International Journal of Applied Research
Journal HP: www.intjar.com; ISSN: 2411-6610

A Review on Non-essential Heavy Metals: Their Bioaccumulation and Bioremediation

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ARTICLE INFO

Article history

Received: 04 December 2023
Accepted: 21 December 2023

Keywords

Heavy metals, bioaccumulation, toxicity, bioremediation

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ABSTRACT

Enormous rise in human subjection to heavy metals has been brought about by the industrial campaigns of the previous century. The most familiar heavy metals to bring about human poisonings have been Cadmium (Cd), Lead (Pb), Mercury (Hg), Arsenic (As), and Aluminium (Al). Here, we have reviewed the bioaccumulation, mechanism of action of toxicity and remediation of the non-essential heavy metals. These non-essential Heavy metals are bioaccumulated in the body, with a variety of noxious effects on different human tissues and organs. Heavy metals have an impact on the effects of apoptosis, differentiation, cellular growth, division and other biological functions. Mechanisms of action also reveal similar ways in which these metals cause toxicity, including ROS production, reduced antioxidant shielding, enzyme dismissal and oxidative stress. However, heavy metals are steady in the environment and do not biodegrade, so remediation is therefore necessary to both prevent heavy metal leaching or mobilization into environmental components and to make their extraction easier. Metal pollutants can be used by microbes as an energy source to change them into less harmful forms. Metal detoxification through bioremediation and phytoremediation using microorganisms and plants is effective, economical, and environmentally beneficial.

Introduction

Increased exposure to pollutants is a major concern for almost all living things on earth. The unrestricted use of a variety of chemicals to maintain the ever-increasing demand for development poses a serious threat to general and public health conditions in developed and developing countries. In the various pollutants associated with industrialization and the most important anthropogenic activities are heavy metals that form a natural combination of earth crust. Since the Earth's formation, these heavy metals have been organically occurring in the Earth's crust. Heavy metal use has skyrocketed aftermath, metallic compounds are now becoming steadily more prevalent in both the tellurian environment and the aquatic environment (Gautam *et al.*, 2016). Heavy metals are those substances which generally go through an atomic number more than 20 and atomic density bigger than 5 g cm^{-3} and demonstrate the attribute of metals (Hazrat *et al.*, 2017).

On account of their function in biological system, Heavy metals can be separated into two groups: those that are necessary and those that are not. Necessary or essential heavy metals like Cu, Zn, Co, Cr, Mn, and Fe, are requisite in trace amounts (10–15 ppm) for biological creatures bring off basic functions such as development, anabolism/ catabolism, for organ growths, as cofactors for enzymes and other proteins. While non-essential trace metals (Cd, Pb, Hg, As, and Al), are not required by organisms for any metabolic activities, even in small concentrations (Collin *et al.*, 2022). Due to their toxicity, inherent persistence, lack of biodegradability, and accumulative characteristics, heavy metal pollution has become a significant issue on a global scale (Islam *et al.*, 2018).

Heavy metal vulnerability has exploded as an outcome of the twentieth century's industrial activity. The most frequent heavy metals that cause human intoxication are mercury, lead, chromium, cadmium, and arsenic. Following exposure to water, air, or food, acute or chronic poisonings can occur. The biological processes of growth, augmentation, differentiation, DNA impairment repair, and apoptosis are all affected by heavy metals (Mahdi *et al.*, 2021). Toxicity of heavy metals and carcinogenicity are depends upon absorbed dose (high, medium, low), route of exposure (oral, peritoneal, and subcutaneous etc.), and duration of exposure (acute, sub chronic and chronic); high dose exposure induces severe reactions in people and other animals that result in increased DNA damage and neurological impairments, (Gorini *et al.*, 2014) by the production of reactive oxygen species (ROS), the inactivation of enzymes, and the suppression of antioxidant systems.

Cite this article: *Sharma, G. & John, P.J. (2023). A review on non-essential heavy metals: Their bioaccumulation and bioremediation. International Journal of Applied Research, 9 (1): 22-34. DOI: 10.5281/zenodo.10726607*

Bioaccumulation of xenobiotic compounds first gained public attention in the 1960s with the invention of DDT and methyl mercury residue in fish and wildlife. When an organism absorbs a compound more rapidly than it is shed or removed by catabolism and excretion, this is known as bioaccumulation. These heavy metals bioaccumulate and have a variety of negative effects on variety of life forms, including human tissues and organs. Fish, which are at the top of the aquatic food chain, can accumulate heavy metals and transfer them down to humans, where they can cause acute or chronic illnesses (figure 2) (Yousuf *et al*., 2000). On the other hand, one of them produces septicemia in a specific arrangement and binds to specific macromolecules. Different heavy metal toxic methods broaden our understanding of their damaging effects on body organs, authorize for carefulness of animal and human intoxications. A review of the literature on heavy metal toxicity and their bioaccumulation processes would help us in place to improve our understanding of their toxic effects on body or organs and hence better manage metal toxicities. The toxicity of non-essential trace metals and their bioaccumulation are the key topics of this review.

Sources of non-essential heavy metals

Sources of heavy metals are broadly two types (figure 1), natural sources and human induced sources, natural sources include soil erosion, natural weathering of earth crust, anthropogenic or manmade sources are major sources like mining, industrial effluents, urban runoff, sewage discharge, dental amalgam, insect or disease control agents like pesticides, fungicides which applied to crop, and many others (Bauvais *et al*., 2015; Morais *et al*., 2012).

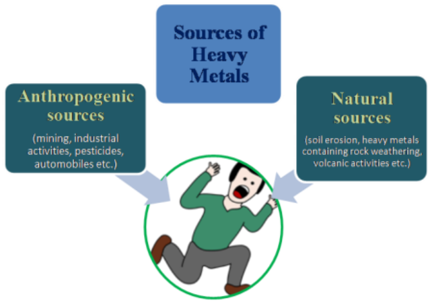

Figure 1: Sources of heavy metals

Table 1: Non-essential trace metals and their respective sources

Non-essential trace metals	Sources	References
Cadmium chloride ($CdCl_2$)	Chloride Mirrors, analytical chemistry, vacuum tubes, lubricants, photocopying, calico printing, dyeing, electroplating, grease, and synthetic intermediary in the manufacture of stabilizers and pigments holding cadmium.	Rani *et al.*, 2013
Cadmium nitrate (Cd(NO3)2)	To produce photographic emulsions, colour glass and porcelain, use nuclear reactors, and generate cadmium hydroxide for use in alkaline batteries.	Rani *et al.*, 2013
Lead (Pb)	Batteries, metal pressure, Paint old houses, furnishings, toys, and crafts Dust, soil, water to drink, air, drugs, ayurvedic treatments, and makeup, jewellery and games for kids.	Pandey *et al*., 2013, New York state department of health.
Mercury (Hg)	Mining, transportation, processing of mercury, ores, plastic, batteries and fertilizers.	Pandey *et al*., 2013, New York state department of health.
Arsenic (As)	Timber treatments, paints and pesticides.	Pandey *et al*., 2013, New York state department of health.
Aluminium (Al)	Mining and processing of aluminium, Aluminium utensils and tea consumption.	ATSDR 2010 and Hardisson *et al.*, 2017.

Toxic effect of non-essential heavy metals

Cadmium (Cd)

According to agency for toxic substance and disease registry (ATSDR) Cadmium is the 7th most toxic metal and group I carcinogenic as per the International Agency for Research on Cancer (IARC). A little quantity of cadmium is naturally present in soil, but the amount is greatly increased by industrial activity, which is the main cause of cadmium contamination of soil, water, and other species, including humans. Cadmium is a byproduct of Zn production, exposure of cadmium generally occurs by means of natural and occupational measures, forest fires, weathering of Cd-containing rocks, and volcanic activity are some examples of natural Cd emissions. Manufacturing of non-ferrous metals, burning of fossil fuels, trash incineration (particularly the burning of plastics and batteries that contain Cd), and the production of phosphate fertilizers are all operations that result in Cd emissions. Tobacco smoking is also a cause of cadmium intoxication; Smokers have roughly two times the amount of cadmium in their blood than non-smokers do (Iwona *et al*., 2019; Batáriová *et al*., 2006).

Bioaccumulation of Cadmium

Due to significant concerns that excessive levels of Cd may have negative effects on marine organisms and may pose issues with their acceptability as food for humans, cadmium bioaccumulation by marine organisms has gained substantial research in recent years. Cd is an industrial and environmental chemical that harms a number of human organs. It was determined many years ago that Cd only occurs in tiny amounts in the marine environment and in aquatic animals, although salinity and temperature have an impact on species. This is quickly absorbed by phytoplankton in the aquatic environment, just like the other heavy metals and bioaccumulate in the progressive food chain, and ultimately reaches to human beings (Tai *et al*., 2020). It is selectively accumulated in some organs such the liver, kidney, gills, and exoskeleton and is not evenly distributed throughout the body. In muscle tissues, the concentrations are several orders of magnitude lower.

Even in a clean environment, marine creatures' ability to bioaccumulate cadmium from sea water varies depending on the species and population. The process of bioaccumulation is influenced by both abiotic (such as the chemical form of Cd in solution, metal interaction, salinity, and temperature) and biotic (such as animal size and features, sex, maturity, etc.) variables. Due to its impact on the animals' metabolic activity, temperature usually causes an increase in the bioaccumulation of cadmium by marine creatures (Jackim *et al*., 1977). The overall concentration of Cd in an organism will rely on a variety of biotic and abiotic factors, as well as how the organisms use the metal during metabolism. Some bivalves may deplete Cd, according to some research; however other creatures effectively retain Cd (Ray *et al*., (1986).

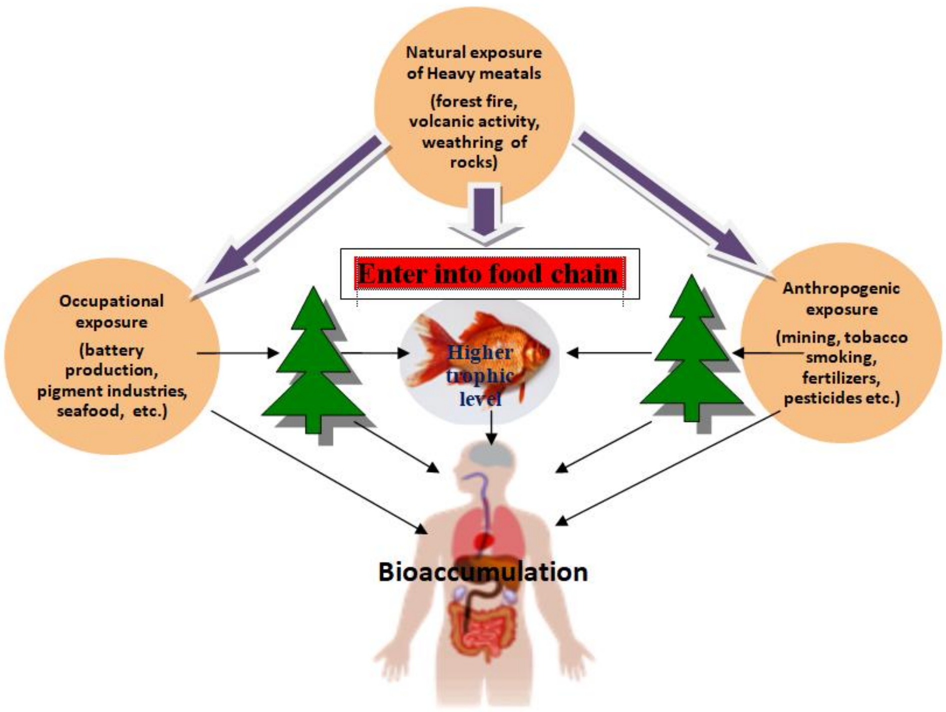

Figure 2: Bioaccumulation of different heavy metals

Hazardous effect on health

Widespread Cd impurity of water and food supplies was the outcome of the Itai-itai illness outbreak in Japan. The people experienced severe degenerative bone disease, kidney failure, and illnesses of the GI and lungs (Nishijo *et al.,* 2017).

Mechanism of toxicity

Cell maturation, differentiation, and death are all altered by cadmium. The mechanism of DNA repair, the production of reaction oxygen species (ROS), and the activation of apoptosis are all affected by these activities. Cadmium binds to the mitochondria at modest concentrations, which can stop cellular respiration and oxidative phosphorylation (Rani *et al.,* 2013). Cadmium's astonishing capacity to prevent DNA damage repair explains why it causes cancer (Giaginis *et al*., 2006). Cadmium is a co-mutagen that makes mammalian cells more susceptible to mutation from UV radiation, alkylation, and oxidation. Cadmium's inhibition of many DNA repair processes, including (BER) base excision repair, (NER) nucleotide excision repair, mismatch repair, and the abolition of the pre-mutagenic DNA antecedent 8-oxodGTP, may account for these effects.

Regarding NER, cadmium prevents the elimination of cyclobutane pyrimidine dimers following Ultra Violet exposure by blocking the initial stage of aforementioned repair process. Additionally, cadmium interferes with the interaction and dissociation of vital NER proteins. After the cells were exposed to a non-cytotoxic level of $CdCl_2$, there was a reduced localization of the Xeroderma pigmentosa C protein (XPC) to UVC-induced DNA damage as a result of lower amounts of XPC nuclear protein. It's interesting to note that the zinc-binding domain of the tumor suppressor protein p53, which is crucial for DNA binding and p53's role in transcription process, is also present in the protein. It has been shown that cadmium chloride affects the structure of p53 in MCF7 cells, prevents it from attaching to DNA, and suppresses the transcriptional activity of a reporter gene (Costa *et al*., 2003).

Remediation

Phytoremediation is a still-evolving technique that heavily relies on chemical, biological, and physical interactions to help contaminants in polluted environments mineralize. There are lots of remediation processes like extraction, volatilization, rhizoremediation, and degradation. Extraction is used to remediate Cd. plant species plays an important role in phytoremediation such as Indian goose grass (*Eleusine indica*), chickweed (*Ageratum conyzoides*), and asthma-plant (*Euphorbia hirta*) have all been proven to significantly lower the levels of Cd in soil, by 51.8%, 52.2%, and 58.8%, individually (Lata *et al*., 2019 ; Fasih *et al*., 2020) . The variables that drive plants to remove Cd from the environment include soil temperature, pH, additional mineral concentrations, and soil toxicity levels (Radziemska *et al*., 2017). It has been demonstrated that phyto-extraction of Cd from rapeseed lowers soil Cd levels by 60% when compared to the control (Kathal *et al.*, 2016).

Organometallic and organic pollutants can be removed with the aid of entities like Fungi, bacteria, and algae. Bacillus species significantly aid in removing the toxicity of contaminants including Uranium, lead, Nickel, Ferrous, Copper, Chromium, Cadmium, and Arsenic from industrial effluents or agricultural soils that have been contaminated. Pseudomonas species have been utilized to successfully remove pollutants like Ni, Pb, Cu, Cr, and Cd (Radhakrishnan *et al*., 2017; Chellaiah *et al*., 2018; Fasih *et al*., 2020).

Resistance to microbial Cd has been associated with sequestration/accumulation, toxic metal deposition in the wall of cells, altered toxic chemicals, alterations in the cell-wall plasma membrane complex, and all of these processes. By using divalent cation absorption methods like Zn2+ (zinc (II) ion) or Mn2+ (Manganese), gene amplification, active Cd efflux, and enhanced metallothionein transcription in genes, cadmium can enter bacterial cells. The primary benefits of using microbes to remediate metals are low running costs, high capacity, metal recovery potential, and effective bio-sorbent regeneration (Chellaiah *et al*., 2018).

Lead (Pb)

Lead (Pb) is a naturally existing metal that frequently reacts with two or more elements to generate lead compounds. Lead forms lead sulphate, lead carbonates, or lead oxide when it reacts with air and water. These substances function as a shield to stop corrosion. Both acids and bases can interact with lead (Collin *et al*., 2022). Lead is the most hazardous and ubiquitous matter in the surroundings. An account of its foremost physico-chemical attributes, its use can be dated back to ancient times. On a global scale, it is a widely used, important, and potentially dangerous environmental chemical. Because of its predominant characteristics, including softness, malleability, ductility, feeble conductivity, and corrosion resistance, it is more difficult to stop using it. Due to its inability to biodegrade and long-term use, its concentration in the ecosystem rises along with associated risks. Leaded petrol, industrial processes like lead smelting and combustion, pottery, boat building, lead-based painting, alloys, vehicle exhaust, burning of fossil fuels, lead-containing pipes, battery recycling, grids, the arm industry, pigments, and book printing are just a few of the sources from which humans are exposed to lead and its compounds. According to recommendations from the Centre for Disease Prevention and Control (CDC), adults who have blood lead levels greater than 5 g/dL are at high risk. However, the World Health Organization (WHO) advises against deeming any blood lead level safe (Prasenjit *et al*., 2021).

Bioaccumulation of lead

Under water life forms can bioaccumulate Pb across their feed and drinking water. Pb builds up in many fish organs, including the digestive system, gills, liver, spleen, and kidneys; these fish uptake by birds and human beings where lead concentration is much higher than low trophic level because of the lower surface to volume ratio (Abdel *et al*., 2020; Jamil *et al.*, 2023). Metal concentrations in the water and the length of exposure are the two main factors affecting the accumulation of contaminants in tissue. Fish are capable of ingesting and accumulating trace metals from the surroundings as well as secondarily through added aquatic animals such as smaller fishes, crustaceans, zooplanktons, and phytoplankton. In fish, pollutants build up in their organs like the liver, and when the levels in these tissues reach an excessive concentration, the effects are evident. Fish can therefore absorb heavy metals through the skin, gills, and alimentary duct when they consume contaminated food. Metals are absorbed by fish and then circulated through the bloodstream to the tissues and organs, where they accumulate as a consequence (Polat *et al*., 2015). These fishes are eaten by humans and other higher trophic level animals, resulting in heavy metals in human tissues.

Mechanism of toxicity

Due to immune-modulating, oxidative, and inflammatory pathways, exposure to Pb can result in neurological, respiratory, urinary, and cardiovascular diseases. Pb may also cause inflammatory reactions in different organs and alter the homeostasis of the oxidant-antioxidant system. Pb exposure has several related disorders and can impair the body's physiological functions (Mahdi *et al*., 2021). Numerous investigations on lead (Pb) neurotoxicity have shown that this metal is a harmful toxin, especially throughout the stages of organisms' development. The sequestration of this metal in brain tissue is carried out by astrocytes. Loss of the buffering function and pathogenic processes are frequently caused by activation of astrocytes. Neuronal cell death occurs along with this phenomenon, which may be related to inflammatory processes brought on by the release of a variety of cytokines and chemokines. In order to look into this putative pro-inflammatory effect, the effects of chronic exposure to Pb on glial activation are studied in young rats (Lidia *et al*., 2006).

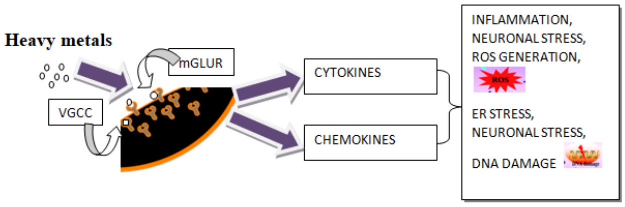

Figure 3: Mechanism of generation of Cell and Neuronal stress by heavy metals, VGCC (voltage-gated calcium channels) and mGLUR (metabotropic glutamate receptors) are receptor for heavy metals entrance

The basis of the ionic mechanism of lead toxicity, which eventually derange cellular metabolism, is the ability of lead metal ions to put back other bivalent cations like Ca2+, Mg2+, and Fe2+ as well as monovalent cations like Na+. miscellaneous biological operations, including cell adhesion, intra- and intercellular transmission, maturation, apoptosis, protein folding, ionic transport, enzyme steadiness, and neurotransmitter reveal, are significantly altered by the ionic system of lead toxicity. Lead can put back calcium even at low concentrations, which affects protein kinase C, a factor in the command of brain excitation and memory storage (Flora ***et al.***, 2012).

Hazardous effect on health

High blood lead levels in pregnant women escalate the risk of premature childbirth or stunted birth weight kids. Even with blood lead concentrations considerably below 25 ng/dL, the fetus may suffer harm. Blood lead levels in the newborn were found to be higher than those in the mother at the same instant. Malnourished ladies who encounter a lot of lead exposure prior to getting pregnant are thought to be at bigger risk (David *et al.,* 2005; Latif *et al*., 2015). Chronic Pb poisoning has a notorious past that includes physiological, neurological, reproductive, hypertension, baldness, anemia (which inhibits the activity of the enzymes porphobilinogen synthase and ferrochelatase), dementia, memory issues, because Pb is an analogue of calcium and, at stubby concentrations, is a selective suppressor of voltage-dependent calcium channels, and death (Wani *et al*., 2015).

Remediation

By excreting extracellular enzymes and organic acids, bacteria have the ability to hydrolyze inaccessible types of heavy metal-bearing minerals from soil, increasing the availability of Pb in the soil. Because they have adapted to these conditions, bacteria that have been isolated from highly contaminated heavy metal zones frequently exhibit a high tolerance to multiple metals. Heavy metal intake in plants is significantly regulated by metal-resistant bacteria (Anindita *et al*., 2021; Drewniak *et al*., 2017). Plant microbe consortium, which is impacted alongside various factors such as soil nutriments, pH, plant species, and their attendant microbial flora, regulates how much heavy metals plants growing in metalliferous soil absorb. By adjusting pH, redox processes, and pollutant adsorption from a polluted environment, bioremediation aims to reduce the solubility of contaminants in the environment. Chemical transformations of dangerous pollutants into less dangerous, safer, less mobile, or inactive compounds are known as redox reactions. Pollutant adsorption is significantly influenced by the pH values, and adsorptive capacity rises as pH decreases (Nnaji *et al.,* 2023). In order to combat trace elements or other abiotic distress, plant growth-promoting rhizobacteria (PGPRs), are formerly employed to increase crop output in farming, and during the bioremediation procedure (Lucy *et al*., 2004).

Mercury (Hg)

Mercury is one of the top 10 substances causing serious public health concerns, according to the World Health Organization (WHO 2013; Alessia *et al.,* 2016). Mercury is a lustrous, silver-white odorless liquid and become colorless and odorless gas when heated. The gaseous configuration of mercury is more threatening than the liquid form. Hg0 splashes due to container breaking, and inhaling massive amounts of Hg fumes can be dangerous. Mercury has been used for centuries in multiple purposes including medicinal use like chlormerodrin, merbaphen, and mercurophylline as diuretics and phenyl mercury nitrate as disinfectant and widespread industrial use like gold extraction, lamp manufacturing factories, for production of fluorescent light bulbs and fungicides to defend plants against infections etc. Because of this, it is a common chemical exposure and environmental pollutant (Shawn *et al*., 2021). The most detrimental things related to mercury toxicity in recent history include Minamata Bay and Niagata, Japan in the 1950s, and Iraq in the 1970s (Clifton *et al*., 2007).

Three different forms of mercury (Hg): organic mercury (Hg), inorganic mercury (Hg+, Hg2+), and elemental or metallic mercury (Hg0) (commonly methyl or ethyl mercury) (Li *et al*., 2017), which leads to different mercury intoxication syndromes. Hg0 <Hg2+, Hg+ < CH3-Hg is the order of increasing toxicity associated with different types of mercury. Organic mercury compounds like methyl mercury (Me-Hg) and ethyl mercury (Et-Hg) are more hazardous than inorganic mercury compounds which exposure usually occurs from ingestion of contaminated seafood, paints containing mercury, or ingestion/injections of thimerasol a mercury-containing preservative (Sakamoto *et al*., 2018). One of the main ingredients in skin-brightening cosmetics that are used to treat freckles and skin spots caused by an excessive deposition of melanin is mercury chloride (HgCl2). Tyrosinase, an enzyme involved in the production of melanin, is inhibited irreversibly by HgCl2 by substituting the copper cofactor (Mahdi *et al*., 2021).

Bioaccumulation of mercury

Mercury from the atmosphere settles in water where it is transformed into organic (methyl or ethyl) mercury by microorganisms. This organic mercury is then devoured by smaller animals that are then eaten by larger fish. Fish at the top of the food chain, such as tuna, swordfish, and sharks, may have high mercury concentrations in their tissues. Human exposure to mercury have occurs through consuming these contaminated fishes and other sea foods

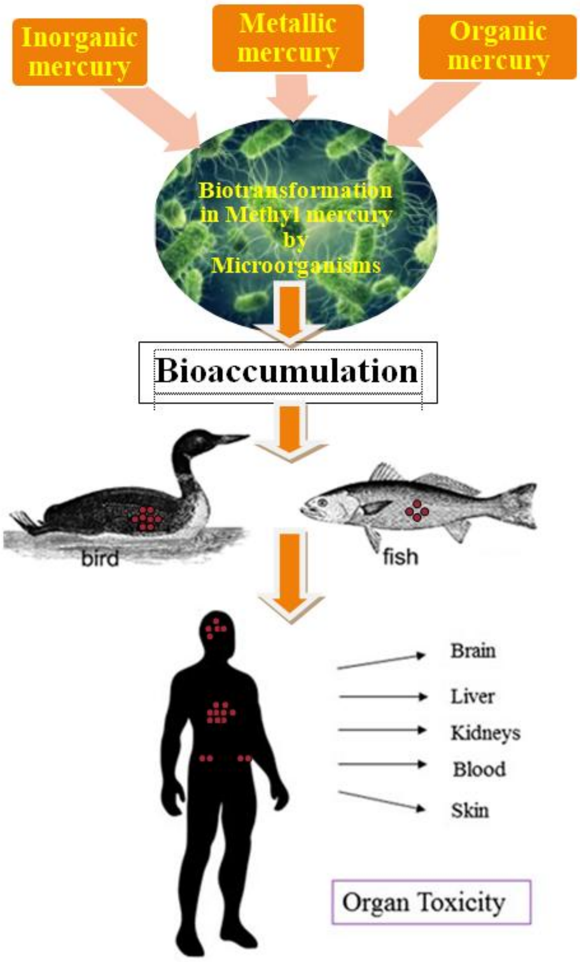

Figure 4: Different form of mercury accumulate in biological system

Hazardous effect on health

The most typical symptoms of elemental mercury inhalation include shortness of breath, cough, fever, nausea, vomiting, diarrhea, headache, metallic taste, salivation, and vision impairment. Severe exposure can lead to emotional excitability, loss of memory, insomnia, depression, fatigue, and in severe cases delirium, hallucination, respiratory discomfort and failure. Acute ingestion of organic salts is frequently accompanied with a metallic taste and graying of the oral mucosa. Intracellular catalase in RBCs converts Hg0 to Hg2+, a divalent form that binds with proteins, particularly hemoglobin, by interaction with sulfhydryl groups which interfere in protein structure mainly tertiary and quaternary. Main target organ for mercury is brain, although other targets include peripheral nerves, the kidneys, the immunological system, the endocrine system, the muscles, and several forms of dermatitis (Robin *et al*., 2011).

Mechanism of toxicity

Protein precipitation, enzyme inhibition, and broad corrosive action are three ways that mercury ions cause harmful consequences. Along with sulfhydryl groups, mercury can also bind to phosphoryl, carboxyl, amide, and amine groups. These readily accessible groups make proteins (including enzymes) sensitive to mercury reactivity. Most proteins are rendered inactive once they are coupled to mercury. The chemical form and oxidative state are both factors in toxicity (organic versus inorganic).

Remediation

Mercury is both tenacious and volatile. It can enter the soil through a variety of channels and can reside there in a variety of forms and seriously polluting the soil. Rhizofiltration, phytostabilization, phytoextraction, phytotransformation (organic), and phytovolatilization, are the major components of phytoremediation of Hg-contaminated soil (Dongye *et al*., 2020).

Bacteria which are belonging to genus *Bacillus, Enterobacter, Klebsiella* and *Acinetobacter*, which can be used for bioremediation of mercury. These bacteria were able to resist high mercury concentrations. The isolated bacteria have an additional benefit for use in bioremediation due to their extensive salinity tolerance. It was observed that the bacteria Bacillus and *Enterobacter* sp. were quite effective at removing up mercury (Bhupendra *et al*., 2019). Hg is carried from the roots to the aboveground portion of the plant through a pertinent organizational structure of the plant during the remediation of Hg-contaminated soil. Hg will interact with each component of the plant in some way during the entire absorption and transportation process, and some particular plants can mend or eliminate Hg in the soil through these processes for soil remediation (Ghosh *et al*., 2005).

Arsenic (As)

Millions of people are distressed by arsenic poisoning globally as a consequence of occupational and environmental subjection, moreover purposeful suicide and homicide attempts. Although arsenic homicides are frequently reported, polluted water, soil, and food products are the main sources of arsenic toxicity for the general organisms. Arsenic (As) is a poisonous metalloid element that is virtually odorless, tasteless, and present everywhere in nature. Arsenic is found in three common forms-inorganic salt, organic salt, and gaseous form-and four ordinary valence states: As (III), As (V), As (o), and arsine gas (Matthew *et al*., 2021).

Bioaccumulation of arsenic

Both its speciation and concentration influence arsenic's toxicity. The International Agency for Research on Cancer (IARC) has categorized organic and inorganic arsenic as carcinogens. Organic arsenic is substantially less hazardous than inorganic arsenic. For marine fish, the total arsenic content has been observed to range between 0.2 and 150 µg/g, and bioaccumulation differs for various tissues. While just 0.02 percent to 11 percent of marine fish have inorganic arsenic, over 90% of arsenic is found in its less hazardous organic form (Zhang *et al*., 2015).

According to studies, the As (V) ingested by marine fish can first be turned into As (III). Once As (III) is present, it can be speedily transformed into monomethylarsonic acid (MMA), dimethylarsinic acid (DMA), and arsenobetaine (AsB), the ultimate obvious form of arsenic (Pei *et al*., 2019).

Hazardous effect on health

In conformity with WHO (world health organization) Arsenic in food and water can cause cancer and skin imperfections when consumed over an extended amount of time. Furthermore, diabetes and cardiovascular disease have been tied to it. A dip in cognitive development has been related to being subjected between conception and the early years of life, and young adult mortality has increased (WHO 2018).

Mechanism of toxicity

Arsenic is offshoot in smelting actions for numerous ores including gold, lead, cobalt, nickel, and zinc (Danielle *et al*., 2016). Arsenic is rarely absorbed through the skin and is often absorbed through inhalation or oral intake. It has a higher rate of absorption in the gastrointestinal tract after oral consumption which is nearly 90%, as compared to other heavy metals. Arsenic that has been ingested deposits in the liver, kidneys, muscle, bone, hair, skin, and nails and attaches to red blood cells. It is primarily eliminated through the urine. Inorganic arsenic compounds may pass through the placenta and impair the development of the embryonic nervous system by inhibiting the activity of numerous enzymes involved in cellular respiration, glutathione metabolism, and DNA synthesis. Arsenic metabolism is a multistep process that starts with the methylation of inorganic arsenic molecules and involves more than five metabolites (Hong *et al*., 2014; Hanlon *et al*., 1977).

The manner of arsenic poisoning Toxic inorganic arsenic molecules are methylated by bacteria, algae, fungi, and humans during the process of arsenic biotransformation to create Mono-methyl-arsonic acid (MMA) and Dimethylarsinic acid (DMA). During this biotransformation process, these inorganic arsenic species (iAs) go through enzymatic conversion to methylated arsenicals, the byproduct and the biomarker of chronic arsenic exposure. Inorganic arsenic that has been methylated and is discharged in the urine as MMA (V) and DMA (V) is a bioindication of chronic arsenic exposure. Biomethylation is a detoxification process.

iAs(V) → iAs(III) → MMA(V) → MMA(III) → DMA(V) (Source: Singh *et al*., 2007).

The intermediate product MMA (III) is, however, not eliminated and stays inside the cell. Comparatively hazardous to other arsenicals, Monomethylarsonic acid (MMA III), an intermediate product, may be responsible for arsenic-induced cancer (Zhang *et al*., 2015).

Remediation

The in-depth analysis of heavy metal-contaminated sites has revealed unique characteristics of the bacteria that thrive there. It is their selective metallophilic characteristics. This is largely because the action of these organisms causes soluble heavy metal oxyanions to change their oxidation state by converting them to an insoluble form (Gault *et al*., 2004). The anionic transport mechanism can deliver metal ions to metal-reducing bacteria in the form of soluble oxyanions. The bacterial species such as, *Shewanella*, *Clostridia*, *Pseudomonas*, *Bacillus*, *Geobacter*, and *Archaea* have the ability to reduce and resist metals. Metal-tolerant Sulfate Reducing Bacteria (SRB). They demonstrate the capability of removing As and other metals from the As mining region. The main substrate for metal precipitation, hydrogen sulphide, is produced by the SRB when the active nitrate-reducing population in the soil is active. The colony of acetogenic bacteria is active, which is a source of carbon and energy (Khatisashvili *et al.* (2021). Arsenic can become mobilized in sediments gathered from a contaminated aquifer by some metal-reducing bacteria (Serrano *et al.,* 2017).

Aluminium (Al)

The most conventional metal in the environment is aluminium (Al), which naturally occurs in the trivalent form (Al+3) as silicates, oxides, and hydroxides. However, it may also mix with other elements like chlorine, sulphur, and fluorine to create complexes, as well as with organic matter (Ikechukwu *et al*., 2020). The lots of people disregard their regular activities' aluminium exposure. Perhaps the way we define "exposed to aluminium" is related to how much metal is found in food sources. The majority of oral consumption of aluminium comes through food, which makes up around 95% of daily caloric intake, and water, which makes up 1-2%. These typically supply 4,000–9,000 mcg of daily consumption (Yokel *et al*., 2008). Environmental conditions, particularly pH, have an impact on Al (Hutchinson *et al*., 1978; Driscoll *et al*., 1984).

Bioaccumulation of aluminium

Aluminium (AI) is widely present in the environment; its insolubility prevents it from entering the food chain. Solubility of Al is mostly depends upon some environmental factor like pH and temperature, in which pH is more important, while most Al exists as the insoluble AI(OH)3 at neutral pH, it is extremely soluble in acidic conditions. Al is also known to accumulate significantly across the soft tissues, the intestines, the digestive system, and the kidney (Elangovan *et al*., 1996).

Hazardous effect of health

Al intake is linked to the agglomeration and precipitation of β-amyloid, which corresponds with Alzheimer's disease (Exley et al., 2006). Peroxidation of lipids, oxidative stress Organ inflammation in the lung, gut, heart, and testis are pro-inflammatory conditions. Immunosuppression causes macrophage dysfunction, lymphocyte death and malfunction, lymphocyte proliferation inhibition, the transformation and denaturation of proteins, whether to stimulate or inhibit an enzyme, Kreb's cycle and glycolysis are compromised, and oxidation of lipids and proteins is encouraged. Genotoxicity: dysneurogenesis, decreased cell division and proliferation. Some of the significant health effects of aluminium include amyloidogenic and anti-amyloidolytic effects (Igbokwe *et al*., 2019).

Mechanism of toxicity

Al enters the body mostly by inhalation and ingestion (through food and water). Al compounds are deposited in the lungs after inhalation. The majority of the time, Al is delivered to the lungs as silicate and other weakly soluble compound particles. Where the Al is localized, the concentration of Al in the lungs tends to rise with ageing and may cause respiratory abnormalities. There is no indication in the literature that particulate or soluble Al is transported from the lungs to other body organs by way of the bloodstream (Ikechukwu *et al*., 2019).

The iron-transporter protein transferrin transports around 90% of the circulating aluminium in the blood, with the remaining aluminium binding to albumin and citrate. The comparatively slower cellular absorption of aluminium in tissues is thought to be mediated via endocytosis and intracellular transfer of the aluminium bound to transferring (Hemadi *et al*., 2003).

The transferrin-receptor may not, however, bind to the Al-transferrin complex, demonstrating the existence of a different mechanism for the uptake of Al by cells (Sakajiri *et al*., 2010). Overall the Al deposition, which causes Al toxicosis, is accelerated by exposure to Al, its ongoing use, as well as by a surge in intestinal absorption and a reduction in the metal's excretion. The systemic toxicosis that is linked to structural and functional abnormalities of the organs is caused by lesions in the cells that are caused by the molecular targets of action, which produce effects in the cell and disrupt cellular homeostasis.

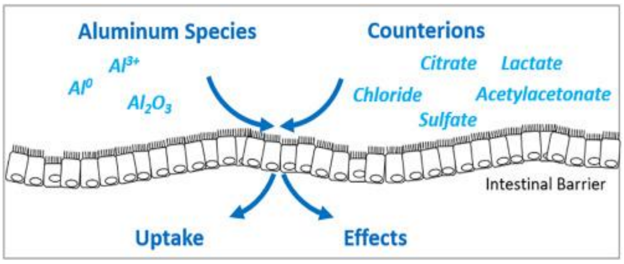

Figure 6: Toxicity Mechanism of Aluminium and their counter ions (Source: Holger Sieg *et al*., 2021)

Remediation

An efficient, affordable, and environmentally benign method for removing metals from environment is phyto- or bioremediation. Water becomes more acidic due to elevated aluminium levels, which may have negative health effects on both people and aquatic animals. One of the finest methods for reducing the toxicity levels of aluminium in industrial waste water is phytoremediation. By detoxifying effluents, bioremediation has made it possible to solve difficulties in the realm of solid waste. The oldest living thing on the planet is blue green algae, which may be used to remediate industrial water that contains heavy metals and is edible. Some studies showing that filamentous *Cyanobacteria spirulina* has the ability to remediate aluminium in efficient way (Murali *et al*., 2014).

Conclusion

The heavy metals enter in the body by variety of ways, including through food, water, air, and even cutaneous contact. Heavy metals are keep hold of after absorption, where they can amass in the body. Harmful metals bioaccumulation has a variety of toxic consequences on various body tissues and organs. Metal toxicity symptoms can be acute or build up over time. Heavy metals interfere with biological functions such as apoptosis, growth, proliferation, and differentiation. Additionally, harmful metals can hearten epigenetic alterations that impact on gene expression. Parallel pathways for these metals that bring toxicity are revealed by their mechanisms of action, including ROS production, a debilitate antioxidant resistance, enzyme deterrent, and oxidative stress. Industrial wastewater discharged into sensitive environmental areas, including soil and rivers, calls for prompt government involvement, frequent monitoring, and treatment using the right techniques. Conventional treatment approaches have drawbacks and ought to be replaced by effective, affordable, and environmentally friendly alternatives like bioremediation, which uses biological agents. A significant challenge is choosing an economical and efficient biosorbent. By performing redox reactions, microorganisms have an impact on the bioremediation processes by immobilizing or mobilizing metal. It will be advantageous for future study to consider additional targets as preventative measures against organ toxicity brought on by heavy metals and converting lab-scale solutions into feasible industrial uses.

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