Summary
5. SUMMARY

Rapid development in the field of industrialization and urbanization in developing countries like India has taken its toll on the environment. Majority of industries particularly the metal related industries like tannery, foundry, welding and electroplating are found to deteriorate the environment. Discharge of various suspended particulate matter, gaseous pollutants and toxic effluents from these industries found to contain various toxic, carcinogenic, mutagenic and teratogenic chemicals and people employed in these industries are exposed to these chemicals. In such situation early identification of hazards through biomonitoring studies is crucial to reduce exposure and carcinogenic risk in persons exposed to industrial toxicants. The mutagenic and carcinogenic effect of genotoxic agents on human populations who are exposed occupationally, accidentally or by life style has been an increasing concern. In all the four industries mentioned above in one or other way, workers are exposed to compounds of metals like Cr, Pb, Cd and Ni, and all these metals have the potential to cause multiple classes of DNA damage and may lead to cancer.

Carcinogenesis is a long lasting multistage, multigenic and multicausal process, which appears to involve DNA damage. DNA damage induced by chemicals appears primarily in the form of alterations of phosphate backbone, sugar or base modification such as alkylation cross links, or formation of bulky DNA adducts, which are substrates for DNA
repair mechanism. For screening large number of subjects exposed to genotoxic agents, blood is the usual source for cells. Since the early 1970s, up to the present time, cytogenetic analysis of peripheral blood lymphocytes has remained the only suitable assay for biological monitoring of the genetic damage induced in somatic cells by excessive exposure to clastogenic agents in the workplace. But these tests have their limitations because they require mitotically active cells with relatively large chromosomes. In this study the SCGE or ‘Comet assay’ known for its multi number of advantages, was applied to measure DNA damage in peripheral blood lymphocytes of persons working in tannery, foundry, metal welding, and electroplating industries. To find out the genotoxicity risks among these workers, peripheral blood samples were collected from the industrial workers and assayed for base level DNA strand breaks (DSBs and SSBs), DNA-DNA cross-links, DNA-protein cross-links, the global repair capacity, Cr, Pb, Cd and Ni concentrations in the blood samples were also estimated. Results of this study clearly show that the persons working in these industries are exposed to the toxic pollutants produced in this environment and are found to suffer from significantly higher level of DNA damage than the control group. The DNA damage parameters measured in blood cells of worker’s samples viz., DSBs, SSBs, global level repair efficiency and the metal concentration were significantly higher than the control group. DNA-DNA cross-links, DNA-protein cross-links were found to be significantly higher only in the electroplater’s blood sample. Apart from metal concentrations
in the blood, age, experience, smoking and alcohol drinking were the other major confounding factors that had significant influence over DNA damage end points in the blood samples of the metal related industrial workers. The correlation observed among various genotoxicity biomarkers (DSBs, SSBs, DNA-DNA cross-links, DNA-protein cross-links, the global repair capacity and Cr, Pb, Cd, Ni and total metal concentration) justify the use of these biomarkers in assessing levels of genotoxic exposure in the study groups.

The comet assay was also applied in this study to estimate the DNA damaging potential of metal compounds such as potassium dichromate, lead (II) acetate, cadmium chloride and nickel (II) sulfate in an in vitro experiment using human peripheral blood lymphocytes. The protective effects of antioxidants like ascorbic acid and Se on DNA damage parameters were assessed.

In the metal induced genotoxicity Cr, Pb, Cd and Ni were found to induce dose dependent increase in DNA damage in the isolated human peripheral blood lymphocytes. The DSBs, SSBs, DNA-protein cross-links were also increased as the concentration of the chemicals (Cr, Pb, Cd and Ni) increases. Treatment with ascorbic acid and Se were found to protect the cells from the genotoxic insult caused by these chemicals. Compare to Se, ascorbic acid was found to be more genoprotective.

In addition, the metals-DNA binding were also analysed by exposing the isolated human genomic DNA with different concentration of chemical salt solutions viz., Potassium dichromate (K$_2$Cr$_2$O$_7$), Lead
acetate (CH₃COO)₂Pb, Cadmium chloride (CdCl₂) and Nickel sulfate (NiSO₄).

The chemical-DNA adduct formation is found to be strictly dose dependent. As the concentration of the chemicals increases the chemical-DNA adducts were also increased.

The blood samples collected from the metal related industrial workers (tannery, foundry, welding and electroplating) were found to confirm that there is a high risk for the workers reflecting in multiple classes of DNA damages. The genotoxic effects in the workers include SSBs, DSBs, DNA-DNA cross-links, DNA-protein cross-links, repair efficiency. Presence of higher concentration of metals in their blood indicates that the working environment is highly prone to genotoxic toxicants.