SUMMARY

The present work was undertaken to study the effect of *H. auriculata* in protecting mercuric chloride induced nephrotoxicity in rats.

- The *in vitro* study of DPPH, NO⁻ and DNA sugar damage showed the free radical scavenging properties of the *H. auriculata*.

- Ethanolic extract of *H. auriculata* showed more significant nephroprotective activity, suggesting the antioxidant effect of *H. auriculata* in HgCl₂ induced nephrotoxicity. HgCl₂ treated rats showed a significant decrease in their body weight and liver weight. *H. auriculata* treated rats reverted back to near normal weights.

- The levels of urinary markers indicated the nephrotoxicity induced by HgCl₂ on renal tubular cells. Enzymes appearing in urine originate owing to leakage from damaged cells or remain in the urine inadequate reabsorption by the proximal tubules. Administration of *H. auriculata* seems to protect the renal tubules and thus prevents the increased excretion of urinary enzymes in HgCl₂ treated rats.

- *H. auriculata* rendered its salubrious effect on changes in the constituents in the urine and blood of experimental animals.

- The marker enzymes such as AST, ALT, ACP, ALP, LDH, cathepsin-D, β-D glucuronidase, N-acetyl-β-D glucosaminidase and γ-GT were found to be altered in HgCl₂ induced kidney damage in rats. *H. auriculata* treatment reverted the activities of marker enzymes to normal in experimental rats.
Nucleic acid (DNA and RNA) synthesis was found to be decreased in HgCl₂ induced nephrotoxicity condition and their levels were normalized in *H. auriculata* treated rats.

Increased renal lipid peroxidations, along with a fall in the activities of enzymic and non-enzymic antioxidants were observed upon HgCl₂ administration.

HgCl₂ induced alterations in the activities of the antioxidant enzymes and in the concentrations of cellular non-enzymic antioxidants were found to be effectively protected by the administration of *H. auriculata* which clearly indicates the protective role of *H. auriculata* by replenishing the cellular antioxidant pool.

Hence it can be concluded that *H. auriculata* acts not only as an antioxidant but also improves the cellular thiol content and energy status, thus mitigating the extent of HgCl₂ mediated toxic changes.

Glycoproteins such as hexose, hexosamine and sialic acid levels were found to be changed in kidney damaged rats may due to alteration in glycoprotein synthesis by HgCl₂ induced animals. These changes in glycoproteins level were normalized in *H. auriculata* treated animals.

Carbohydrate metabolizing enzymes viz. glycolytic enzymes such as hexokinase, phosphoglucoisomerase, aldolase and gluconeogenic enzymes such as glucose-6-phosphatase and fructose-1,6-di phosphatase activities were altered in HgCl₂ induced animals. Administration of *H. auriculata* brought back
these changes to near normal values, which justifies the membrane stabilizing property of *H.auriculata*.

- Increased levels of lipid profile in serum and decreased levels in kidney were observed in HgCl₂ treated rats. Administration of *H.auriculata* brought backs all these lipid levels to normal and modified the lipid profile.

- Membrane bound ATPase such as Na⁺/K⁺-ATPase and Mg²⁺-ATPase were decreased, whereas Ca²⁺-ATPase was increased in renal damaged animals due to HgCl₂ induced lipid peroxidation. The activities of these ATPases were noticeably reverted in *H.auriculata* treated animals due to the free radical scavenging property of plant extract.

- The observed alterations undoubtedly reflect mitochondrial dysfunction which is due to accumulation of mercury in the subcellular organelle. *H.auriculata* treatment reduced the renal and hepatic burden of mercury by favouring its urinary excretion.

- Administration of *H.auriculata* effectively modulated the alterations in glycolytic and gluconeogenic enzymes along with the TCA cycle enzymes to near normal levels. This demonstrates the efficacy of *H.auriculata* in maintaining the mitochondrial membrane integrity, preventing lipid peroxidation and also the possible regeneration of renal proximal tubules, hence reflects the cytoprotective effect of *H.auriculata*.

- Since mercuric chloride affects the renal mitochondria extensively, the mitochondrial susceptibility to Hg²⁺ toxicity was also studied. It is worth mentioning that Hg²⁺ ion an
important component of energy production system-ICDH, SDH, MDH and α-KDH ultimately led to decreased respiratory coupling ratio and subsequent cellular ATP depletion.

Phase I biotransformation enzymes such as cyto-P<sub>450</sub>, cyto-b<sub>5</sub>, NADPH and cyto-C reductase were decreased in HgCl<sub>2</sub> treated animals due to microsomal damage caused by HgCl<sub>2</sub> induced free radicals. On the other hand, GST and UTPGT were increased in nephrotoxicity induced rats due to the involvement in HgCl<sub>2</sub> metabolism.

The renal tubular function was affected in the cases as evidenced from an extensive damage to brush border membrane. *H. auriculata* administration had an ameliorating effect on the above mentioned changes in the experimental model studied.

Inhibition of erythrocyte membrane ATPase activity by HgCl<sub>2</sub> is considered to be one of the possible mechanism of HgCl<sub>2</sub> induced nephrotoxicity. Administration of *H. auriculata* clearly indicates its special role in maintaining renal function and membrane structure against HgCl<sub>2</sub> induced alterations seen in membrane bound ATPases.

Mercuric chloride toxicity altered the level of calcium and lead to the accumulation of mercury, thereby damaging the cells. *H. auriculata* protected the tubular damage by normalizing the levels of calcium in experimental animals. On the other hand *H. auriculata* elevated the excretion levels of mercury.

The histopathological examinations of kidney further substantiate the efficacy of *H. auriculata* against HgCl<sub>2</sub> induced
nephrotoxicity with reference to biochemical parameters studied.

✓ From this study, it may be suggested in general that *H. auriculata* may be used as an effective protective agent against various pathological conditions especially in nephrotoxicity.