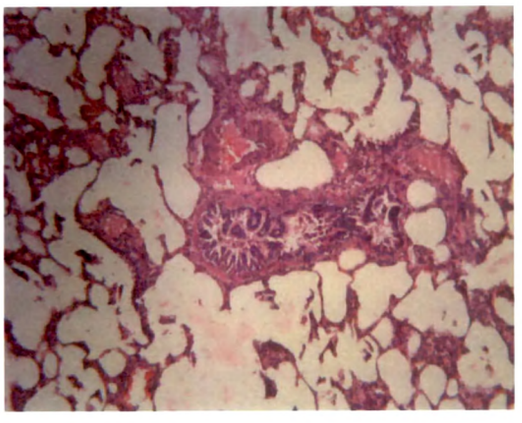


Peribronchial lymphoid hyperplasia & hyperaemia

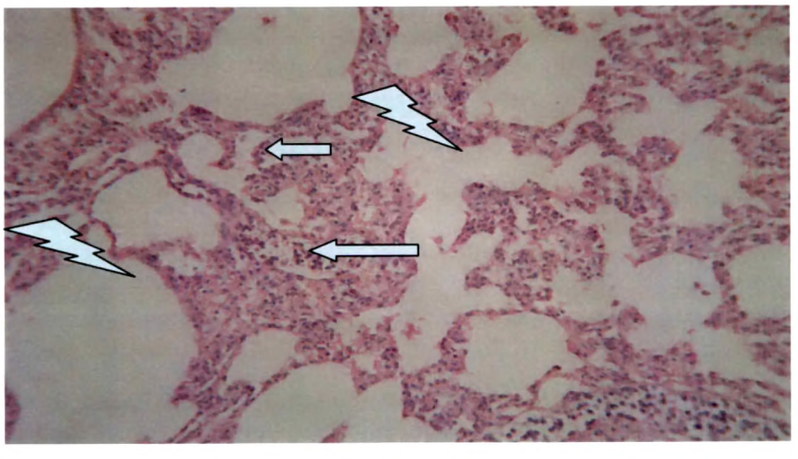
Fig: 4.57.



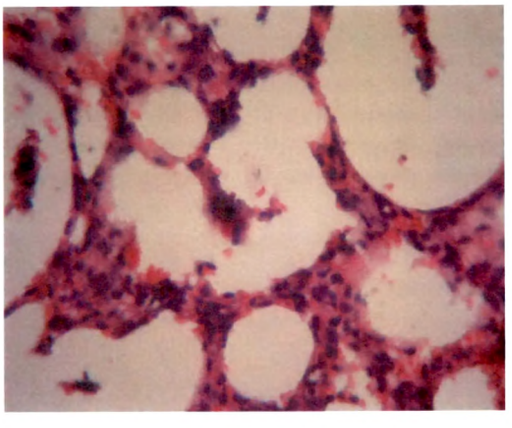
Control



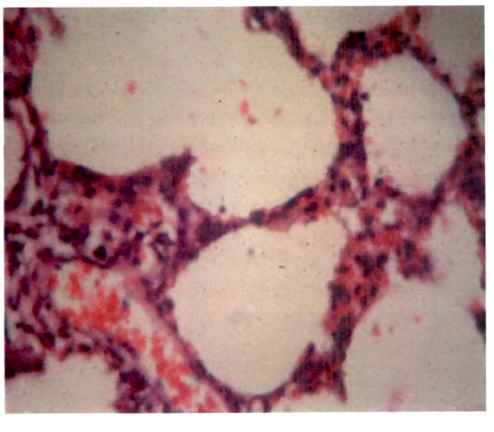
Alpha lipoic acid+Cadmium



Cadmium



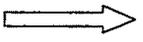
Selenium+Cadmium



Coenzyme Q10+Cadmium

Fig: 4.58. PHOTOMICROGRAPHS SHOWING HEART OF RATS AFTER FOLLOWING TREATMENTS (MAGNIFICATION 40 X)

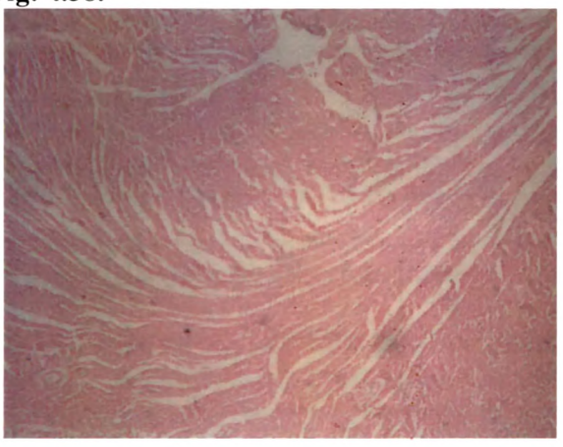
A. Control
B. 100 ppm Cadmium
C. Alpha lipoic acid+ 100 ppm Cadmium
D. Selenium + 100 ppm Cadmium
E. Coenzyme Q10 + 100 ppm Cadmium



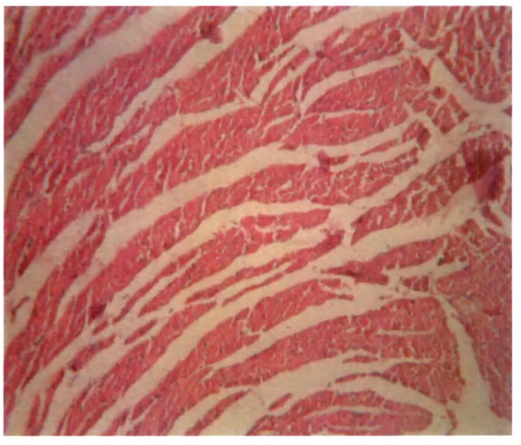
Swelling

Occasional inflammatory cells

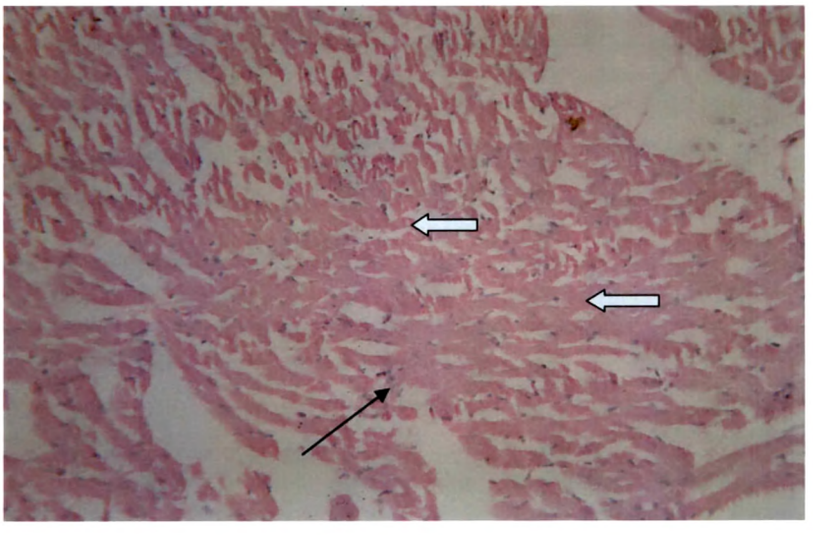
Fig: 4.58.



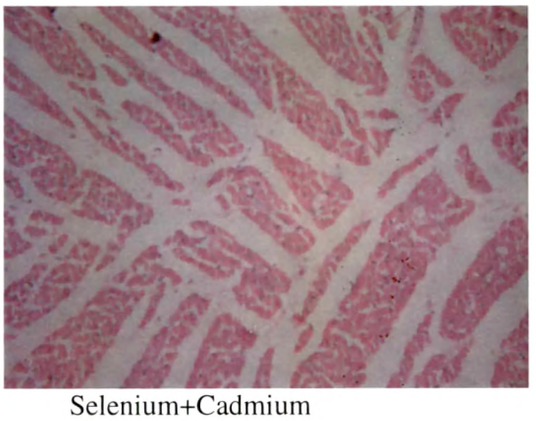
Control



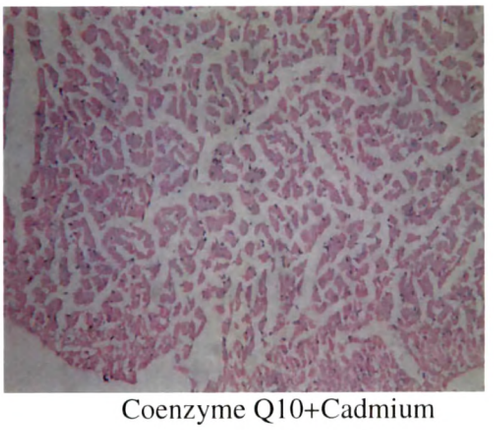
Alpha lipoic acid+Cadmium



Cadmium



Selenium+Cadmium



Coenzyme Q10+Cadmium

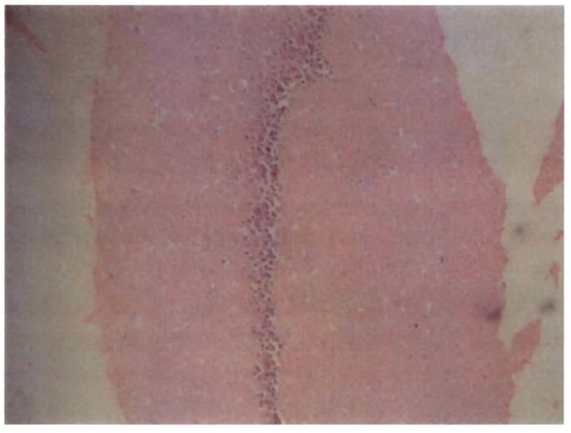
Fig: 4.59. PHOTOMICROGRAPHS SHOWING BRAIN OF RATS AFTER FOLLOWING TREATMENTS (MAGNIFICATION 40 X)

A. Control
B. 100 ppm Cadmium
C. Alpha lipoic acid + 100 ppm Cadmium
D. Selenium + 100 ppm Cadmium
E. Coenzyme Q10 + 100 ppm Cadmium

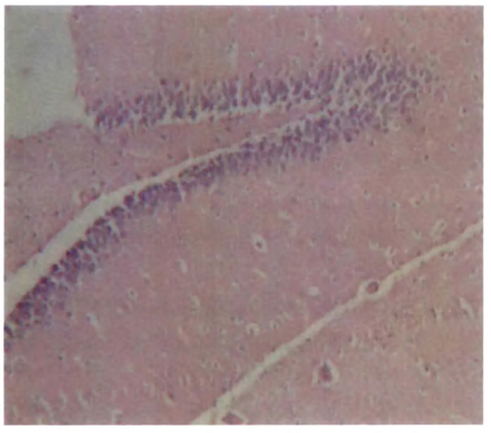
⇨ **Inflammatory cells**

→ **Fatty infiltration**

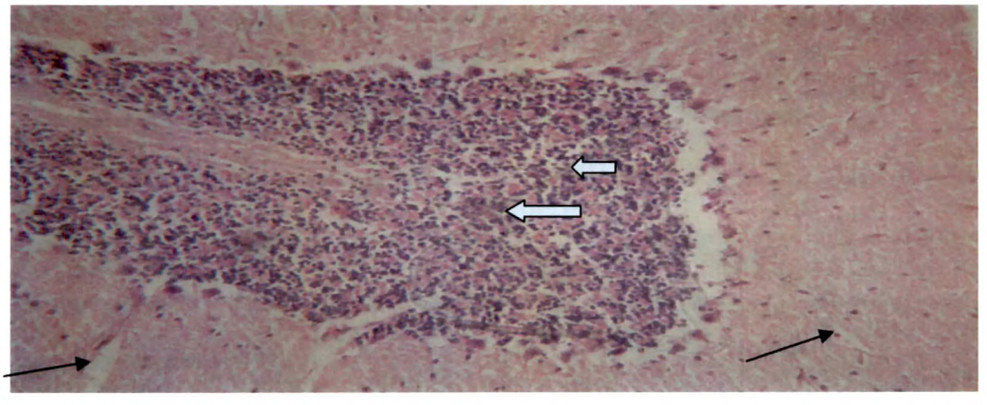
Fig: 4.59.



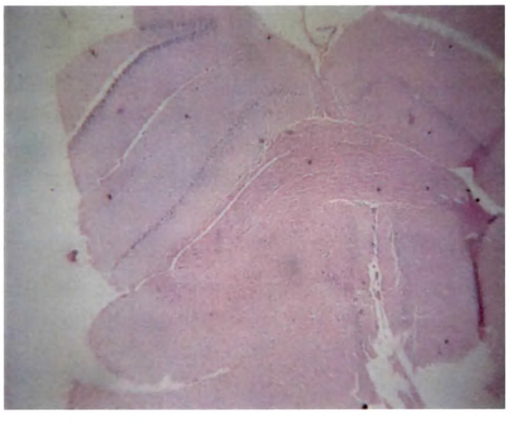
Control



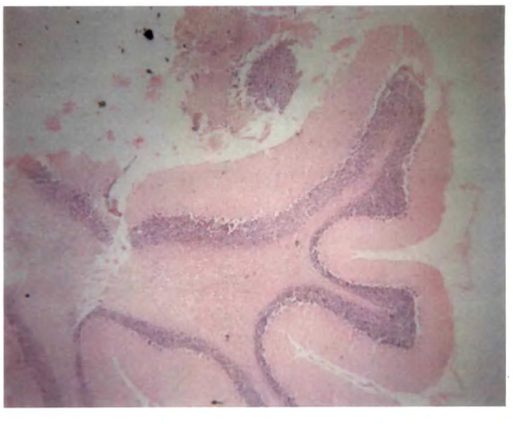
Alpha lipoic acid+Cadmium



Cadmium



Selenium+Cadmium



Coenzyme Q10+Cadmium