Some Hazardous Effects of Cadmium on Human Health: A Short Review

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Abstract
Heavy metals can be emitted into the environment by both natural and anthropogenic causes. The anthropogenic sources of emission are the various industrial point sources including former and present mining sites, foundries and smelters, combustion byproducts and traffics [1](UNEP/GPA, 2004). The objective of this paper is to review available information on possible toxicities of cadmium on human health [3]. Cadmium is a hazardous substance having global concern as it is a potent environmental pollutant as well as it causes enduring health hazards. Cadmium (Cd) is a toxic heavy metal which can be accumulated in human body and environment long term. Cadmium (Cd) has been ranked at the sixth of the toxic substances for significant human health by U.S poison and disease registry. Cadmium (Cd) exposure occurs mainly in Japan and China. In other countries the intensity and duration of cadmium exposure and the injury occurring in populations are in a relatively low level, with related little literature reported [4].

Accumulation of cadmium is a major ecological concern, especially because of its ability to accumulate very quickly. It is responsible for increased hypertension, emphysema, kidney, tubular damage impaired liver function and cancer [12]. The environment in which we claim to “live” in has become a huge reservoir of toxic metals. Human health is under constant risk of deterioration due to increasing chronic exposure of such metals that adversely affect the quality of life of people. Exposure to cadmium has long been recognized as a health hazard, both in industry and in general populations with high exposure. However, cadmium is toxic at very low exposure levels and has acute and chronic effects on health and environment which is thus the cause of great concern. The parts of body that are potentially affected from exposures to cadmium mainly involve the kidney, liver, lung, heart and bone.

The purpose of this paper is to review relevant literature regarding the threat posed by potential cadmium contamination its toxicity and effect on water bodies [5]. Cadmium (Cd) is toxic to aquatic organisms at low concentrations. Clean water act fresh water criteria- criteria continuous concentration: 0.25 micro grams per liter the highest concentration to which on aquatic community can be exposed briefly without resulting in an unacceptable effect. Criteria maximum concentration: 2.0 micro grams per liter (an estimate of the highest concentration to which an aquatic community can be exposed indefinitely without resulting in an unacceptable effect).[6].

Rivers and lake shores are the areas primarily affected by diluted cadmium waste from industrial facilities in big cities. The cadmium related contamination of the aquatic habitat has greatly increased in the last decades, resulting in an increase of cadmium deposits in tissues of aquatic organisms in all food chain systems. It is important to note that cadmium is a highly toxic element for all mammals and fish [8].

1. Introduction
Heavy metals which adversely affect human health can be emitted into the environment by both natural and anthropogenic causes. The anthropogenic sources of emission are the various industrial point sources including former and present mining sites, foundries and smelters, combustion byproducts and traffics [1](UNEP/GPA, 2004). The objective of this paper is to review available information on possible toxicities of cadmium on human health [3]. Cadmium is a hazardous substance having global concern as it is a potent environmental pollutant as well as it causes enduring health hazards. Cadmium (Cd) is a toxic heavy metal which can be accumulated in human body and environment long term. Cadmium (Cd) has been ranked at the sixth of the toxic substances for significant human health by U.S poison and disease registry. Cadmium (Cd) exposure occurs mainly in Japan and China. In other countries the intensity and duration of cadmium exposure and the injury occurring in populations are in a relatively low level, with related little literature reported [4].

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of research journals, reports of international organizations and newspaper reports.

2. Cadmium Background its Behavior and Toxicity

Cadmium is released as a byproduct of zinc (and occasionally lead) refining. Cadmium (Cd) exposure is through Nickel-cadmium exposure batteries and artists paints [11]. Many literatures reported that impact of Cadmium (Cd) on human reproductive system [13]. Falcon reported that pregnant women exposed to environmental cadmium might have an adverse effect in parental period that is fetal growth retardation, low birth weight, birth deformities and premature. Nishio et.al. [14] [15] reported that mothers with higher urinary Cadmium (Cd) concentration would be company with higher levels of Cd and lower calcium concentration in their breast milk. Cd exposure may be a possible cause of mate infertility. A significant negative correlation was observed between serum Cadmium (Cd) level and all examined biophysical semen characteristics except serum volume [16]. Chronic exposure to Cadmium (Cd) could increase popular mortality and shorter life expectancy.

The research data on nonspecific hazards of environmental Cadmium (Cd) pollution was not too much, because the health effects of population were characterized by target organ damage in the early stage of chronic Cadmium (Cd) poisoning, which has lead main studies focusing on effects of Renal injury, a special effects in a long time, yet few investigations on the change of popular mortality and morbidity of environmental Cadmium (Cd) exposure [17]. Cadmium (Cd) is a metal with no known beneficial properties that support life there is no evidence that it is either biological necessary or beneficial[18]. At low concentrations it is toxic to all life, including plants, fish, birds, mammals (including humans) and microorganisms. In one study that used comparative acute toxicity testing of 63 heavy metals, cadmium was the most toxic metal. In its elemental form cadmium does not break down but it can change form into different species and compound. Source of cadmium are coal and other fossil fuels, and scale. It can also be released to the atmosphere during volcanic eruption. It can enter atmosphere during volcanic eruption. It can enter atmosphere during the burning of coal and household wastes, and can enter water around a sulfide mine as a byproduct of acid mine drainage [6]. Most Cadmium (Cd) is released from human activities such as mining and smelting of sulfide ores, fuel combustion and application of phosphate fertilizers or sewage sludge [19].

Cadmium is a silver white, blue tinged, lustrous metal that melts at 321 degrees and boils at 765 degree centigrade. This divalent element has atomic weight of 112.4 and an atomic number of 48. The availability of cadmium to living organisms from their immediate physical and chemical environs depends on numerous factors including adsorption and desorption rates of cadmium from terrigenous materials, pH, chemical speciation, and many other modifiers [20].

3. Sources of Cadmium

1. Cadmium is produced mainly as a byproduct from mining, smelting and refining sulfide ores of zinc, and to a lesser degree, lead and copper. Cadmium minerals do not occur in concentrations and qualities sufficient to justify mining them in their own right. Small amounts of cadmium, about 10-15% of consumption, are produced from secondary sources, mainly from dust generated by recycling of iron and steel scrap [21].

2. The general trend in the global cadmium consumption over last two decades has been a steep increase in the use of cadmium for batteries[22]

<table>
<thead>
<tr>
<th>Economic sector</th>
<th>Air Emission (Tones)</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stationary fossil fuel combustion</td>
<td>691</td>
<td>23</td>
</tr>
<tr>
<td>Non-ferrous metal production</td>
<td>2,171</td>
<td>73</td>
</tr>
<tr>
<td>Iron and Steel production</td>
<td>64</td>
<td>2.0</td>
</tr>
<tr>
<td>Cement production</td>
<td>17</td>
<td>0.6</td>
</tr>
<tr>
<td>Waste disposal (incineration)</td>
<td>40</td>
<td>1.3</td>
</tr>
<tr>
<td>Total</td>
<td>2,983</td>
<td></td>
</tr>
</tbody>
</table>

3. Natural activities, such as volcanic activity (both on land and in the deep sea). Weathering, erosion and river transport [23].

4. Human activities such as Tobacco smoking, mining, smelting and refining of non ferrous metals. Fossil fuel combustion, incineration of municipal waste (especially cadmium containing batteries and plastics), manufacturing of phosphate fertilizers and recycling of cadmium plated steel scrap and electric and electronic waste. The metal content in the tobacco comes from the soil, which is being taken up by tobacco plants. Cadmium is also used in cigarette paper to make the paper burn slower. These metals are either released into the air by tobacco smoke or are retained in the cigarette ash. It has been reported that the cigarette tobacco contains about 0.5 to 2.0μg of cadmium and about 10% of the cadmium content is inhaled when cigarette is smoked[24] (WHO 1992) and the non-smoker may passively inhale significant amount of cadmium as well. Workers exposed to cadmium-containing fumes have been reported to develop acute respiratory distress syndromes (ARDS). Thus, smoking tobacco is an important source of exposure, and the daily intake may exceed that from food in the case of heavy smokers [25].

5. Recombination of historic sources such as the contamination of water sources by drainage water from metal mines.

6. The majority of cadmium present in the atmosphere is the result of human activities, especially smelting of non-ferrous metal ores.

7. Cadmium contained in the soil and water can be
taken up by certain crops and aquatic organisms and accumulate in food chain. Food constitutes the main environmental source of cadmium for non smokers. Highest cadmium levels are found in the kidney and liver of mammals feed with cadmium rich diets and certain species of oysters, scallops, mussels and crustaceans.

8. Impurities in the Zinc of galvanized pipes and solders in fittings, water heaters, water coolers and taps can sometimes lead to increase of cadmium levels in drinking water. Food is the most important source of cadmium exposure in the general non-smoking population in most countries.

9. The tobacco plant naturally accumulates relatively high concentration of cadmium in its leaves. Thus, smoking tobacco is an important source of exposure, and the daily intake may exceed that from food in the case of heavy smokers. From a study by the Centre for Control of Chronic Diseases in Bangladesh (CCCDDB) conducted in three rural settings of the country, it was found that tobacco smoking was higher among the lower socio-economic groups in both rural and urban areas in Bangladesh which suggests that the risk of exposure to cadmium is greater in low-income groups of people. The study also revealed that men from low-income groups not only smoke more frequently, but also they consume more cigarettes compared to men from high-income groups. Therefore, it indicates that men among the low-income groups are at higher risk of developing cadmium body burden [28-29].

10. The major source of occupational cadmium exposure are melting and refining of zinc, lead and copper ores, electroplating, manufacturing of cadmium alloys and of pigments and plastic stabilizers, production of Ni-Cd batteries and welding[26-27].

Table 2 Cadmium in the Products in the US, 2001, Source N Kolika and Benedict, 2004 [51]

<table>
<thead>
<tr>
<th>Cadmium Products</th>
<th>Abundance of Products (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nickle-Cadmium batteries</td>
<td>75.0%</td>
</tr>
<tr>
<td>Pigments</td>
<td>12.0%</td>
</tr>
<tr>
<td>Plating</td>
<td>8.0%</td>
</tr>
<tr>
<td>Stabilizers</td>
<td>40.0%</td>
</tr>
<tr>
<td>Others</td>
<td>1.0%</td>
</tr>
</tbody>
</table>

4. Cadmium Intake via Food Chain
Dissolved cadmium is a poison, which enters the food chain in different ways; plants absorb cadmium ions from water in the ground. The cadmium ions may have reached surface water in the ground. The cadmium ions may have reached surface water through a generally increased leaching in an acid environment. On arable land the presence of cadmium may also be a result of leaching of phosphate fertilizers and digested sludge. Cadmium absorbed in crops, example rice and wheat, reaches people and animals [30]. Soil contaminated by heavy metals from either aerial depositions or irrigation are likely to induce a corresponding contamination in harvested crops [16]. Animals accumulate cadmium in their bodies (“body burden”) can be eaten up by others, and so on, such that cadmium will both accumulate and bio magnify in the food chain[5]. *Fish can accumulate cadmium from the water and eating foods contained with cadmium (contaminated food chain). It is important to note that bioaccumulation occurs when a substance cannot be easily metabolized or excreted [32]. Leafy vegetables such as lettuce, spinach, potatoes and grain foods are also found to have a higher concentration of cadmium. Moreover, the cadmium entering the aquatic ecosystem may not directly impart toxicity to the organisms being in low concentrations; however it can be accumulated in aquatic organisms through bio-concentration, bioaccumulation and the food chain process, and eventually threaten human health because of consumption of fishes and other organism with bio-accumulated concentration of metal species [33]. Some have estimated that 98% of the ingested cadmium comes from terrestrial foods such as rice, vegetables while only 1% comes from aquatic foods such as fish and shellfish and 1% arises from cadmium in drinking water.

Table 3 Global Release of Cadmium to Land [52-53]

<table>
<thead>
<tr>
<th>Source Category</th>
<th>% Discharge to land</th>
</tr>
</thead>
<tbody>
<tr>
<td>Agriculture and food waste</td>
<td>6</td>
</tr>
<tr>
<td>Animal waste and manure</td>
<td>3</td>
</tr>
<tr>
<td>Logging and other wood wastes</td>
<td>4</td>
</tr>
<tr>
<td>Urban refuse</td>
<td>15</td>
</tr>
<tr>
<td>Municipal sewage sludge</td>
<td>0.7</td>
</tr>
<tr>
<td>Solid waste, Metal manufacturing</td>
<td>0.1</td>
</tr>
<tr>
<td>Coal fly ash, Bottom fly ash</td>
<td>26</td>
</tr>
<tr>
<td>Fertilizer</td>
<td>0.5</td>
</tr>
<tr>
<td>Peat( agriculture and fuel use)</td>
<td>0.2</td>
</tr>
<tr>
<td>Wastages of commercial products</td>
<td>4</td>
</tr>
<tr>
<td>Atmosphere fall out</td>
<td>19</td>
</tr>
</tbody>
</table>

5. Target Organ Damage
Cadmium (Cd) is toxic at extremely low levels. In humans long term exposure results in renal dysfunction, characterized by Tubular proteinuria. Severe exposure may result in pulmonary edema and death. Pulmonary effects (emphysema, bronchiolitis and alnoliitis) and renal effects may occur following sub chronic inhalation exposure to Cd
and its compounds. [34] The researches on human specific injury caused by cadmium exposure have focused on injury bio monitoring of bones and urogenital systems. Cadmium cause bone demineralization, either through direct bone damage or indirectly as a result of renal dysfunction [35]. Result of study indicated that excretion of urinary vitamin D-binding protein (DBP, which binds, transports and activates vitamin D, plays role in cadmium homeostasis and Bone turnover) in urine may be linked to renal tubular dysfunction and possibly bone lesions in the inhabitants of cadmium polluted areas .Cadmium indicates the disorders of normal osteoblasts and bone metabolism through disruption calcium messenger systems, led to osteomalacia, increased the dissolution of calcium, decreased BMD, and caused osteoporosis[36].

5.1 Renal Damage
Cadmium is a major toxic metal, well known for its occupational health risks. It is also of increasing concern as a pollutant of the general environment with implications for public health. Cadmium accumulates in the human body (half-life 15–20 years) and may particularly affect the kidney, which is considered to be the critical target organ in cases of chronic exposure [37]. Cadmium thus accumulates in renal tubular cells, until the synthetic capacity for metallothionein is exceeded. When the concentration of cadmium in the kidney reaches a critical concentration, renal dysfunction is likely to occur. Most of the absorbed cadmium is retained; some excretion of cadmium occurs through the urine, and urinary excretion increases with renal damage (ATSDR 1999). Signs of renal dysfunction are the first indication of chronic cadmium toxicity. Cadmium is accumulated mainly in the liver and kidneys, and, in general, the highest concentrations are found in the renal cortex (14). The cadmium concentration in the kidneys increases with age up to about 50-60 years, after which it decreases.

5.2 Tubular Damage
Friberg[39] was the first to observe proteinuria among cadmium-exposed workers .Butler & Flynn[40] , in 1958, revealed that the proteinuria was of a tubular type. In severe cases of cadmium-induced nephrotoxicity, several signs of tubular damage are evident, for example renal glucosuria, aminoaciduria, hyper phosphaturia, hyper calcuria, polyuria due to decreased concentration capacity, and a deteriorated. Ability to handle an acid (ammonium chloride) load. Cadmium-exposed workers sometimes show slightly increased urinary excretion of transferring, albumin, and other high molecular-weight plasma proteins. The interpretation of this occurrence has been debated.

5.3 Neurological Effect
Cadmium is known to alter neurotransmitter levels in the brain, and may inhibit calcium entry into neurons (ATSDR 1999; Nation et al. 1989). Elevated cadmium exposure may also be associated with learning disability as well as special education for children [28].

5.4 Bone
Osteopenia may be caused by both osteomalacia and osteoporosis, the latter being by far the most common. Osteomalacia is characterized by an abnormally high ratio of inadequately mineralized bone matrix to mineralized bone. The most common causes of osteomalacia are impaired vitamin D metabolism and loss of renal tubular phosphate. The most common forms of generalized osteoporosis is senile osteoporosis, which is a gradual loss of skeletal mass with advancing age [43]. Such factors may therefore further increase a woman's risk of developing postmenopausal osteoporosis. Postmenopausal osteoporosis is more common in white and Asian women than in women of other races [44].

5.5 Carcinogenic effect
In its latest evaluation of the carcinogenic risk of cadmium Exposure, IARC concluded that there was sufficient Evidence to classify cadmium as a human carcinogen, and the overall evaluation was that cadmium and Cadmium compounds are carcinogenic to man. The estrogen receptor independent of estradiol[45]. The International Agency for Research on Cancer (IARC) in their most recent evaluation (IARC 2012) reconfirmed that there is sufficient evidence of Cadmium being a human carcinogen, mainly based on lung cancer in studies of workers. Studies of Cadmium exposure and cancer in the general population have found positive associations. The National Toxicology Program (NTP 2001):[46] has classified cadmium and cadmium compounds as human carcinogens, based on sufficient evidence of carcinogenicity from studies in humans. When modeling the dose-response relationship using restricted cubic spines, it was found that increased risks with increasing urinary cadmium (U-Cd) concentrations for overall, smoking-related, lung and pancreatic cancer mortality with no statistically significant departures from linearity.

5.6 Mammary gland
Pregnant women exposed to environment containing Cadmium have adverse effect in parental period like retardation in the fetal growth, low birth weight, birth deformities and premature. Mothers with high urinary cadmium concentration would be company with higher levels of cadmium and lower calcium concentration in there breast milk. Gundacker et al. (2007)[14] showed that breast milk samples of Austrian subjects contained, on average, a cadmium content of 0.086 pg/L and that breast milk cadmium content was lower among nonsmokers who took vitamins and mineral supplements (p < 0.05). In a study by Kippler et al. (2008) [15], the median cadmium level in breast milk from Bangladeshi subjects was 1.6-fold higher than was the level from Austrian subjects. The investigators observed a correlation between cadmium and the elemental composition of milk, including manganese, iron, and calcium levels. Their findings suggest a potential influence of cadmium on mammary gland metal transport and secretion.

5.7 Respiratory Effect
Long-term inhalation exposure to cadmium and cadmium compounds may also lead to decrease in lung function and emphysema, which may be manifested by an increased mortality in exposed populations. Surveys of workforces exposed to cadmium published in the 1950s already indicated that long-term occupational exposure to cadmium can cause emphysema [47]. Several mortality studies in cadmium workers in the United Kingdom found that those who have experienced high exposure had an increased rate of mortality from bronchitis. In copper-cadmium alloy producers, a marked excess of deaths from chronic non-
malignant respiratory disease has also been found related to cadmium exposure. Cadmium found in dye and pigments was found to cause lung cancer [48].

6 Conclusions and Recommendations in Order to Avoid the Health Hazards of Cadmium

1. Restriction on the use of Cadmium in the packaging material.
2. Tax on batteries and accumulator containing more than 0.025% cadmium by weight.
3. Legal arrangements on labeling and recycling of Ni-Cd batteries exist in several states.
4. Rise awareness on the importance of minimizing waste discharge of cadmium on global scale.
5. Improve working condition in the non-ferrous smelting industry and dissemination of information on the proper use of fertilizers in order to reduce cadmium exposure.
6. Ban use of cadmium and cadmium compounds as colorants in plastic and paints and also the stabilizers in plastics.
7. Limit the use of cadmium in electrical and electronic equipments.
8. Limit on the content of cadmium in fertilizers.
10. Monitor dumping of waste to prevent deposition in soil.

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