CHAPTER II

AIMS AND SCOPE OF THE PRESENT WORK
With the advancement of technology and rapid industrialization, the use of metals and their alloys has become many folds higher in the present time. With the result, there is continuous contamination of metals in the environment. Environmental pollution of metals has, therefore, posed a global concern. One of the industrially important metals is nickel. Exposure to nickel may occur during mining, electroplating, polishing, welding, manufacture of alloys, battery cells, inks and cement and during the hydrogenation of oils, etc. The notable toxic effects of nickel include skin irritation, dermatitis, kidney and liver dysfunction, lung and nose cancers, etc.

The metal binding proteins (occasionally rich in sulfhydryl content) are known to play crucial roles in the storage, transport and detoxication of heavy metals (Eaton et al., 1980; Wong and Klassen, 1980; Maines and Kappas, 1977). It was, therefore, necessary to study the nature of bioligands which bind to nickel in cytosolic fractions of liver and kidney.
It has been documented that TETA, d-penicillamine and several other polyaminocarboxylic acid drugs are effective antidote of nickel (Dwivedi et al., 1978; Sunderman et al., 1976). However, these drugs show several deleterious toxic effects which may be implicated to their indiscriminate interaction with the essential metals even in the presence of toxic amounts of nickel (Williams, 1982; Sillen and Martell, 1964). Thus prolonged treatment with these drugs may lead to the condition of metal deficiency. It was, therefore, important to develop a suitable therapeutic measure having specificity for nickel.

Essential trace metals are building blocks of the body systems. Various disorders have been reported in the homeostasis of essential trace metals after the administration of nickel and leads to the impairment in physiological and biochemical processes in normal rats (Chmielnicka et al., 1982; Nielson et al., 1979; Nielson, 1976; Schroeder and Nason, 1976; Schroeder et al., 1974; Whanger, 1973).

It was also necessary to make a comparative account of existing and newly developed chelating drugs to evaluate their comparative effects on the levels of essential trace metals and some biochemical parameters. This study will provide the knowledge regarding the inherent toxicity of chelating drugs.

Finally, it was equally important to assess the efficacy of existing and newly developed chelating drugs to
set on the nickel mediated alterations in the levels of hepatic and renal trace metals and some biochemical parameters.

In view of these considerations, the following experiments have been performed to get an insight whether the removal of nickel from the body organs simultaneously brings about the reversal of the biochemical alterations mediated by nickel:

i) Kinetics of nickel binding bioligands in hepatic and renal cytosol of radioactive nickel-63 treated rats.


iii) Effect of chelating drugs on the trace metals metabolism and biochemical parameters.

iv) Reversal of nickel induced biochemical and trace metal metabolism by chelating drugs.

v) Pharmacokinetik studies on the mobilization of nickel by chelating drugs from the liver and kidney of nickel treated rats.