Environmental Biology and Pathophysiology of Cadmium

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Basic chemistry/biochemistry

Cadmium (Cd) is a soft, silver-white metal being together with zinc and mercury in group II b in the periodic table. It's melting and boiling point are 320.9 ^{0}C and 765 ^{0}C, respectively. Cd is rapidly oxidized into cadmium oxide in the air.

When reactive gases such as carbon dioxide, sulphur dioxide, sulphur trioxide and hydrogen chloride or water vapour are present in the air, cadmium vapour reacts to produce cadmium carbonate, cadmium sulphite, cadmium sulphate, cadmium chloride or cadmium hydroxide. These compounds may be formed in chimneys and emitted into the environment. It is indicated that zinc-bearing coals of the central United States and carboniferous age coals of other countries contain large sub economic resources of cadmium (Tolcin 2009). Although some cadmium compounds such as acetate, chloride and sulphate are soluble in water; cadmium oxide, carbonate and sulphide are insoluble (WHO 2000).

Cadmium in the environment

Cadmium is not found in the pure state in nature and occurs mainly in association with the sulphide ores of zinc, lead and copper. It is a by-product of the zinc industry and the estimated world identified resources of cadmium were about 6 million tons, based on identified zinc resources of 1.9 billion tons containing about 0.3% cadmium (Tolcin 2009). Before the First World War, cadmium was not usually recovered from zinc and other nonferrous metal plants. This situation caused uncontrolled cadmium contamination of the environment for decades (WHO 2000).

The percentage of cadmium consumed globally for NiCd battery production has been increasing, while the percentage for the other end uses of cadmium-specifically coatings, pigments and stabilizers-have gradually decreased, owing to environmental and health concern. Approximately 85% of the global NiCd battery market was concentrated in Asia (Tolcin 2008). Certain cadmium refining countries are China (3400 tons), Japan (2100 tons), Republic of Korea (3600 tons) and Kazakhstan (2000 tons). World cadmium refining capacity was estimated 20 000 tons. The average annual production of cadmium throughout the world was about 20 tons in 1920s, 12 000 tons in 1960s and in recent years was 20 000 tons in 1999; 20 800 tons in 2000; 18 800 tons in 2001; 16 800 tons in 2002 and 16 900 tons in 2003 (Kuck and Plachy 1996; Tolcin 2008).

Cadmium uses have changed through time. Before 1960 it was mainly used in the electroplating of metals, the production of pigments or stabilizers for plastics. Between 1960 – 1990 the coatings and plating sector consumed over half the cadmium produced worldwide. In the mid-1990s, the nickel - cadmium battery industry consumed

1996, NiCd batteries accounted for 56% of the rechargeable battery market. By 2006, that percentage had decreased to 18%. Global sales of NiCd batteries also decreased during 2006 by approximately 16% from that of 2005. Li-ion and Ni-metal hybrid batteries are replacing NiCd batteries in some applications. However, the higher cost of these substitutes restricts their use in less expensive products. Coatings of zinc or vapour-deposited aluminium can be substituted for cadmium in many plating applications, except where the surface characteristics of a coating are critical such as fasteners for aircraft. Cerium sulphide is used as a replacement for cadmium pigments, mostly in plastics. Sources indicate that barium/zinc or calcium/zinc stabilizers can replace barium/cadmium stabilizers in flexible polyvinylchloride applications. However, cadmium demand may increase owing to several new market opportunities for NiCd batteries, particularly in industrial applications. NiCd batteries currently power approximately 80% of battery electric vehicles in circulation and are also used as a source of power in a limited number of hybrid electric vehicles (Tolcin 2008, 2009).

Human exposure to certain cadmium sources and their relative importance are as follows: phosphate fertilisers (41.3 %), fossil fuel combustion (22.0 %), iron and steel production (16.7 %), natural sources (8.0 %), non-ferrous metals (6.3 %), cement production (2.5 %), cadmium products (2.5 %) and incineration (1.0 %) (Van Assche 1998). Former cadmium sources have actual importance because of the long life and accumulation characteristics of cadmium in the environment.

It is assumed that 15 % of cadmium absorbed follows a pulmonary route (WHO 2000). Much of the cadmium which enters the body by ingestion comes from terrestrial foods such as contaminated plants and animals feeding on these plants. Some have estimated that 98 % of the ingested cadmium comes from terrestrial food while only 1 % comes from aquatic foods and 1 % comes from drinking water (Van Assche 1998).

The cadmium content of the soil and the plants grown on it, are principally derived from natural sources, air born particles, phosphate fertilisers and sewage sludge (De Meeus et al. 2002; Navarro Silvera and Rohan 2007). Phosphate fertiliser has been the major source of the cadmium addition to agricultural soil in Australia as the traditional sources of rock phosphate often contain elevated levels of cadmium (Yu-Jing 2003). Phosphate rocks of igneous origin normally contain less than 15 mg cadmium per kilogram P_2O_5 (phosphate fertiliser) compared with 20 to 245 mg cadmium in sedimentary counterparts. Therefore, European fertilizer producers had put forward a limit of 60 mg Cd/kg for importing phosphate fertilisers by the year 2005 (Kuck and Plachy 1996) and the Czech Republic has notified the European Commission it wishes to maintain its pre-accession upper limit of 50 mg Cd/kg P_2O_5 for phosphate fertilizers in 2005 (SCHER 2006).

The soil pH is the important parameter determining cadmium uptake of plants. In the soil, increasing pH from 5.5 to 7.0 has significantly decreased cadmium concentrations in clover, lettuce, carrot, rye grass and to a lesser extent in wheat (Gray 1999). Also, soil acidification (e.g. by acid rain) can lead to an increased content of cadmium in food (Nigam et al. 2001). Liming of soil can reduce soil acidity and therefore reduce the mobilisation and uptake of cadmium by plants (Tsadilas et al. 2005).

Cd / Zn ratio in soil is another important factor influencing plant uptake of soil cadmium. Most livestock and wildlife have no increase of cadmium in tissues used as food even when crop cadmium is increased substantially as long as Cd / Zn ratio is near natural levels. Zinc inhibits cadmium absorption and / or retention in tissues, even liver and kidney. Most plant species exclude cadmium relative to zinc during the formation of grain, fruits, or storage roots. However, rice grown in flooded soils has an opposite pattern in which grain cadmium is substantially increased, while grain zinc remains at background levels. Fe, Zn and Ca in

rice are deficient for subsistence human diets, increasing risk (Yu-Jing 2003).

Microorganisms are the invisible constituents of ecosystems, having importance preparing inorganic substances for plants. Low (10 mg kg^{-1}) and medium (20 mg kg^{-1}) concentrations of cadmium in soil have stimulated a proliferation of organotrophic bacteria while high rates of cadmium (30 – 40 mg kg^{-1}) cause a significant decrease in the number of oligotrophic, oligotrophic - sporulating, copiotrophic and copiotrophic – sporulating bacteria in soil, especially at the yellow lupine (*Lupinus* spp.) shoots elongation phase (Wyszkowska and Wyszkowski 2002).

Food constitutes the principal environmental source of cadmium. The lowest concentrations (≈1 μg / kg) are found in milk. Cadmium concentrations is in the range 1 - 50 $\mu g\ kg^{-1}$ in meat, fish and fruit and 10-300 $\mu g\ kg^{-1}$ in staple foods (wheat, rice and potatoes). The highest cadmium concentrations (100 – 1000 $\mu g\ kg^{-1}$) are found in the internal organs (kidney and liver) of mammals and certain species of mussels, scallops and oysters. In cadmium–polluted soil, rice can accumulate a considerable amount of cadmium (more than 1000 $\mu g\ kg^{-1}$) (WHO 2000).

Cadmium treated *Brassica rapa* seedlings exhibit the deficiency symptoms of calcium, magnesium and manganese including decreasing levels of chlorophyll a, chlorophyll b, and carotenoids. In addition, cadmium treated plants display the reduction of height and formation of primary leaves, and fresh and dry weights. Furthermore, increased concentration of cadmium causes severe bending of seedlings (Wang and Zhou 2005). In wheat seedlings (*Triticum durum*), uptake of potassium and nitrate, transpiration and shoot growth is inhibited by adding cadmium to the nutrient medium. A sharp reduction in cytokinin content is observed within two hours of supplying cadmium (Veselov et al. 2003).

Animals can accumulate cadmium from their foods in the kidney, liver, pancreas, testes, lung (by inhalation) with negligible amounts in the muscle (WHO 2000; Bernard 2008). The level of cadmium in the liver and kidneys generally increases with the age of the animals. The harmful effects of cadmium observed in animals are having higher blood pressure, iron-poor blood, liver diseases and nerve or brain damage (Bernard 2008). In chronically intoxicated animals, cadmium gives rise to a nephropathy very similar to that described in humans and characterised functionally by the appearance of a tubular or mixed-type proteinuria, aminoaciduria, glucosuria and hypercalciuria and morphologically, by lesions predominantly involving the tubules. The critical concentration of cadmium in the renal cortex associated with these changes in rats is around 200 mg kg^{-1}, as in humans. Other chronic effects in animals treated with cadmium by inhalation include lung emphysema and inflammation, disturbances in calcium and vitamin-D metabolism resulting in bone lesions, hepatic damage and effects on the pancreas, testes and cardiovascular system. Cadmium can also produce embryotoxic, teratogenic and carcinogenic effects (WHO 2000). In farm animals, the consumption of high levels of cadmium produce depressed appetite, decreased milk production, abortion and birth defects (Ishitobi and Watanabe 2005; Golub 2006; Robinson et al. 2009).

Absorption by human body

Acute toxicity of cadmium was discovered as early as the 19th century. Chronic effects of Cd such as pulmonary, bone and renal lesions in industrial workers were recognized within the first half of 20th century. In the 1960's there was the outbreak of the Itai-Itai bone disease in Japan.

The World Health Organization has established a provisional tolerable weekly intake for cadmium at 7 $\mu g\ kg^{-1}$ of body weight. This value corresponds to a daily tolerable intake level of 70 μg of cadmium per day for the average 70 kg man and 60 μg of cadmium for the average 60 kg women. For the populations living in non-contaminated areas, the average daily intake from food is in the range of 10 to 25 μg which means that

approximately 0.5 to 1.0 μg is retained in the body. Smokers absorb about 1 to 3 μg of extra cadmium per day from smoking cigarettes (McElroy et al. 2006; Navarro Silvera and Rohan 2007; Bernard 2008).

Smoking is an important source of cadmium exposure. Several studies have compared the blood cadmium concentration between smokers and non-smokers. Blood and urinary Cd concentrations in the smokers have been reported to be 2–4 times higher than in the non-smokers in Poland (Galażyn-Sidorczuk et al. 2008) and in the similar experiments in Turkey, the blood cadmium concentration of female smokers were found to be highest 2.62±0.72 ng ml^{-1} and that of nonsmokers lowest 0.67±0.57 ng mL^{-1} (El-Agha and Gökmen 2002). It is interestingly reported that cigarette smoking resulted in the absorption of 1.9 μg cadmium per pack (Ellis et al. 1979).

The main deposition sites of cadmium in the body are the liver and the kidney. In the case of low-level exposures, such as occurring in general environmental conditions, about 30-50 % of the cadmium body burden is stored in the kidneys alone, with concentrations in the cortex about 1.25 times higher than in the kidney as a whole. In non-occupationally exposed people the concentration of cadmium in the liver increases continuously with age. The concentration in the renal cortex also increases but only until the age of 50-60 years, after which it levels off or even decreases. In Europe, mean concentrations of cadmium in the renal cortex in the age group 40-60 years are in the range 15-50 mg kg^{-1}. Concentrations are usually 50-100 % higher in current or ex-smokers than in non-smokers. In industrial workers, cadmium concentration in the renal cortex may be as high as 300 mg kg^{-1}. The amount of cadmium excreted in urine is very small, it is about 0.005-0.01 % of the total body burden which corresponds to a biological half-life for cadmium of about 20-40 years (WHO 2000).

Consequently, the health effects of cadmium-contaminated soil, air and water depends on the nature and extent of exposure of a person. Food and cigarette smoke are the biggest sources of cadmium exposure of people in the general population. Therefore, it is important to inform people that kidney is the critical organ for cadmium accumulation and transport to man and that the restrictions on smoking will prevent the harmful effects of cadmium on people also who are passive smokers.

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