

Toxic Effects of Heavy Metals on the Human Organism

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Summary

The toxic effects of these metals, even though they do not have any biological role, remain present in some or the other form harmful for the human body and its proper functioning. They sometimes act as a pseudo element of the body while at certain times they may even interfere with metabolic processes. Few metals, such as aluminium, can be removed through elimination activities, while some metals get accumulated in the body and food chain, exhibiting a chronic nature. Various public health measures have been undertaken to control, prevent and treat metal toxicity occurring at various levels, such as occupational exposure, accidents and environmental factors. Metal toxicity depends upon the absorbed dose, the route of exposure and duration of exposure, i.e. acute or chronic. This can lead to various disorders and can also result in excessive damage due to oxidative stress induced by free radical formation. This review gives details about some heavy metals and their toxicity mechanisms, along with their health effects.

Key words: heavy metals, metal toxicity, oxidative stress, free radicals.

Introduction

The main objective of this review is to provide insight into the sources of heavy metals and their harmful effects on the environment and living organisms. Heavy metals are generally referred to as those metals which possess a specific density of more than 5 g/cm³ and adversely affect the environment and living organisms (Järup, 2003). These metals are quintessential to maintain various biochemical and physiological functions in living organisms when in very low concentrations, however they become noxious when they exceed certain threshold concentrations. Although it is acknowledged that heavy metals have many adverse health effects and last for a long period of time, heavy metal exposure continues and is increasing in many parts of the world. Heavy metals are significant environmental pollutants and their toxicity is a problem of increasing significance for ecological, evolutionary, nutritional and environmental reasons (Jaishankar *et al.*, 2013; Nagajyoti *et al.*, 2010). The most commonly found heavy metals in waste water include arsenic, cadmium, chromium, copper, lead, nickel, and zinc, all of which cause risks for human health and the environment (Lambert *et al.*, 2000). Heavy metals enter the surroundings by natural means and through human activities. Various sources of heavy metals include soil erosion, natural weathering of the earth's crust, mining, industrial effluents, urban runoff, sewage discharge, insect or disease control agents applied to crops, and many others.

Arsenic

Arsenic is one of the most important heavy metals causing disquiet from both ecological and individual health standpoints. It has a semimetallic property, is prominently toxic and carcinogenic, and is extensively available in the form of oxides or sulfides or as a salt of iron, sodium, calcium,

copper, *etc.* (Singh *et al.*, 2007). Arsenic is the twentieth most abundant element on earth and its inorganic forms such as arsenite and arsenate compounds are lethal to the environment and living creatures. Humans may encounter arsenic by natural means, industrial source, or from unintended sources. Drinking water may get contaminated by use of arsenical pesticides, natural mineral deposits or inappropriate disposal of arsenical chemicals. Deliberate consumption of arsenic in case of suicidal attempts or accidental consumption by children may also result in cases of acute poisoning (Mazumder, 2008; Saha *et al.*, 1999). Arsenic is a protoplasmic poison since it affects primarily the sulfhydryl group of cells causing malfunctioning of cell respiration, cell enzymes and mitosis (Gordon & Quastel, 1948).

Lead

Lead is a highly toxic metal whose widespread use has caused extensive environmental contamination and health problems in many parts of the world. It begins to tarnish on contact with air, thereby forming a complex mixture of compounds, depending on the given conditions. The sources of lead exposure include mainly industrial processes, food and smoking, drinking water and domestic sources. The sources of lead were gasoline and house paint, which has been extended to lead bullets, plumbing pipes, pewter pitchers, storage batteries, toys and faucets (Thürmer *et al.*, 2002).. Some is taken up by plants, fixation to soil and flow into water bodies, hence human exposure of lead in the general population is either due to food or drinking water. Lead is an extremely toxic heavy metal that disturbs various plant physiological processes and unlike other metals, such as zinc, copper and manganese, it does not play any biological functions.

A plant with high lead concentration fastens the production of reactive oxygen species (ROS), causing lipid membrane damage that ultimately leads to damage of chlorophyll and photosynthetic processes and suppresses the overall growth of the plant (Najeeb *et al.*, 2014). Some research revealed that lead is capable of inhibiting the growth of tea plant by reducing biomass and debases the tea quality by changing the quality of its components (Yongsheng *et al.*, 2011).

Mercury

The metallic mercury is a naturally occurring metal which is a shiny silver-white, odorless liquid and becomes colorless and odorless gas when heated. Mercury is very toxic and exceedingly bioaccumulative. Its presence adversely affects the marine environment and hence many studies are directed towards the distribution of mercury in water environment. Major sources of mercury pollution include anthropogenic activities such as agriculture, municipal wastewater discharges, mining, incineration, and discharges of industrial wastewater. Mercury exists mainly in three forms: metallic elements, inorganic salts and organic compounds, each of which possesses different toxicity and bioavailability. These forms of mercury are present widely in water resources such as lakes, rivers and oceans where they are taken up by the microorganisms and get transformed into methyl mercury within the microorganism, eventually undergoing biomagnification causing significant disturbance to aquatic lives. Consumption of this contaminated aquatic animal is the major route of human exposure to methyl mercury. Mercury is extensively used in thermometers, barometers, pyrometers, hydrometers, mercury arc lamps, fluorescent lamps and as a catalyst. It is also being used in pulp and paper industries, as a component of batteries and in dental preparations such as amalgams.

Cadmium

Cadmium is the seventh most toxic heavy metal as per ATSDR ranking. It is a by-product of zinc production which humans or animals may get exposed to at work or in the environment. Once this metal gets absorbed by humans, it will accumulate inside the body throughout life. This metal was first used in World War I as a substitute for tin and in paint industries as a pigment. In today's scenario, it is also being used in rechargeable batteries, for special alloys production and also present in tobacco smoke. About three-fourths of cadmium is used in alkaline batteries as an electrode component, the remaining part is used in coatings, pigments and platings and as a plastic stabilizer. Humans may get exposed to this metal primarily by inhalation and ingestion and can suffer from acute and chronic intoxications. Cadmium distributed in the environment will remain in soils and sediments for several decades. Plants gradually take up these metals which get accumulated in them and concentrate along the food chain, reaching ultimately the human body. In the US, more than 500,000

workers get exposed to toxic cadmium each year as per The Agency for Toxic Substances and Disease Registry (Bernard, 2008; Mutlu *et al.*, 2012). Researches have shown that in China the total area polluted by cadmium is more than 11,000 hectares and its annual amount of industrial waste of cadmium discharged into the environment is assessed to be more than 680 tons. In Japan and China, environmental cadmium exposure is comparatively higher than in any other country (Han *et al.*, 2009). Cadmium is predominantly found in fruits and vegetables due to its high rate of soil-to-plant transfer (Satarug *et al.*, 2011). Cadmium is a highly toxic nonessential heavy metal that is well recognized for its adverse influence on the enzymatic systems of cells, oxidative stress and for inducing nutritional deficiency in plants (Irfan *et al.*, 2013).

Aluminum

Aluminum is the third most abundant element found in the earth's crust (Gupta *et al.*, 2013). Aluminum occurs naturally in the air, water and soil. Mining and processing of aluminum elevates its level in the environment. Recent investigations on environmental toxicology revealed that aluminum may present a major threat for humans, animals and plants in causing many diseases (Barabasz *et al.*, 2002). Many factors, including pH of water and organic matter content, greatly influence the toxicity of aluminum. A pH of surface layer of soil below 5 (pH<5) can lead to soil acidity which is a major concern around the world that affects crop production. Due to aluminum toxicity, the crop production was constrained to 67% of the total acid soil area in the world. Aluminum is one of the most commonly found elements in the earth crust. Due to acid soils (pH<5), silicon gets leached leaving behind aluminum in solid form known as aluminum ox hydroxides, such as gibbsite and boehmite. These unstable forms of aluminum discharge phytotoxic Al^{3+} well-known as $Al(OH)^{63+}$ in soil (Ermias Abate *et al.*, 2013). The interaction of Al^{3+} with apoplastic, plasma membrane, and symplastic targets leads to toxicity and distracts the physical and cellular processes in plants. The common manifestations are root growth inhibition, cellular modification in leaves, small and dark green leaves, yellowing and death of leaves, chlorosis, purpling and foliar necrosis (Gupta *et al.*, 2013). Enzymes such as hexokinase, phosphodiesterase, alkaline phosphatase and phosphoxidase are inhibited by aluminum since it has a greater affinity to DNA and RNA. Metabolic pathways in the living organism involving calcium, phosphorous, fluorine and iron metabolism are affected by aluminum. Aluminum has been found to be very harmful to nervous, osseous and hemopoietic cells.

Iron

Iron is the second most abundant metal on the earth's crust (EPA, 1993). Iron is a most crucial element for growth and survival of almost all living organisms (Valko *et al.*, 2005).

It is one of the vital components of organisms like algae and of enzymes such as cytochromes and catalase, as well as of oxygen transporting proteins, such as hemoglobin and myoglobin (Vuori, 1995). Iron is an attractive transition metal for various biological redox processes due to its inter-conversion between ferrous (Fe^{2+}) and ferric (Fe^{3+}) ions (Phippen *et al.*, 2008). The source of iron in surface water is anthropogenic and is related to mining activities. The production of sulphuric acid and the discharge of ferrous (Fe^{2+}) takes place due oxidation of iron pyrites (FeS_2) that are common in coal seams (Valko *et al.*, 2005). A study of iron toxicity on aquatic plants, particularly rice, reported that the growth of species of aquatic reed was found to be inhibited by concentration of 1 mg/L total iron (Phippen *et al.*, 2008). Acid soils restrict rice production and together with Zn deficiency cause a macronutrient disorder in wetland rice. The production of lowland rice was greatly affected by high concentrations of reduced iron (Fe^{2+}) in the flooded soils. The features of iron toxicity in rice include high uptake of Fe^{2+} by roots, acropetal translocation into leaves, bronzing of rice leaves and yield loss (Becker & Asch, 2005).

Effects of heavy metals on humans

There are 35 metals that are of concern for us because of residential or occupational exposure, out of which 23 are 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 (Mosby *et al.* 1996). These heavy metals are commonly found in the environment and diet. In small amounts they are required for maintaining good health but in larger amounts they can become toxic or dangerous. Heavy metal toxicity can lower energy levels and damage the functioning of the brain, lungs, kidney, liver, blood composition and other important organs. Long-term exposure can lead to gradually progressing physical, muscular, and neurological degenerative processes that imitate diseases such as multiple sclerosis, Parkinson's disease, Alzheimer's disease and muscular dystrophy. Repeated long-term exposure of some metals and their compounds may even cause cancer.

Arsenic effects

Most of the paints, dyes, soaps, metals, semi-conductors and drugs contain arsenic. Certain pesticides, fertilizers and animal feeding operations also release arsenic to the environment in higher amounts. The inorganic forms of arsenic such as arsenite and arsenate are found to be more dangerous to human health. They are highly carcinogenic and can cause cancer of lungs, liver, bladder and skin. Humans are exposed to arsenic by means of air, food and water. Drinking water contaminated with arsenic is one of the major causes for arsenic toxicity in more than 30 countries in the world (Chowdhury *et al.*, 2000). Water may get contaminated through improperly disposed arsenical chemicals, arsenical pesticides or by natural mineral deposits. Arsenic

toxicity can be either acute or chronic and chronic arsenic toxicity is termed as arsenicosis. Most of the reports of chronic arsenic toxicity in man focus on skin manifestations because of its specificity in diagnosis. Pigmentation and keratosis are the specific skin lesions that indicate chronic arsenic toxicity (Martin & Griswold, 2009).

Figure 1 shows arsenic keratosis, so called "raindrops on a dusty road".



Figure 1. Arsenic keratosis, so called "raindrops on a dusty road"



Figure 2. Skin lesions due to arsenicosis

Lower levels of arsenic exposure can cause nausea and vomiting, reduced production of erythrocytes and leukocytes, abnormal heart beat, pricking sensation in hands and legs, and damage to blood vessels. Long-term exposure can lead to the formation of skin lesions, internal cancers, neurological problems, pulmonary disease, peripheral vascular disease, hypertension and cardiovascular disease and diabetes mellitus (Smith *et al.*, 2000). Chronic arsenicosis results in many irreversible changes in the vital organs and the mortality rate is higher. In spite of the magnitude of this potentially lethal toxicity, there is no effective treatment for this disease (Mazumder, 2008).

Lead

Human activities such as mining, manufacturing and fossil fuel burning has resulted in the accumulation of lead and its compounds in the environment, including air, water and soil. Lead is used for the production of batteries, cosmetics, metal products such as ammunitions, solder and pipes, *etc.* (Martin & Griswold, 2009). Lead is highly toxic and hence its use in various products, such as paints, gasoline, *etc.*, has been considerably reduced nowadays. The main sources of lead exposure are lead based paints, gasoline, cosmetics, toys, household dust, contaminated soil, industrial emissions (Gerhardsson *et al.*, 2002). Lead poisoning was considered to be a classic disease and the signs that were seen in children and adults were mainly pertaining to the central nervous system and the gastrointestinal tract (Markowitz, 2000). Lead poisoning can also occur from drinking water. The pipes that carry the water may be made of lead and its compounds which can contaminate the water (Brochin *et al.*, 2008).

According to the Environmental Protection Agency (EPA), lead is considered a carcinogen. Acute exposure can cause loss of appetite, headache, hypertension, abdominal pain, renal dysfunction, fatigue, sleeplessness, arthritis, hallucinations and vertigo. Acute exposure mainly occurs in the place of work and in some manufacturing industries which make use of lead. Chronic exposure of lead can result in mental retardation, birth defects, psychosis, autism, allergies, dyslexia, weight loss, hyperactivity, paralysis, muscular weakness, brain damage, kidney damage and may even cause death (Martin & Griswold, 2009).

Mercury

Mercury poisoning is referred to as acrodynia or pink disease. Mercury is released into the environment by the activities of various industries such as pharmaceuticals, paper and pulp preservatives, agriculture industry, and chlorine and caustic soda production industry (Morais *et al.*, 2012). Mercury has the ability to combine with other elements and form organic and inorganic mercury. Exposure to elevated levels of metallic, organic and inorganic mercury can damage the brain, kidneys and the developing fetus (Alina *et al.*, 2012). Mercury is present in most foods and beverages in the range <1 to 50 µg/kg. In marine foods it is often seen at higher levels. EPA has declared mercuric chloride and methyl mercury to be highly carcinogenic. The nervous system is very sensitive to all types of mercury. Increased exposure of mercury can alter brain functions and lead to shyness, tremors, memory problems, irritability, and changes in vision or hearing. Exposure to metallic mercury vapors at higher levels for shorter periods of time can lead to lung damage, vomiting, diarrhea, nausea, skin rashes, increased heart rate or blood pressure. Symptoms of organic mercury poisoning include depression, memory problems, tremors, fatigue, headache, hair loss, *etc.* Since these symptoms are common also in other conditions, it may be difficult to diagnose such cases (Martin & Griswold, 2009).

Cadmium

Cadmium is a metal of the 20th century. It is a byproduct of zinc production. Soils and rocks, including coal and mineral fertilizers, contain some amount of cadmium. Cadmium has many applications, *e.g.* in batteries, pigments, plastics and metal coatings and is widely used in electroplating (Martin & Griswold, 2009). presents a relative contribution of different sources to human cadmium exposure (Regoli, 2005). Cadmium and its compounds are classified as Group 1 carcinogens for humans by the International Agency for Research on Cancer (Henson & Chedrese, 2004). Cadmium is highly toxic to the kidney and it accumulates in the proximal tubular cells in higher concentrations. Cadmium can cause bone mineralization either through bone damage or by renal dysfunction. Inhaling higher levels of cadmium can cause severe damage to the lungs. If cadmium is ingested in higher amounts, it can lead to stomach irritation and result in vomiting and diarrhea. On very long exposure time at lower concentrations, it can

become deposited in the kidney and finally lead to kidney disease, fragile bones and lung damage. Tobacco is the main source of cadmium uptake in smokers as tobacco plants, like other plants, can accumulate cadmium from the soil.

Aluminum

The main routes of aluminum consumption by humans are through inhalation, ingestion and dermal contact and sources of exposure are drinking water, food, beverages, and aluminum containing drugs. Symptoms that indicate the presence of higher amounts of aluminum in the human body are nausea, mouth ulcers, skin ulcers, skin rashes, vomiting, diarrhea and arthritic pain. Aluminum exposure is probably a risk factor for the onset of Alzheimer disease (AD) in humans, as hypothesized by the WHO, Contact dermatitis and irritant dermatitis were seen in persons who were exposed to aluminum in their place of work. Aluminum showed adverse effects on the nervous system and resulted in loss of memory, problems with balance and loss of co-ordination (Krewski *et al.*, 2009). People suffering from kidney diseases find it difficult to eliminate aluminum from the body, resulting in aluminum accumulation in the body leading to bone and brain damage. Some factors that would likely be the reason for the development of aluminum toxicity are life in dusty environments, long-term intravenous nutrition, diminished kidney function, hemodialysis, drinking or ingesting substances that are high in aluminum content, working in an environment that contains high levels of aluminum. Patients undergoing kidney dialysis may get exposed to aluminum present in contaminated dialysates and phosphate binders.

Iron

Iron poisoning has always been a topic of interest mainly to pediatricians. Children are highly susceptible to iron toxicity as they are exposed to a maximum of iron-containing products (Albretsen, 2006). Iron toxicosis occurs in four stages. The first stage which occurs after 6 hrs of iron overdose is marked by gastrointestinal effects such as gastrointestinal bleeding, vomiting and diarrhea (Osweiler *et al.*, 1985). The second stage progresses within 6 to 24hrs of overdose and it is considered as the latent period, a period of apparent medical recovery. The third stage occurs between 12 to 96 hrs after the onset of certain clinical symptoms. This stage is characterized by shocks, hypotension, lethargy, tachycardia, hepatic necrosis, metabolic acidosis and sometimes death (Hillman, 2001). The fourth stage occurs within 2–6 weeks of iron overdose. This stage is marked by the formation of gastrointestinal ulcerations and development of strictures. Excess iron uptake is a serious problem in developed and meat eating countries and it increases the risk of cancer. It is said that asbestos associated cancer is linked to free radicals. Loose intracellular iron can also promote DNA damage. Iron can initiate cancer mainly by the process of oxidation of DNA molecules.

Conclusion:

In this review we reviewed the effects of some heavy metals, *i.e.* arsenic, lead, mercury, cadmium, aluminum and iron, on the environment and living organisms, mainly human beings. Effective legislation, guidelines and detection of the areas where there are higher levels of heavy metals are necessary. Failure to control the exposure will result in severe complications in the future because of the adverse effects imposed by heavy metals. Occupational exposure to heavy metals can be decreased by engineering solutions. Monitoring the exposure and probable intervention for reducing additional exposure to heavy metals in the environment and in humans can become a momentous step towards prevention. National as well as international co-operation is vital for framing appropriate tactics to prevent heavy metal toxicity.

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