Summary and Conclusion
Chapter 6: Summary and Conclusion

The present study was aimed to examine the possible beneficial role of selected dietary nutrients in individual and combined supplementation during Cd exposure in rats. The physiological response of Cd intoxication on the albino rats was evaluated towards haematotoxicity, hepatotoxicity and nephrotoxicity based on various biochemical and histopathological variables. The protective effects of dietary nutrients were analyzed separately as acute, sub chronic and pretreatment studies for five, twenty one and thirty days respectively.

The results of present study shows the effects of dietary nutrients in rats exposed to cadmium (2 mg/kg) subcutaneously with particular reference to liver, kidney and blood. The overall toxic effects of continuous exposure to cadmium were assessed by monitoring body weight and organ-body weight ratio in rats. A significant decrease was observed (p<0.05) in body weight of rats exposed to cadmium as compared to control rats. Individual supplementation with methionine, selenium, melatonin, Zinc, NAC, thiamine, cystine and Vit-E as well as combination of dietary nutrients were considered more effective showing increase in body weight of albino rats as compared to Cd exposed rats. Exposure of rats to Cd significantly increased (p<0.05) the organ body weight ratio as compared to the control groups. However, Cd exposed rats when concomitantly treated with dietary nutrients tended to normalize the organ body weight ratios very close to untreated controls.

Exposure to cadmium showed 2.0, 2.5 and 2.7 fold increase in Cd concentration in blood liver and kidney respectively. It is evident from data that accumulation of Cd was found maximum (1.1 fold higher) in kidney as compared to liver. Administration of Vit-B₅ and cystine showed non significant decrease in Cd concentration in the tissue while co-administration of melatonin with Cd provided the best effect in reducing Cd concentration from these tissues than any other treatment groups.
Results presented in this study clearly show that administration of Cd resulted in a significant (p<0.05 and p<0.01) decrease of Hb, GSH and PCV. Further, treatment with dietary nutrients alone and their combination recovered almost normal values. There was a significant increase in the levels of serum creatinine, ALT, AST and urea in CdCl₂ administered group compared to controls (p<0.05). Exposure to Cd resulted in gradual increase in hepatic and renal markers in blood serum. However, Cd exposed rats following treatment with dietary nutrients individually and in combination showed a marked improvement in serum variables.

Reduced levels of antioxidant enzymes activities were observed in Cd treated rats compared to control rats. Oral supplementation of dietary nutrients with simultaneous Cd treatment increased the antioxidant enzyme activities in liver and kidney when compared to rats treated with Cd alone. Our results showed that combination of dietary nutrients (Met+NAC+Vit-B₁+Zn) was most effective in reducing the toxic effects of cadmium.

TBARS levels were measured as an index of malondialdehyde production to denote lipid peroxidation. Results indicated a significant increase of TBARS in Cd treated rats. However, combined or individual supplementation of dietary nutrients in rats to co-exposed with Cd was effective in reversing TBARS level almost close to control.

Histopathological examination of liver in control rats showed normal hepatocytes, central vein and portal triad. The liver of Cd treated rats exhibited marked pathological lesions such as cytoplasmic vacuolization, karyolysis, pycnosis in hepatocytes and centrilobular necrosis. The kidney of control rats showed normal glomeruli and renal tubules. Whereas, cadmium intoxicated rats evinced cellular glomeruli congestion. Moreover, combined administration with dietary nutrients showed almost normal architecture with mild residual degeneration in hepatic and renal tissues similar to that of control rats.

Additionally, the present study also evaluated the protective effects of *Spirulina* against the Cd-induced nephro-, hepato- and haematotoxicity in rats. In this study,
pretreatment with *Spirulina* significantly attenuated the Cd-induced toxicity and this effect has been attributed to its antioxidative property.

In this work, rats exposed to cadmium alone showed significant accumulation of cadmium in blood and tissue. Exposure to Cd alone significantly enhanced Cd concentration with a notable decrease in the levels of Cu and Zn. Pretreatment with *Spirulina* was found to have a protective effect by decreasing cadmium content in blood and tissues while the increase of Cu and Zn concentration. Cadmium treated rats showed not only a significant increase in TBARS and serum variables but also a significant decrease in the blood and biochemical variables in the selective tissues of albino rats reversed these changes by pretreatment of *Spirulina platensis*. These alterations have been confirmed by the histological examination of liver and kidney of *Spirulina platensis* pretreated group.

The present investigation suggests that the selected dietary nutrients have effective antioxidant properties and could well scavenge excess free radicals. Our results, further evinced that combined treatment of zinc (essential metal), methionine (amino acid), Vit-B₁ (vitamin) and NAC (antioxidant) was most effective than either of them alone in reversing Cd induced changes in the selected vital organs of albino rats.

The results thus led to conclude more or less similar protective role of *Spirulina platensis* pretreatment and combination group of dietary nutrients (Zn, Met, Vit-B₁ and NAC). However, still it remains to be seen if pretreatment with individual dietary nutrients may provide significant recovery.

Conclusions drawn from the present study are summarized as under:-

- Cd exposure induced reduction in body weight which was enhanced by 1.2 fold (approx.) after 21 days on dietary supplementation.
- Elevation in organ body weight ratio in Cd intoxicated rats was declined by the administration of dietary nutrients.
- Accumulation of cadmium in selected tissues was of following order: Kidney> Liver> Blood
Cd exposed rats showed a significant decrease in haematological variables till the end of experiment. However, administration of dietary nutrients and their combination improved Hb, GSH and PCV levels.

Cadmium toxicity resulted into anemia, hepatic necrosis, renal corpuscles deformities and numerological reduction of renal tubules in experimental specimens.

There was a notable increase in the activity of TBARS in Cd exposed rats which was more pronounced in liver than in kidney. Dietary nutrients supplementation significantly inhibited the activity of TBARS in liver (54%) and kidney (61%) after 21 days.

Cd intoxication resulted in significant decrease in the activity of SOD, GPx, ALP and total protein in both the tissues.

Kidney exhibited a more marked inhibition in the GPx activity while ALP and total protein levels were more declined in liver in contrast to kidney.

Supplementation with dietary nutrients enhanced the activity of SOD (136 % and 143 %), GPx (112 % and 149 %), ALP (162 % and 143 %) and total protein (380 % and 169 %) in liver and kidney respectively after 21 days Cd exposure.

The activity of hepatic markers (AST and ALT) and renal markers (urea and creatinine) was significantly increased in Cd intoxicated rats which was normalized after dietary supplementation.

Dietary nutrients restored a decreased GSH concentration and thereby ameliorated histopathological changes in the liver and kidney induced by cadmium toxicity.

Among different dietary nutrients studied individually, melatonin, NAC and methionine were found to play more effective role against Cd induced toxicity.

Co-treatment with dietary nutrients (Met, Zn, NAC and Vit-B₁) was most effective than either of them alone in reversing Cd induced toxicity.

In the pretreatment study, activity of SOD, GPx and total protein was decreased more in comparison to liver, in contrast to ALP of Cd exposed rats.
Pretreatment with *Spirulina* prior to Cd intoxication attenuated the levels of AST and ALT as marker for liver function and URE and CRE levels as a marker for kidney function.

In the pretreatment study, Cd exposure led to varying degree of lipid peroxidation and changes in the activities of antioxidant enzymes in liver and kidney of rats. However, prophylactic supplementation of *Spirulina platensis* resulted in tissue protection from oxidative damage due to cadmium.

Antioxidant and antiperoxidative effects of *Spirulina platensis* protected Cd-induced toxicity more efficiently than the combinational group of dietary nutrients.

The selected dietary nutrients as well as *Spirulina* pretreatment played a significant role in modifying the cadmium induced toxic haematological, biochemical and histopathological effects and reducing cadmium concentration in blood, liver and kidney.