Chapter 4

Summary

The current study was undertaken to evaluate the protective effect of p-coumaric acid in cadmium chloride-induced toxicity in rats under the following heads.

1. Protective role of p-coumaric acid against cadmium chloride-induced hepato-renal toxicity in rats
2. Protective efficacy of p-coumaric acid on pro-inflammatory cytokines levels in the serum of cadmium chloride-induced rats.

PROTECTIVE EFFECT OF P-COUMARIC ACID AGAINST CADMIUM CHLORIDE-INDUCED HEPATO-RENAL TOXICITY IN RATS

- In phosphomolybdenum assay, p-coumaric acid showed strong dose dependent reducing activity.
- In reducing power assay, dose dependent increase in reducing power of Fe$^{3+}$ to Fe$^{2+}$ was observed.
- Liver functional markers such as alanine transaminase (ALT), aspartate transaminase (AST), alkaline phosphatase (ALP), gamma glutamyl transaminase (GGT) and total bilirubin (TB) levels in serum were found to be increased in cadmium chloride alone treated rats.
- Kidney functional markers such as urea, uric acid and creatinine levels were found to be increased in serum and decreased in urine in cadmium chloride alone treated rats.
- Total cholesterol, triacylglycerides, low density lipoprotein (LDL) and very low density lipoprotein (VLDL) levels were found to be increased and high density lipoprotein (HDL) was significantly decreased in cadmium chloride-induced rats.
- Lipid peroxidation was found to be increased in plasma, liver and kidney of cadmium chloride-induced rats. Whereas, decreased levels of the antioxidants – superoxide dismutase, catalase, glutathione-S-transferase,
glutathione peroxidase, glutathione reductase and reduced glutathione were observed in the plasma, liver and kidney of cadmium chloride-induced rats.

- The activities of lysosomal enzymes were found to be significantly increased in the plasma, liver and kidney of cadmium chloride-induced rats.

- The levels of glycoproteins such as sialic acid and hexosamine were found to be increased in the plasma, liver and kidney of cadmium chloride-induced rats.

- The levels of membrane bound ATPases such as total ATPases, Na$^{+}$K$^{+}$ATPase, Mg$^{2+}$ATPase and Ca$^{2+}$ATPase were found to be decreased in the plasma, liver and kidney of cadmium chloride-induced rats.

- The administration of $p$-coumaric acid along with cadmium chloride protected the above biochemical parameters to near normal levels which were found to be similar to that of silymarin in liver and kidney of rats.

- The activities of tricarboxylic acid cycle and electron transport chain enzymes such as isocitrate dehydrogenase, $\alpha$-ketoglutarate dehydrogenase, succinate dehydrogenase, malate dehydrogenase, NADH dehydrogenase and cytochrome-c-oxidase were found to be significantly decreased in cadmium chloride alone treated rats.

- The administration of $p$-coumaric acid along with cadmium chloride protected the above enzyme activities to near normal levels in liver and kidney tissues of rats.

- The level of serum glucose was found to be significantly increased in cadmium chloride alone treated rats.

- The tissue glycogen level was found to be significantly decreased in cadmium chloride alone treated rats.

- The levels of carbohydrate metabolizing enzymes such as glucose-6-phosphatase, fructose 1, 6-bisphosphatase, lactate dehydrogenase were found to be increased and hexokinase and pyruvate kinase levels were decreased in cadmium chloride-induced rats.
- The administration of $p$-coumaric acid along with cadmium chloride prevented the above biochemical alterations which were found to be similar to that of silymarin in liver and kidney tissues of rats.

- The metallothionein and cadmium content in liver and kidney tissue homogenates were found to be increased in cadmium chloride-induced rats.

- The administration of $p$-coumaric acid to cadmium chloride-induced rats increased the metallothionein content and decreased the cadmium concentration compared to the cadmium chloride alone treated rats.

- In histopathological analysis, the liver and kidney sections of cadmium chloride alone treated rats showed severe hepatocyte degeneration and severe tubular epithelial cell degeneration respectively.

- On the other hand, $p$-coumaric acid treatment along with cadmium chloride showed mild hepatocyte degeneration and mild tubular epithelial cell degeneration in liver and kidney tissues respectively similar to that of silymarin treated rats.

PROTECTIVE EFFICACY OF $p$-COUMARIC ACID ON PRO-INFLAMMATORY CYTOKINES LEVELS IN THE SERUM OF CADMIUM CHLORIDE-INDUCED RATS

- The levels of serum TNF-$\alpha$ and IL-1$\beta$ were found to be increased significantly when compared to the control rats.

- The administration of $p$-coumaric acid to cadmium chloride-induced rats markedly decreased the pro-inflammatory cytokines to near normal levels in the serum similar to that of silymarin treated rats.
CONCLUSION

The abnormalities observed in the liver and kidney tissues of cadmium chloride-induced rats with respect to tissue markers, lipid peroxidation, antioxidants, lysosomal enzymes, glycoproteins, mitochondrial tricarboxylic acid cycle and electron transport chain enzymes, carbohydrate metabolizing enzymes, cadmium and metallothionein content, pro-inflammatory cytokines and histopathology were significantly prevented in $p$-coumaric acid treated cadmium chloride-exposed rats.

Hence this study ascertained the usefulness of $p$-coumaric acid as a dietary compound to counteract the cadmium chloride-induced toxicity. This study paved the foundation to evaluate the efficacy of $p$-coumaric acid at molecular level for overcoming the challenges elucidated by cadmium chloride-induced toxicity.