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THE CHARACTERISTICS, TOXICITY AND EFFECTS OF CADMIUM

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ABSTRACT

Cadmium is a heavy metal that occurs as a natural constituent in earth's crust along with Copper, Lead, Nickel and Zinc. Cadmium is vastly used in batteries, coating, plating, alloys etc. in various industries. Humans are commonly exposed to cadmium by inhalation and ingestion. Cadmium enters in air and bind to small particles where it can combine with water or soil causing contamination of fish, plants and animals in nanoform. Spills at hazardous waste sites and improper waste disposal can cause cadmium leakages in nearby habitats. Foodstuffs like liver, mushrooms, shellfish, mussel, cocoa powder and dried seaweed are cadmium rich increasing the concentration in human bodies. Cigarettes contains tobacco smoke that transports cadmium into lungs and then to the rest of the body through blood. The bioaccumulation of cadmium in human body and in food chain leads to acute and chronic intoxications due to biomagnification. Health effects includes diarrhea, stomach pains, Bone fracture, Reproductive failure and possibly even infertility, damage to the central nervous system and immune system, psychological disorders, etc. Cadmium can also cause the transformation of normal epithelial cells into carcinogenic cells by inhibiting the biosynthesis of protein. Cadmium waste streams from the industries end up in soil which can pollute both soil and surface water. The organic matter in the soil absorbs cadmium increasing the risk of survival of various plants and also increases the uptake of this toxic metal in food. This review is about the study of toxicity mechanism of cadmium in human beings and plants and the biological phenomena involved.

Keywords: Cadmium ion, cadmium induced toxicity, cadmium related diseases

INTRODUCTION

Cadmium (Cd) is a silvery-white, soft, ductile chemical metal with atomic number 48 and belonging to the group 12 element in d block and period 5. It was discovered by German chemist F.Strohmeyer in 1817 as a constituent of smithsonite ($ZnCO_3$) from zinc ore. Electronic configuration of the cadmium is [Kr] 4d10 5s2. Cadmium concentration in the earth crust is 0.15ppm and the most common cadmium mineral is greenockite (CdS).[1] Cadmium is recovered as a by-product from sulfide deposits, mainly those containing lead, zinc, and copper. Cadmium level in human increases with the age, it reach to an average of about 30mg in the age range 40-50 and after that decreases slightly. [2] Cadmium is hazardous to both environment and human beings. Cadmium present in atmosphere, water, or food when exposed to human in low concentration cause serious health problems and probably the death.[1] Sources of cadmium human exposures are fossil fuels, iron and steel production, cement nonferrous metals production, waste incineration, smoking, fertilizers, etc. Activities like volcanic eruption, mining and use of phosphate fertilizers provides cadmium exposures indirectly as toxin from earth crust. Plants take up cadmium from the soil and form the major source of cadmium intake in non-smoking, non-occupationally exposed populations. There is a significant use of this heavy toxic metal in batteries, pigments, coating, plating, PVC stabilizers and alloys in industries. [3]Renal disease and emphysema are observed in the workers working in battery plant due to the inhalation of the cadmium oxide dust over a long period of time. Due to excessive intake of cadmium in water and rice and low intake of calcium and vitamin D, there is effect in pregnancy and lactation. Cadmium in small amount absorbeKd in the kidney cause proteinuria when kidney concentration reaches a certain value. Interaction between Cd, Cu and Zn results in cadmium toxicology [4]. Cadmium is also adsorbed

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and distributed in the other organ and tissues such as liver, spleen, pancreas, heart and testis. In human, the biological half life of cadmium is 10-30 years. [5]. As cadmium is very harmful ,its sources of emission and its direct and indirect interaction with soil, plants, water and animal is to be understood properly.[1] Total usage of cadmium is small due to its toxic properties of the soluble salts. In 1968, metal production increases from about 100,000 lb per year to 31,000,000 lb per year due to its metallurgical properties such as corrosion resistance. [4] Regulatory limits have been decided at various levels according to EPA 5 parts per billion (ppb) or 0.005 parts per Million (ppm) of cadmium in drinking water, Food and Drug Administration (FDA) concentration In bottled drinking water should not exceed 0.005 ppm (5 ppb) and OSHA has an average permissive concentration of 5 micrograms per cubic meter in workplace air according to 8-hours workday, 40-hours work week. [6]

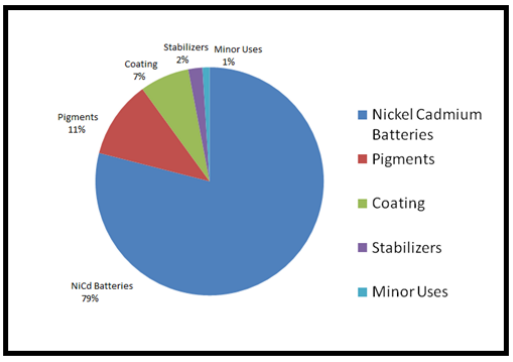

Figure 1: Cadmium uses in industries (Adapted from International cadmium association 2003)

BIOLOGICAL ROLE OF CADMIUM

Under the condition of low zinc, cadmium enhances the growth rate of marine diatom Thalassiosira weissflogii at low partial pressure of CO2. Even though the major intracellular Zn-requiring isoform of CA (TWCA1) in T. weissflogii remain low, there is increase in the carbonic anhydrase (CA) activity reflecting the enhanced growth rate. Marine organism controls oceanic primary production by distributing many nutrients in the sea. Similar to the distribution of the major nutrients, there is water column distribution of biologically important trace metals in oceanic system. At the surface, metal present extremely at low concentration where photosynthetic activity depletes algal nutrients and due to the decomposition of the organic matter and remineralization, the metal concentration is increases at depth.[10]Cadmium is a good example of metal which has a nutrient like profile and the accumulation of the cadmium in fossilized tests of marine invertebrates is used as a measure of past nutrient concentrations in the sea by correlating its concentration to that of phosphate.[11-12] Cd may replace Zn under the conditions of Zn limitation and enhance the growth rate of marine phytoplankton.[13-15]By using X-ray absorption fluorescence spectroscopy (XAFS),[16] it is observed that in marine diatoms with low zinc concentration cadmium performs the function carried out by zinc in other anhydrases.[17-18] Cadmium can be used to block calcium channels in chicken neurons. [19]

CADMIUM INDUCED TOXICITY

Cadmium is considered as a toxic metal and is hazardous to both human and wild life. It acts as a mitogen and promotes cancer in a number of tissues. It also stimulates cell proliferation, inhibit DNA repair and inhibit apoptosis. On the one hand it induces the cell death which leads to tissue damage in kidney. In cell culture systems, cadmium at low concentration cause apoptosis and with increase in concentration necrosis become evident. Cadmium also affects the renal function when exposed to the environment. [20] When the cadmium acetate is administered to the rat in varying concentration, there is interaction between the Cd^{2+} and the enzyme molecule which inhibits the activity of superoxide dismutase (SOD) to increase the lipid peroxidation in liver and kidney. It is indicated that Cd-induced elevation in lipid peroxidation is not only due to the inhibition of the activity of the superoxide dismutase (SOD) but also due to the direct action of Cd^{2+} on the peroxidation reaction. [21]The role of cadmium in induction of atherosclerosis in rabbits. Effect of the cadmium has determined in various tissues of the rabbits for a period of 6 months on histopathological changes and biochemical alterations of profiles. Before and at the end of cadmium treatment, no ECG changes were observed. Histopathological studies of the coronary artery revealed that the atherosclerotic changes occur due to the toxic effect of the cadmium. It leads to total increase of lipids, cholesterol, free fatty acids and phospholipids , Triglyceride in heart and kidney and decrease in serum and liver. [22] Cadmium-induced hepatic and renal injury in chronically exposed rats: likely role of hepatic cadmium-metallothionein in nephrotoxicity. When cadmium is injected in rat, cadmium level in liver and kidney

TABLE 1: Properties and applications of cadmium

Physical properties	Chemical properties	Geochemical properties	Applications
• silvery-white, soft, ductile chemical metal [7]	• atomic number-48 • atomic weight-112.40 • has 8 isotopes- 106Cd,1.22%b; 108Cd, 0.88%o; "0Cd, 12.39%o; 111Cd,12.75%; 112Cd,24.07%o; 118Cd,12.26%o; 1"4Cd,28.86%o; 116Cd, 7.58.o	• Strong chalcophilic Element.	• Nickel cadmium (NiCd) batteries.
• Insoluble in water.[8]	• Transition metal in Group IIb of the periodic table	• Abundance of cadmium in earth crust is 0.15-0.2ppm	• cadmium pigments
• Inflammable[8]	• Form more stable compound due to the presence of 14 additional electrons in fourth orbital.	• Low concentration in igneous rocks. • Ratio of Zn/Cd varies in all igneous rocks.	• cadmium coatings
• Density-8.645	• Oxidation state is +2 but few compounds show +1 oxidation state.[9]	• Cadmium concentration occurrence is high in oceanic, shale's, and lacustrine sediments, oceanic manganese and phosphorites nodules	• stabilizers in polyvinyl chloride plastics
• Vapor pressure at 400°C is 1.4mm and at 500°C is 16 mm. • Form CdO in air as vapor is very reactive.	• Have greater tendency to form covalent bonds with sulphur.		• used in rods in nuclear reactors to control atomic fission
• Melting point-321.069°C,609.924°F,594.219K	• With cyanine's and ammines, form soluble complexes.		• Used in electroplating and prevents corrosion.
• Boiling point-767°C,1413°F,1040K	• For fourfold coordination, cadmium ionic radius is 0.88A°		• Used in alloys
• CAS number-7440-43-9	• For six fold coordination, cadmium ionic radius is 1.03A°		• Used in herbal preparation. • Used in fungicides, phosphors, ceramics, and others.

increases linearly for the first few weeks but

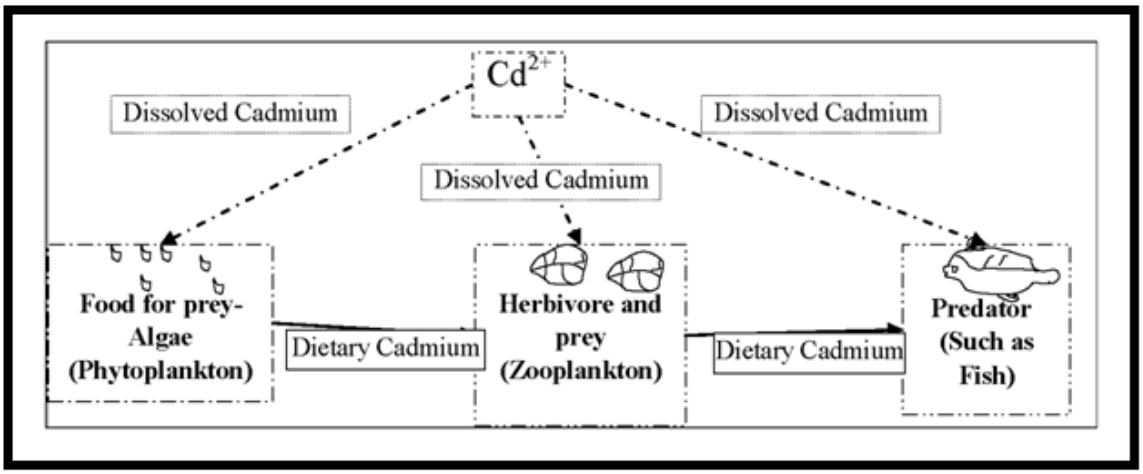

Figure 2: Dietary cadmium exposures at tropical levels. Adapted from Toxicity of Dietary Cadmium to Aquatic Organisms Part 1)

thereafter content of cadmium in kidney remain constant and hepatic concentrations of cadmium decreased. During the first 12 weeks of cadmium treatment, metallothionein (MT) increases linearly in

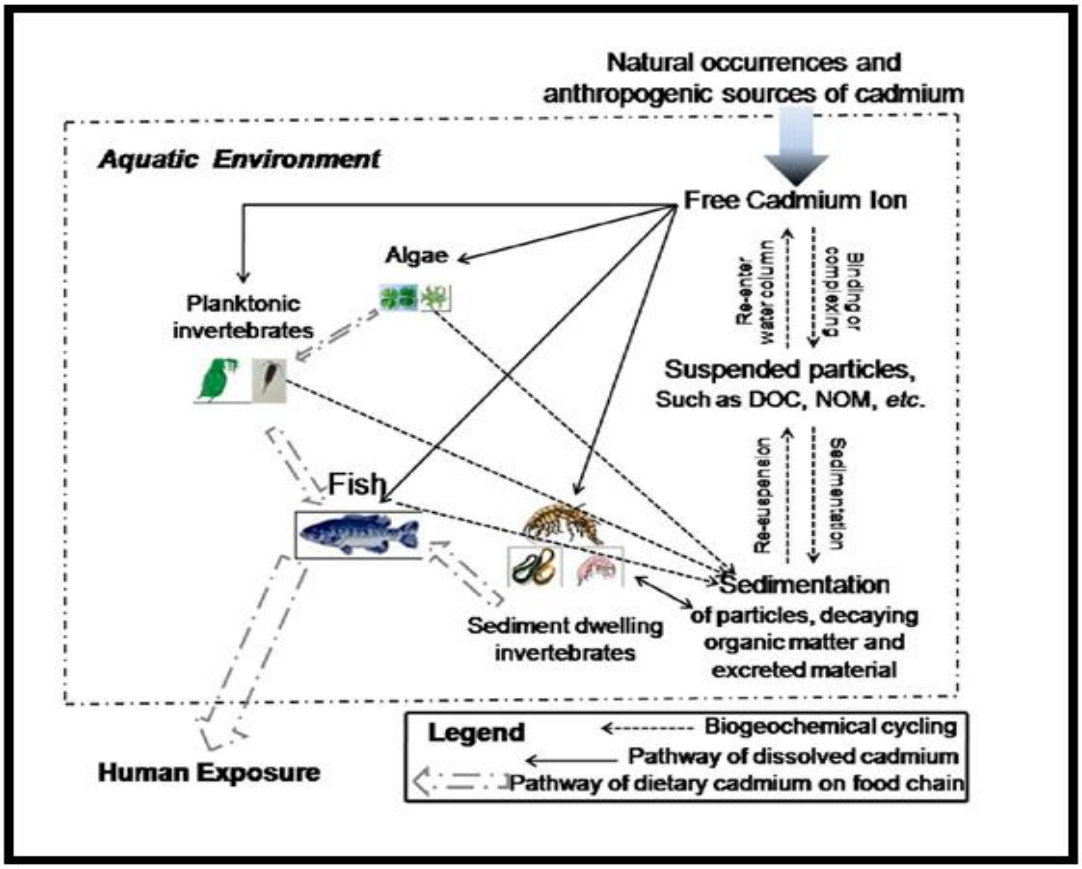

Figure 3: Exposure of cadmium at various levels (Adapted from Toxicity of Waterborne Cadmium to Saltwater Aquatic Organisms Part 1)

liver and kidney and thereafter rose slightly. Activity of alanine and aspartate aminotransferase enzyme in plasma increases sharply after 10 to 12 weeks of dosing. Hepatic damage, renal injury and urine outflow increases after cadmium exposure began. This indicates that Cd-induced hepatic injury via release of Cd-MT plays an important role in nephrotoxicity by affecting the liver. [23]

cadmium exposures may lead to genomic instability and tumor genesis by inhibiting DNA repairs at various levels [31].

Infertility: Sperm concentration in semen is very important factor in reproduction cadmium exposures decreases sperm count in semen. [32] Cadmium enters the testicular cells in ion

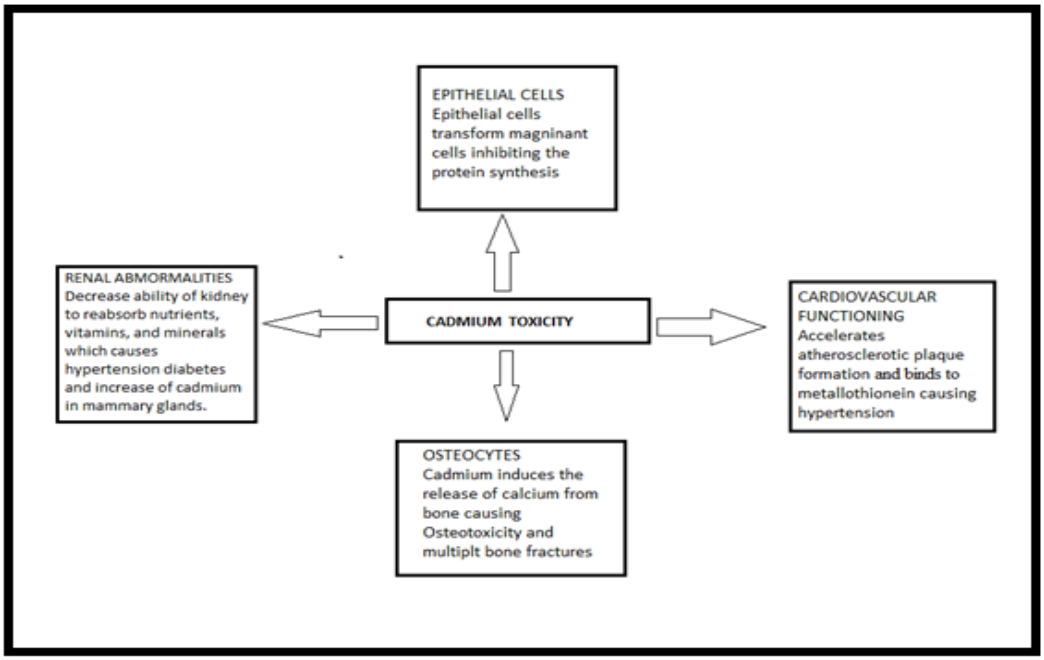

Figure 4: Health effect of cadmium in humans

CADMIUM INDUCED HUMAN DISORDERS

According to International Agency for Research on Cancer (IARC) [24] Cadmium is considered one of the hazardous metals to human health [25]. Cadmium acute exposures may lead to inflammation followed by cough, dryness and irritation of the nose and throat, headache, dizziness, chest pain, pneumonitis, and pulmonary edema [26]

Carcinogenesis: Long-term exposures to cadmium may turn carcinogen in humans, where normal epithelial cells transform to malignant cells inhibiting the biosynthesis of DNA, RNA, and proteins [27].Cadmium inhibits binding of xeroderma pigmentosum group A (XPA) to DNA which recognizes DNA damages. Cadmium also reduces the binding efficiency of tumor suppressor p53 to DNA [28-29] that is responsible for base excision repair of UV light exposure in DNA [30].Cadmium inhibits an enzyme Human 8-oxo-dGTPase that protects against the incorporation of 8-oxo-dGTP into DNA. Thus

transporter chains and voltage-dependent calcium channels. Sertoli and testicular germ cells contains expression of sperm-head voltage-dependent calcium channeling [33-34]where with elevated testicular cadmium levels[35-36] there is a deletion in exons 7 and/or 8 which cadmium levels decreasing the sperm count.[36]

Cardiovascular abnormality: Cadmium found in tobacco, air and food by in-vitro exposures effects endothelial dysfunctions and in-vivo accelerates atherosclerotic plaque formation (artery wall thickening) causing cardiovascular diseases. [37] Cadmium interferes with anti-oxidative stress by binding to metallothionein [38] (protein that regulates zinc homeostasis and free radical scavenger [39-40] and increase reactive oxygen species formation. [41]

Osteotoxicity: There are many Cadmium-induced hormone disturbances like affect in vitamin D metabolic pathways [42] that is cadmium-related

bone changes due to release of calcium from bone occurring in the absence of circulating parathyroid hormone, and calcitonin [43]. In estrogen hormone pathways, cadmium concentrations activate the estrogen receptor (ER) and blocks it's binding to estrogen indirectly affect the skeleton causing Osteotoxicity and multiple bone fractures. [44]

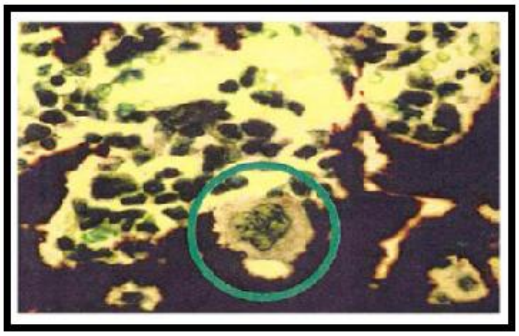

Figure 5: Multinucleated osteoclast-like cell associated with osteopetrotic bone of a 45-days old mouse (Adapted from Toxicology and applied pharmacology 2009)

Renal disorder: Exposures to high-dose cadmium causes Itai-itai disease characterized by severely impaired tubular and glomerular function [45]. Long-term exposure of low-dose cadmium leads to tubular impairment include zinc and copper bound to the metal binding protein metallothionein (MT), glucose, amino acids, phosphate, calcium, β2-MG, and retinol-binding protein (RBP) losses[46]. Kidney reabsorptive capacity for nutrients, vitamins, and minerals decreases. There is abnormal urination with low-molecular-weight proteins, calcium, amino acid, phosphate and glucose similar in Fanconi's syndrome, a genetic disorder of renal tubular transport develops kidney damage, and blood cadmium as the indicator. [47]

Other disorders: Urinary cadmium has various effects on other tissues such as lungs, periodontal tissues, hypertension, diabetes and mammary glands. There is a reduction of forced expiration (reflection of lung function) with increased urinary cadmium in smoking individuals [48]. Urinary cadmium with creatinine level is estimated to be to more in periodontal disease affected individuals than the unaffected individuals [49]. It was studied that the cadmium blood pressure association disorder was greatest among nonsmokers, intermediate among former smokers, and small or absent among current smokers. [50] Increased urinary cadmium level increases the risk of prediabetes and diabetes. The estimated risk for abnormal individuals fasting glucose and diabetes were almost the same. [51] Cadmium level in breast milk with elemental composition of milk, including manganese, iron, and calcium levels had changes [52], due to mammary gland metal transport chain [53].

CONCLUSION

Cadmium is heavy metal hazardous to all living organisms here its effect on various organisms were studied. Cadmium involves different machineries to induce its harmful effect on many biological activities in humans, animals and various other organisms. In humans cadmium adverse effect is not only restricted to kidney and bone but it includes almost every organ and tissue where it accumulates which argues needs for public health measures aimed at reducing exposure. There are many methods by which this heavy metal can be suppressed in its activities forming the future prospective for reduced metal toxicity involving cadmium. The preventive measures in high-risk patients must be practiced and it is important to make population-based preventive strategies, such as promoting public and private smoke-free environments, reviewing food safety policies maintaining cadmium safety standards, and limiting cadmium industrial releases into the environment helping to avoid cadmium toxicity.

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