CHAPTER 1

Introduction
Nature provides human society with a rich spectrum of starting materials. In practice, the metal minerals constitute the largest set of these resources more than sixty different elements in all. Modern technology is totally dependent on perhaps four of them - iron and manganese that (with minor amounts of other metals) form structural steels, the aluminium widely used in transportation, the lead used for storage batteries, and the copper that transmits power from the generator to the user. Cases nearly as strong could be made for perhaps four others the chromium and nickel that (together with iron) form the stainless steels, the zine that inhibits metal corrosion, and the tin that is essential to modern electronics.

There are many individual metals causing varying degrees of illness based on acute and chronic exposer of them, generally it termed as heavy metal toxicity. Heavy metal is a term used for a group of elements which have specific weight characteristics or it can also be say that "Heavy metals" are chemical elements which have, specific gravity about 5 times the specific gravity of the water. The specific gravity of water is 1 at 4°C (39°F). Simply stated, specific gravity is a measure of density of a given amount of a solid substance when it is compared to an equal amount of water.

Heavy metal poisoning remains a widespread problem in most industrial nations. Exposure to these toxicants is not confined only to occupational workers but also to the general population at large by means of increased deforestation, contaminated reservoirs, and indiscriminate use of food preservatives (Passos and Mergler, 2008). Toxicity is more likely to result through inhalation or ingestion route (Hodgson, 2004). It affects a number of important body functions including central nervous and haematopoietic systems, besides hepatic and renal functions. Metal toxicity has also been reported to cause oxidative stress, leading to various physiological malfunctions (Kalia and Pavani, 1993). Heavy metals such as lead (Pb), cadmium (Cd) and arsenic (As), are specifically known, to bind to proteins and interfere with protein functions, besides inducing neurotoxicity (Wright and Baccarelli, 2007).

Some of heavy metals, which have unstable nuclei are known as radio-isotopes. At present, more than 3000 nuclides have been discovered so far, and most are unstable. Unstable nuclei decay by spontaneous fission, α-particle, β-particle, or γ-ray emission, or electron capture in order to achieve stability. The stability of a nuclide is governed by the structural arrangement and binding energy of
the nucleons in the nucleus. Radioactive decay by particle emission or electron capture changes the
atomic number of the radionuclide, whereas decay by γ-ray emission does not. Radionuclides may
decay by any one or a combination of six processes: spontaneous fission, u-decay, β-decay, β+
decay, electron capture, and isomeric transition.

Use of radionuclides on phenomenal increase throughout the globe in the in healthcare, food
processing and energy production.(Conklin et al., 1987). The extensive use of radionuclides leads to
larger handling of radioactive materials, and thus making the society more vulnerable to
radionuclide accidents. However, strict controls over the use of radionuclides have been imposed
by the regulatory bodies like in India Bhabha atomic research centre (BARC) approves the
laboratories/institutes for using radionuclide, even after this, nuclear accidents have occurred in the
past. The contamination/spillage can be cause intentional nuclear detonations and ever increasing
terrorist threats like use of radioactive dispersal devices (RDD). This leads to the contamination of
flora and fauna. In a nuclear detonation, about 400 radionuclides are released out which 40 are of
vital concern. Externally spilled radionuclides are comparatively easy to handle than the
radionuclides which have gained entry in the body though different portals like ingestion,
inhalation, percutaneous absorption or though wounds. Within the body, these radionuclides
represent a state of either internal contamination or incorporation. In internal contamination,
radiouclides reside mainly in the respiratory and gastrointestinal tracts and have not crossed the
mucous membranes. In case of incorporation, radionuclide is transported across mucous
membranes, or it is injected or absorbed through the skin or a wound. Organ specific radionuclides
like strontium in bone, cesium in muscle and iodine in the thyroid, is most difficult to be removed
from the body.

The possibilities of radiological accidents involving unsealed radioactive material are always
there, where radioactive material is used.(Dunning 1957). Most radioactive metal-salts produce
alpha/beta/gamma radiation or a combination thereof. Radiation poisoning, also called radiation
sickness or a creeping dose, is a form of damage to organ tissue due to excessive exposure to
ionizing radiation. Presence of radionuclides in body poses serious health problems due to their
emission characteristics in the form of alpha, beta particles or gamma rays. Although they are
present in microquantities which are far below the metal toxicity level, but the radiotoxicity may
be very high. As long as these radionuclides remain in the body, they pose significant health
risks. The potential for development of cancers of the lung, liver, thyroid, stomach, and bone, among others, are principal long-term health concerns, as are fibrotic changes in tissues such as lung, which may lead to restrictive lung disease and other chronic debilitating conditions. Radiation exposure can also increase the probability of contracting some other diseases, mainly genetic damage. The only effective method of reducing these risks is the removal of radioactive contaminants from the body. A number of important factors like absorption, excretion, concentration and effective half-life must be understood for the removal of radionuclides from the body.

Once radioisotopes incorporated in the body tissues, these are very difficult to remove and are extremely harmful. These shall require decorporation therapy to reduce the incidence of cancer and early death due to systemic tissue damaged. Removal of internalized radionuclides is a vast problem due to

- Large number of radionuclides
- Their different chemical form and solubility
- Physical decay
- Multiple route of entry &
- Biokinetics & organo-specificity.

Thus, removal strategy for radionuclides is based on the chemical nature rather than on emission characteristics of radionuclides. Therefore, chemical agents that are used for heavy metal removal may also be used in radionuclide removal. They are known as decorporating agents. Decorporating agent is a broad term that includes all agents that can either prevent the incorporation of the radionuclides or decorporate the incorporated radionuclides. These agents may be categorized as blocking agents, chelating agents, diluting agents and ion exchanger. Blocking agents can enhance elimination of the radionuclide or decrease the quantity incorporated. After incorporation, chelating agents that can mobilize the radionuclides, are much less effective. It should be obvious that the lesser incorporation will occur with early administration of the proper decorporating agent. Chelating agents bind metals into complexes, thus preventing tissue uptake and allowing urinary
excretion. Dilution of the radionuclide involves administering large amounts of a stable nuclide so that the hazardous radionuclide is diluted. Thus, the decorporating agents can be used at three different levels in the body:

1. Prevention of heavy metal/radionuclides’ absorption from GIT to the systemic circulation

2. Hastening the elimination of absorbed metal/ radionuclides from the blood stream.

3. Decorporation of heavymetal/radionuclides from their target organ.

Although the use of chelating agents against metal toxicity was employed decades back, introduction of ethylene diamine tetraacetic acid (EDTA) as a chelator is considered as a breakthrough in chelation therapy (Kalia and Flora, 2005). Use of EDTA and other chelating agents is the medically accepted treatment for lead and other heavy metal poisoning (Goyer, 1995; Henge-Napoli et al., 2000; James et al., 2007). However, clinical utility of EDTA and related member of the family, diethylene triamine pentaacetic acid (DTPA) has been severely compromised by the need to administer them intravenously through slow infusion. This necessitates a development of novel decorporation and radioprotective formulation, that may be more effective than the existing one and must be cost-effective to ensure availability at mass scale for local and systemic relief from heavy metal or radiation poisoning.
2.1 **HEAVY METAL TOXICITY**

Heavy metals are chemical elements, which are commonly present in our environment, without realizing it; we all are exposed to heavy metals on a daily basis. However, the quantities that we inhale, ingest or come into contact with the skin are so small that they are usually harmless. In fact, small amounts of some heavy metals in our diet are essential for good health. These are referred to as trace elements and include iron, copper, manganese, zinc, plus others, which are commonly found naturally in fruits and vegetables.

Heavy metal is a term used for a group of elements that have particular weight characteristics, or we can say that "Heavy metals" are chemical elements with a specific gravity that is at least 5 times the specific gravity of water (specific gravity = 1 at 4°C (39°F)). Some well-known toxic metallic elements with a specific gravity that is 5 or more times that of water are arsenic 5.7, cadmium 8.65, iron 7.9, lead 11.34, and mercury 13.546 (Lide et al., 1992). Some heavy metals such as cobalt, copper, iron, manganese, molybdenum, vanadium, strontium and zinc are essential to health in trace amounts. Others are non-essential and can be harmful to health in excessive amounts. These include cadmium, antimony, chromium, mercury, lead and arsenic, these last three being the most common in cases of heavy metal toxicity.

There are 35 metals that concern us because of occupational or residential exposure; 23 of these are the heavy elements or "heavy metals": antimony, arsenic, bismuth, cadmium, cerium, chromium, cobalt, copper, gallium, gold, iron, lead, manganese, mercury, nickel, platinum, silver, tellurium, thallium, tin, uranium, vanadium, and zinc (Glanze et al., 1996). Interestingly, small amounts of these elements are common in our environment and diet and are necessary for good health, but large amounts of any of them may cause acute or chronic toxicity (poisoning). Heavy metal toxicity can result in damaged or reduced mental and central nervous function, lower energy levels, and damage to blood composition, lungs, kidneys, liver, and other vital organs. Long-term exposure, may result in slowly progressing physical, muscular, and neurological degenerative processes that mimic Alzheimer's disease, Parkinson's disease, muscular dystrophy, and multiple sclerosis. Allergies are not uncommon and repeated long-term contact with some metals or their compounds may even cause cancer (International Occupational Safety and Health Information Centre 1999).