1. INTRODUCTION

Heavy metals are chemical elements with specific gravity that is at least five times the specific gravity of water (Passow et al., 1961; Hawkes, 1997). Heavy metals are too well known as environmental pollutants with dangerous effects on human health due to their wide usage in many industrial branches. They are present everywhere in the air, water and soils (Boguszewska and Pasternak, 2004). With the rapid development of urbanization and industrialization in recent years, heavy metal contamination has become a topic of extensive study with many reports in the recent literatures (Hu et al., 2006; Huang et al., 2006; Liu et al., 2006; Rodrigues et al., 2006; Shi et al., 2007; Chen et al., 2008). Heavy metals are of considerable environmental concern due to their toxicity, wide sources, non-biodegradable properties and accumulative behaviors (YU et al., 2008). Although some metals are essential nutrients, excess concentrations of all heavy metals lead to various toxic effects such as oxidative stress and inhibition of enzymes (Dietz et al., 1999; Pohlmeier, 1999). It is generally considered that heavy metals originate from two primary sources: natural inputs (e.g. parent material weathering) and anthropogenic inputs (e.g. metalliferous industries and mining, vehicle exhaust, agronomic practices, etc.) (Zhang, 2006). Concentrations of heavy metals in the environment fluctuate, due to, e.g. tidal currents, storm runoff flooding, changes in speciation or variable emissions from anthropogenic sources (Broman et al., 1994; Montes-Botella and Tenorio, 2003; Shomar et al., 2005; Alagarsamy, 2006).Metals generate many of their deleterious effects through the formation of free radicals, resulting in DNA damage, lipid peroxidation, depletion of protein, sulfhydryls (eg, glutathione), and other effects. These reactive radicals include a wide range of chemical species, including oxygen, carbon, and sulfur radicals originating from the superoxide radical, hydrogen peroxide, and lipid peroxides, and also from chelates of amino acids, peptides, and proteins complexed with the toxic metals (Valko et al., 2005).

Cobalt is a naturally occurring element found in rocks, soil, water, plants, and animals. Cobalt, an essential nutrient, serves at low doses as a cofactor for the activation of several enzymes, the formation of vitamin B12 and other cobalamines (Lee and Herbert, 1999). At high doses, it exhibits diverse effects in several tissues like heart, thyroid, liver and kidney (ATSDR, 2001). Sources of environmental cobalt are both natural and anthropogenic (Barceloux, 1999). Natural sources include erosion (wind-blown continental dusts), weathering of rocks and soil, seawater spray, volcanoes, forest fires, extraction by plants, and continental and marine biogenic emissions (Lantzy and Mackenzie, 1979; Nriagu, 1989). The major anthropogenic sources of environmental cobalt include mining and processing (smelting) of cobalt-bearing ores, the use of cobalt-containing sludge or phosphate fertilizers on soil, the disposal of cobalt-containing waste, and atmospheric deposition from activities such as the burning of fossil fuels and smelting and refining of metals (Smith and Carson, 1981). Cobalt is suspected to be toxic to many cell types, including neural cells (Yang et al., 2004) and can induce cell death by apoptosis and necrosis (Huk et al., 2004). Cobalt can cause DNA fragmentation (Zou et al., 2001), activation of caspases (Zou et al., 2002) and increases production of reactive oxygen species (ROS) leading to oxidative stress (Olivieri et al., 2001).

Chelation therapy is an established treatment for the removal of metal toxins by converting them to a chemically inert form that can be excreted in the urine (current

procedural terminology, 2012). Chelation therapy is thought to not only remove contaminating metals but also to Decrease free radical production (Lamas and Ackermann, 2000).

EDTA chelation therapy is an often used treatment aimed at reducing calcium deposits, removing heavy metals, controlling lipid peroxidation resulting from free radical pathology, and reducing platelet aggregation in the clinical management of atherosclerosis and related disorders (Halstead, 1979).

Cyclam Is macrocyclic Ligand which is capable of binding to metal ions. Cyclam can bind to metal ions by forming four bonds to it – the four bonds from nitrogen atoms in amino groups.