CHAPTER-II

AIM AND SCOPE OF THE STUDY

The researches embodied in this dissertation had basic aim to study i) influence of protein malnutrition, ii) role of trace metal supplementation, and iii) effect of alcoholism, on toxic manifestations of Cd intoxication, and iv) develop suitable prophylactic measures.

The toxic potentials of cadmium pollution are well recognised. Protein malnutrition may alter the response of the organism to environmental pollutants in a manner different to that observed in the fully nourished state of the body. The incidence of protein malnutrition among industrial workers particularly in developing countries is fairly high. Keeping
this in view, attempts were made to simulate this condition in experimental animals. There may be synergism or antagonism between effects of Cd and protein malnutrition particularly Cd-induced hepatotoxicity, nephrotoxicity or alterations in carbohydrate metabolism. The influence of low protein diet on the uptake of Cd and Cd-induced biochemical alterations in liver, kidney and blood of rats was investigated to evaluate the severity of Cd intoxication under condition of protein malnutrition. The profile of such alterations with duration of exposure, was monitored.

The disturbed iron metabolism is an important factor in Cd toxicosis as suggested by occurrence of anaemia in industrial workers exposed to Cd. Exposure to Cd may be more hazardous when Fe intake is inadequate. In view of the occurrences of skeletal defects and cardiovascular lesions in both chronic Cd toxicity and Cu deficiency, there is a need for assessment of the interaction between Cd and Cu. The toxicity of environmental pollutants are known to be affected markedly by the nutritional status of the body; there is evidence that dietary factors influence not only absorption but also distribution of Cd in the body. Therefore, the influence of trace metals viz. Cu, Fe or their combination on Cd intoxication in protein malnourished animals was studied in order to ascertain their mode of action and to understand
the physiological implications of metal-metal interactions.

The abusive consumption of alcoholic beverages deranges normal function of body system in various ways. Chronic alcoholism may have profound effects on mineral, carbohydrate, protein and lipid metabolism. Ethanol has been found to enhance the absorption of lead in body and alcoholics have been reported to be more susceptible to Pb intoxication. A significant section of industrial workers and general population are alcohol addicts, who may also be exposed to Cd. Interpretation of an association between alcohol ingestion and incidence of Cd poisoning, is difficult. Therefore, the effect of ethanol ingestion on susceptibility to Cd toxicity and influence of ethanol-Cd co-exposure on Cd sensitive biochemical parameters, tissue accumulation of Cd, essential trace element status and metallothionein synthesis was investigated.

The development of effective chelation therapy for Cd has been extremely difficult because of intracellular binding of Cd within a short duration following exposure, which prevents most of the chelating agents from removing the metal. The influence of selective lipophilic and hydrophilic metal chelating agents viz. calcium trisodium diethylenetriaminepentaacacetate (CaNa$_3$DTPA), 1,2-cyclohexane diaminetetraacetic acid (CDTA), sodium diethyldithiocarbamate (NaDDC) and triethylenetetramine (TETA) on cellular distribution of Cd, trace
metals and tissue metallothionein was investigated. Further, in view of strikingly similar effects of Cd on pancreatic cells, as in case of diabetes mellitus, the effect of a commonly used hypoglycemic agent, 1-((p-(2-chloro-o-anisamido)-ethyl)phenyl) sulfonyl)-3-cyclohexyl urea (Glibenclamide), on amelioration of Cd toxicity and also its modulatory effect, if any, on efficacy of CaNa$_3$DTPA as an antidote of Cd intoxication was studied.