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Review Article

Environmental Chemistry and Ecotoxicology of Hazardous Heavy Metals: Environmental Persistence, Toxicity, and Bioaccumulation

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Heavy metals are well-known environmental pollutants due to their toxicity, persistence in the environment, and bioaccumulative nature. Their natural sources include weathering of metal-bearing rocks and volcanic eruptions, while anthropogenic sources include mining and various industrial and agricultural activities. Mining and industrial processing for extraction of mineral resources and their subsequent applications for industrial, agricultural, and economic development has led to an increase in the mobilization of these elements in the environment and disturbance of their biogeochemical cycles. Contamination of aquatic and terrestrial ecosystems with toxic heavy metals is an environmental problem of public health concern. Being persistent pollutants, heavy metals accumulate in the environment and consequently contaminate the food chains. Accumulation of potentially toxic heavy metals in biota causes a potential health threat to their consumers including humans. This article comprehensively reviews the different aspects of heavy metals as hazardous materials with special focus on their environmental persistence, toxicity for living organisms, and bioaccumulative potential. The bioaccumulation of these elements and its implications for human health are discussed with a special coverage on fish, rice, and tobacco. The article will serve as a valuable educational resource for both undergraduate and graduate students and for researchers in environmental sciences. Environmentally relevant most hazardous heavy metals and metalloids include Cr, Ni, Cu, Zn, Cd, Pb, Hg, and As. The trophic transfer of these elements in aquatic and terrestrial food chains/webs has important implications for wildlife and human health. It is very important to assess and monitor the concentrations of potentially toxic heavy metals and metalloids in different environmental segments and in the resident biota. A comprehensive study of the environmental chemistry and ecotoxicology of hazardous heavy metals and metalloids shows that steps should be taken to minimize the impact of these elements on human health and the environment.

1. Introduction

Environmental pollution is one of the major challenges in the modern human society [1]. Environmental contamination and pollution by heavy metals is a threat to the environment and is of serious concern [2, 3]. Rapid industrialization and urbanization have caused contamination of the environment by heavy metals, and their rates of mobilization and transport in the environment have greatly accelerated since 1940s [4, 5]. Their natural sources in the environment include weathering of metal-containing rocks and volcanic eruptions, while principal anthropogenic sources include industrial emissions, mining, smelting, and agricultural activities like application of pesticides and phosphate fertilizers. Combustion of fossil fuels also contributes to the release of heavy metals such as cadmium (Cd) to the environment [6]. Heavy metals are persistent in the environment, contaminate the food chains, and cause different health problems due to their toxicity. Chronic exposure to heavy metals in the environment is a real threat to living organisms [7].

Metal concentrations above threshold levels affect the microbiological balance of soils and can reduce their fertility [8]. Bioaccumulation of toxic heavy metals in biota of the riverine ecosystems may have adverse effects on animals and humans [9]. Higher levels of heavy metals in biota can have negative effects on the ecological health of aquatic animal species and may contribute to declines in their populations [10]. Heavy metals are strong neurotoxins in fish species. The interaction of heavy metals with chemical stimuli in fish may interrupt the communication of fish with their environment [11]. Heavy metals have been found associated with fish deformities in both natural populations and in the laboratory. Generally, such deformities have negative effects on fish populations because deformities affect their survival, growth rates, welfare, and external image. These deformities in fish can serve as excellent biomarkers of environmental heavy metal pollution [12]. Hartl [13] remarks that "metals, of natural or anthropogenic origin, are ubiquitous in the aquatic environment, and therefore understanding their behavior and interaction with aquatic organisms, particularly fishes, a major source of protein for human consumption, is of a great socioeconomic importance."

This article comprehensively reviews the different aspects of heavy metals as hazardous materials with a special focus on their environmental persistence, toxicity for living organisms, and bioaccumulative potential. The bioaccumulation of these elements and its implications for human health are discussed with a special coverage on fish, rice, and tobacco. The article will serve as a valuable educational resource for both undergraduate and graduate students and for researchers in environmental sciences.

2. Metals and Their Essentiality for Life

Chemically, metals are defined as "elements, which conduct electricity, have a metallic luster, are malleable and ductile, form cations, and have basic oxides" [14]. Terms usually used in relation to metals in biological and environmental studies are metal, metalloid, semimetal, light metal, heavy metal, essential metal, beneficial metal, toxic metal, abundant metal, available metal, trace metal, and micronutrient [15]. Metals have very diverse applications and play an important role in the industry-dominated human society. Some metals have critically important physiological and biochemical functions in biological systems, and either their deficiency or excess can lead to disturbance of metabolism and therefore to various diseases. Some metals and metalloids are essential for (biological) life. They play important physiological and biochemical roles in the body as they may be part of biomolecules such as enzymes, which catalyze biochemical reactions in the body.

2.1. Heavy Metals (HMs). According to Csuros and Csuros [16], a heavy metal is defined as "a metal with a density greater than 5 g/cm^3 (i.e., specific gravity greater than 5)." According to Duffus [15], "the term "heavy metals" is often used as a group name for metals and semimetals (metalloids) that have been associated with contamination and potential toxicity or ecotoxicity." Very recently, we have proposed a broader definition for the term, and heavy metals have been defined as "naturally occurring metals having atomic number greater than 20 and an elemental density greater than 5 $g{\cdot}cm^{-3}$" [17].

2.2. Essential and Nonessential HMs. Regarding their roles in biological systems, heavy metals are classified as essential and nonessential. Essential heavy metals are important for living organisms and may be required in the body in quite low concentrations. Nonessential heavy metals have no known biological role in living organisms. Examples of essential heavy metals are Mn, Fe, Cu, and Zn, while the heavy metals Cd, Pb, and Hg are toxic and are regarded as biologically nonessential [18–21]. The heavy metals Mn, Fe, Co, Ni, Cu, Zn, and Mo are micronutrients or trace elements for plants. They are essential for growth and stress resistance as well as for biosynthesis and function of different biomolecules such as carbohydrates, chlorophyll, nucleic acids, growth chemicals, and secondary metabolites [22]. Either deficiency or excess of an essential heavy metal leads to diseases or abnormal conditions. However, the lists of essential heavy metals may be different for different groups of organisms such as plants, animals, and microorganisms. It means a heavy metal may be essential for a given group of organisms but nonessential for another one. The interactions of heavy metals with different organism groups are much complex [23].

2.3. Environmentally Relevant Most Hazardous HMs and Metalloids. Heavy metals are among the most investigated environmental pollutants. Almost any heavy metal and metalloid may be potentially toxic to biota depending upon the dose and duration of exposure. Many elements are classified into the category of heavy metals, but some are relevant in the environmental context. List of the environmentally relevant most toxic heavy metals and metalloids contains Cr, Ni, Cu, Zn, Cd, Pb, Hg, and As [24]. Heavy metal pollutants most common in the environment are Cr, Mn, Ni, Cu, Zn, Cd, and Pb [25]. In 2009, China has suggested four metals, i.e., Cr, Cd, Pb, Hg, and the metalloid As, as the highest priority pollutants for control in the "12th 5-year plan for comprehensive prevention and control of heavy metal pollution" [26]. Some other heavy metals are also hazardous to living organisms depending upon dose and duration of exposure. For example, Mansouri et al. [27] have found Ag as more toxic than Hg to a freshwater fish.

2.4. Sources of Heavy Metals in the Environment. Sources of heavy metals in the environment can be both natural/geogenic/lithogenic and anthropogenic. The natural or geological sources of heavy metals in the environment include weathering of metal-bearing rocks and volcanic eruptions. The global trends of industrialization and urbanization on Earth have led to an increase in the anthropogenic share of heavy metals in the environment [28]. The anthropogenic sources of heavy metals in the environment include mining and industrial and agricultural activities. These metals (heavy metals) are released during mining and extraction of different elements from their respective ores. Heavy metals released to the atmosphere during mining, smelting, and other industrial processes return to the land through dry and wet deposition. Discharge of wastewaters such as industrial effluents and domestic sewage add heavy metals to the environment. Application of chemical fertilizers and combustion of fossil fuels also contribute to the anthropogenic input of heavy metals in the environment. Regarding contents of heavy metals in commercial chemical fertilizers, phosphate fertilizers are particularly important.

In general, phosphate fertilizers are produced from phosphate rock (PR) by acidulation. In the acidulation of single superphosphate (SSP), sulfuric acid is used, while in acidulation of triple superphosphate (TSP), phosphoric acid is used [29]. The final product contains all of the heavy metals present as constituents in the phosphate rock [30]. Commercial inorganic fertilizers, particularly phosphate fertilizers, can potentially contribute to the global transport of heavy metals [31]. Heavy metals added to agricultural soils through inorganic fertilizers may leach into groundwater and contaminate it [29]. Phosphate fertilizers are particularly rich in toxic heavy metals. The two main pathways for transfer of toxic heavy metals from phosphate fertilizers to the human body are shown below [29]:

(i) Phosphate rock ⟶ fertilizer ⟶ soil ⟶ plant ⟶ food ⟶ human body

(ii) Phosphate rock ⟶ fertilizer ⟶ water ⟶ human body

Combustion of fossil fuels in industries, homes, and transportation is an anthropogenic source of heavy metals. Vehicle traffic is among the major anthropogenic sources of heavy metals such as Cr, Zn, Cd, and Pb [32]. Higher concentrations of environmentally important heavy metals have been reported in soils and plants along roads in urban and metropolitan areas. Regarding anthropogenic sources of heavy metals, emissions from coal combustion and other combustion processes are very important [5]. During coal combustion, Cd, Pb, and As are partially volatile, while Hg is fully volatile. In China, combustion of coal is one of the major sources of atmospheric emissions of hazardous trace elements [33]. Table 1 lists some environmentally important data for eight key hazardous trace elements (HTEs), of prime environmental concern, in Chinese coals.

The anthropogenic sources of Cr include electroplating industries, leather tanneries, textile industries, and steel industries [34]. Globally, about 50,000 t/year of Cr may be emitted from coal combustion, wood burning, and refuse incineration [5]. Fertilizers also usually contain significant contents of Cr [35]. Globally, about 60,000 t/year of Ni may be generated from coal combustion; its greater portion remains in the ash [5]. The natural sources of Cd in the environment are volcanic action and weathering of rocks, whereas an anthropogenic source is nonferrous metal mining, especially processing of Pb-Zn ores [36]. Globally, about 7,000 t/year of Cd may be emitted from coal combustion, and sewage sludge incineration is also a source of Cd [5]. Anthropogenic increases in Cd concentrations are also caused by excessive application of chemical fertilizers [37]. P-containing fertilizers contain Cd as a contaminant at concentrations ranging from trace quantities to 300 ppm on dry weight basis and hence may be a main source of input of this metal to agricultural systems [38]. Pb is released to the environment from different sources including acid batteries, old plumbing systems, and lead shots used for hunting of game birds. Combustion of leaded gasoline is also a source of Pb in the environment. Although use of the tetraethyl lead as an antiknock agent in gasoline has been banned, it is still used in some developing regions of the world.

3. Contamination of Natural Waters, Sediments, and Soils by Heavy Metals

Toxic trace metals pose an important threat to both aquatic and terrestrial ecosystems [39]. After release from both natural and anthropogenic sources, heavy metals contaminate natural water bodies, sediments, and soils. Heavy metals released into the atmosphere in volcanic eruptions and in different industrial emissions also ultimately return to the land and cause contamination of waters and soils. Since heavy metals are persistent in the environment, they either accumulate in biota or leach down into ground waters. Contamination of biota and groundwater with potentially toxic heavy metals has important implications for human health. It is important to assess the degree of heavy metal pollution in riverine ecosystems by investigating the concentrations of these elements and their distribution [40]. Figure 1 shows a conceptual schematic of contamination of an aquatic (riverine) ecosystem with heavy metals. Different physicochemical and climatic factors affect the overall dynamics and biogeochemical cycling of heavy metals in the environment.

3.1. Water. It is said that water is the "life-blood of the biosphere." Since water is a universal solvent, it dissolves different organic and inorganic chemicals and environmental pollutants. Aquatic ecosystems, both freshwater and marine, are vulnerable to pollution. Contamination of water resources by heavy metals is a critical environmental issue which adversely affects plants, animals, and human health [41]. Heavy metals are extremely toxic to aquatic organisms even at very low concentrations [42]. These elements can cause significant histopathological alterations in tissues of aquatic organisms such as fish [43]. Aquatic ecosystems are contaminated by heavy metals from different sources. One source of heavy metals in the aquatic ecosystems is effluents from mining operations [44]. Other sources of water contamination with heavy metals include different industrial effluents, domestic sewage, and agricultural run-off. The release of industrial effluents without treatment into the aquatic bodies is a major source of pollution of surface and groundwater water [45]. Pollution of water bodies with heavy metals is a worldwide

Table 1: Some environmentally important data for key hazardous trace elements (HTEs), of prime environmental concern, in Chinese coals [33].

Element	Simulated mean conc. (ppm)	Emissions from coal use in China in 2007 (t)
Cr	30.37	8217.8
Ni	17.44	2308.4
Cd	0.61	245.4
Pb	23.04	12547.0
Hg	0.20	305.9
As	5.78	2205.5
Se	3.66	2353.0
Sb	2.01	546.7

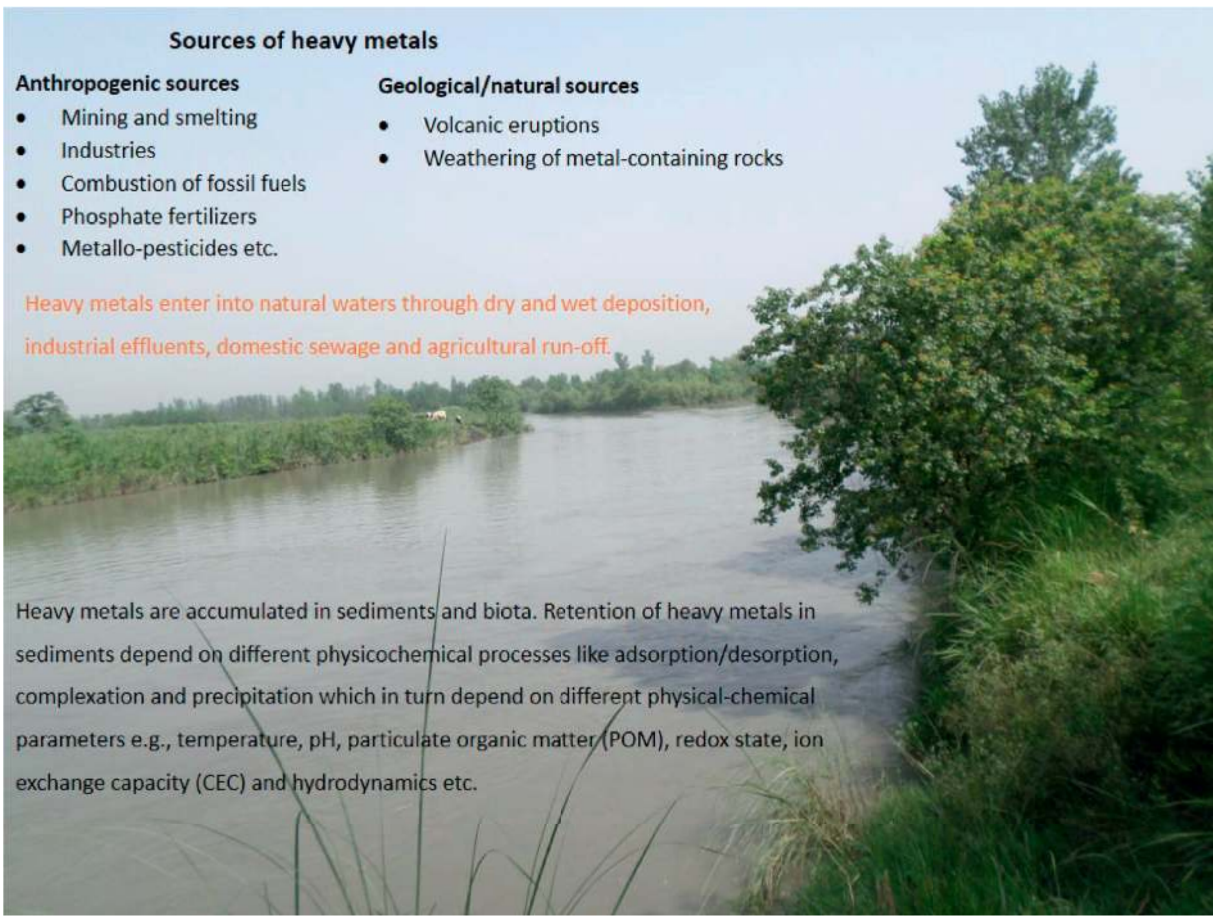


Figure 1: Schematic showing contamination of a river with heavy metals.

problem because of the environmental persistence, bioaccumulation, and biomagnification in food chains and toxicity of these elements [46].

3.2. Sediments. Contamination of sediments with heavy metals is an environmentally important issue with consequences for aquatic organisms and human health. Sediments act as the main pool of metals in the aquatic environment. Their quality can indicate the status of water pollution [47]. Sediments serve as both sink and source of heavy metals, releasing them into the water column [48]. Continuing deposition of heavy metals in sediments can also lead to contamination of groundwater with these pollutants [49]. The adsorption, desorption, and subsequent concentrations of heavy metals in sediments are affected by many physicochemical factors such as temperature, hydrodynamic conditions, redox state, content of organic matter and microbes, salinity, and particle size [50]. Distribution of heavy metals in sediments is affected by chemical composition of the sediments, grain size, and content of total organic matter (TOM) [51]. An important determinant of metal bioavailability in sediments is pH. A lowering in pH increases the competition between metal ions and H^+ for binding sites in sediments and may result in dissolution of metal complexes, thereby releasing free metal ions into the water column [52]. Higher concentrations of toxic heavy metals in riverine sediments may pose ecological risk to benthos (bottom-dwelling organisms) [53].

3.3. Soils. Heavy metals and metalloids are released into soils from the parent material (lithogenic source) and different anthropogenic sources [54]. Factors affecting the presence and distribution of heavy metals in soils include composition of parent rock, degree of weathering, and physical, chemical, and biological characteristics of soil and climatic conditions [55]. Significant enrichment of heavy metals has been reported in soils receiving more input of fertilizers and Cu fungicide compared to virgin soils and soils receiving low inputs [56]. In urban areas, soils may be contaminated with heavy metals from heavy vehicular traffic on roads. Soil samples in urban areas have elevated concentrations of Pb, out of which 45–85% is bioaccessible [57]. The bioavailability of heavy metals in soils is very important for their fate in the environment and for their uptake in plants. Different heavy metals have different bioavailabilities in soils, and this bioavailability is dependent on metal speciation and on different physicochemical properties of soils.

4. Heavy Metals as Hazardous Materials

Heavy metals are considered as hazardous chemicals in the environment. Nonessential heavy metals are toxic to plants, animals, and humans at very low concentrations. Even the essential heavy metals also cause adverse health effects at high concentrations [58]. Procedures developed for hazard identification of chemical contaminants in the aquatic environments consider three characteristic features: persistence, bioaccumulation, and toxicity (Figure 2). Toxic substances which are both persistent and bioaccumulative are more hazardous [59].

Toxicity refers to the property of a chemical to affect survival, growth, and reproduction of an organism. Certain heavy metals have been reported to be carcinogenic, mutagenic, and/or teratogenic to different species depending on dose and duration of exposure. Heavy metals affect both wildlife and human health. Some species are more sensitive to heavy metals than others. The mechanisms by which heavy metals affect different organs, tissues, and systems in different organisms are very complex, and so far some of them are not fully explored. Exposure of the bivalve *Anodonta anatina* to Cd has been found to affect carbonic anhydrase (CA) in its tissues, an enzyme playing a role in osmoregulation and Ca metabolism [60]. Cd has been considered as one of the factors likely responsible for the decline in populations of freshwater mussels due to its high toxicity, bioaccumulation potential, and transfer through food chains [61].

5. Trophic Transfer of Heavy Metals

Since heavy metals are persistent in the environment, they accumulate in living organisms and are transferred from one trophic level to another in the food chains. The extent of accumulation of heavy metals in biota depends on their rate of accumulation and their rate of elimination from the body. Thus, different heavy metals have different half lives in different species.

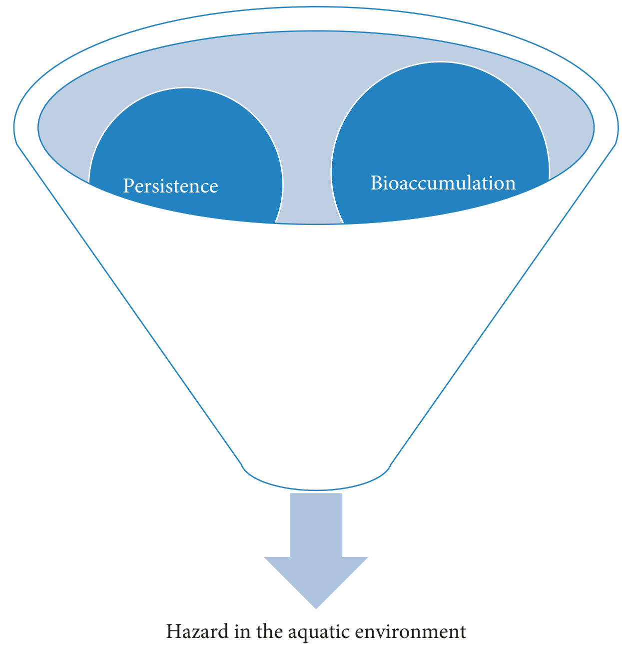


Figure 2: Hazard of a substance in the aquatic environment is a function of its persistence, bioaccumulation, and toxicity (PBT).

Heavy metals may enter the body of an organism directly from the abiotic environment, i.e., water, sediments, and soil or may enter the organism body from its food/prey. For example, heavy metals may enter the fish body directly from water or sediments through the fish gills/skin or from the fish food/prey through its alimentary canal. The concentration of a heavy metal may increase or decrease along successive trophic levels in a food chain. The retention of heavy metals in the body of an organism depends on many factors such as the speciation of the metal concerned and the physiological mechanisms developed by the organism for the regulation, homeostasis, and detoxification of the heavy metal. Methylated forms of heavy metals such as Hg are accumulated in biota to a greater extent and therefore biomagnified in food chains due to their lipophilicity. Certain plants have the ability to thrive on metal-rich habitats and are called metallophytes. These special plants have developed special mechanisms for coping with higher heavy metal concentrations in soil and are divided into three categories, i.e., excluders, indicators, and hyperaccumulators. Certain terms are used to describe the trophic transfer of heavy metals (Figure 3) (for details, refer [62]).

6. Heavy Metal Transfer from Soil to Plant

The soil-to-plant transfer of heavy metals is a very important step in the trophic transfer of such metals in food chains. These metals are taken up by plants from polluted soil and subsequently transferred to herbivorous animals along the food chain [63]. Regarding contamination of the human food chain, contamination of crops such as cereals and vegetables is a very serious issue. Consumption of cereals contaminated with toxic heavy metals may cause risk to human health [64]. Heavy metals in higher concentration ranges have been reported in vegetables grown with

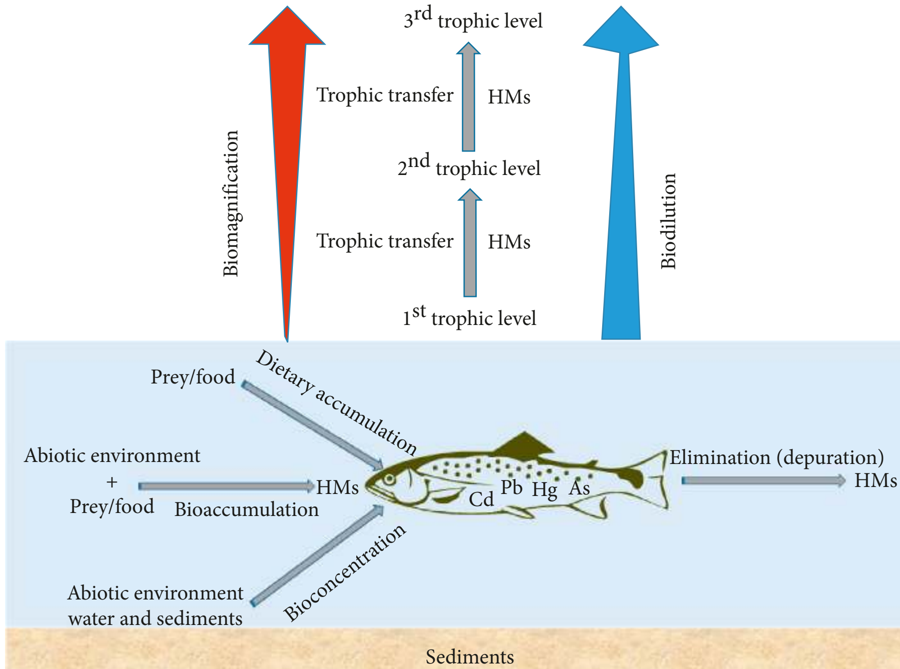


FIGURE 3: Schematic summarizing terms and concepts involved in trophodynamics of heavy metals ([62], used with permission of Tailor and Francis).

wastewaters compared to those grown with groundwater. Furthermore, higher concentrations of these metals have been found in leafy vegetables compared to those in other types of vegetables such as bulbs and tubers [65].

7. Quantification of Trophic Transfer of Heavy Metals

Certain terms have been used to quantify the degree or extent of accumulation of heavy metals in biota. Some of these quantitative terms are bioconcentration factor (BCF), bioaccumulation factor (BAF), bioaccumulation coefficient (BAC), etc. Some of these terms are discussed below.

7.1. Bioconcentration Factor (BCF). BCF is indicative of the degree of enrichment of a heavy metal in an organism relative to that in its habitat. It is defined as "the ratio of the concentration of a heavy metal in an organism tissue to its concentration in the abiotic medium (water and sediments)." It is calculated by the following equation:

$$\mathrm{BCF} = \frac{C_{\text{organism tissue}}}{C_{\text{abiotic medium}}}, \quad (1)$$

where C_{organism} is the metal concentration in the organism tissue and $C_{\text{abiotic medium}}$ is the metal concentration in the abiotic medium.

Some authors use the alternative terms transfer factor (TF), metal transfer factor (MTF), accumulation factor (AF), bioaccumulation factor (BAF), and biota-sediments accumulation factor (BSAF) and calculate them accordingly. However, all these indices show the magnitude of accumulation of a heavy metal in the organism relative to that in the environment where it grows/lives.

7.2. Bioaccumulation Coefficient (BAC). BAC is calculated by the following equation [66]:

$$\mathrm{BAC} = \frac{C_{\text{plant}}}{C_{\text{soil}}}, \quad (2)$$

where C_{plant} is the metal concentration in plant and C_{soil} is the metal concentration in soil.

It is evident that the values of BCF, BAF, BAC, etc. depend on the concentration of the heavy metal in the organism and in the concerned environmental medium. Since the values of these indices are inversely related to the metal concentration in the environmental medium (water, sediments, and soil), the values of these indices should be used with caution for assessment of heavy metal contamination in biota. For example, the BCF value for a heavy metal in muscles of a fish dwelling in less contaminated water may be higher than for the fish dwelling in more contaminated water simply because of the lower metal concentration in the habitat of the former fish. It has been reported that bioconcentration factor (BCF) values of seven typical heavy metals in crop grains decreased exponentially with average concentrations of the metals in soil [67].

8. Bioaccumulation of Heavy Metals in Biota

Since heavy metals are persistent in the environment, they enter from the environment to the organisms and accumulate therein. As mentioned earlier, the uptake and bioaccumulation of heavy metals in biota depend on several factors. For example, the uptake of heavy metals in plants depends on bioavailability of the metal in soil, which in turn depends on several factors such as metal speciation, pH, and organic matter contents in soil. Metals which are more bioavailable in soil may be accumulated in plants more easily and thus will have more bioaccumulation potential. An assessment of bioaccumulation of heavy metals in plants may be used for an estimation of bioavailability of the metals in soil. Such an assessment may also be used for knowing the contamination status of the environment. It has been reported that plants seem to be more sensitive to environmental changes than soils [68]. Different plant species have been suggested as bioindicators of heavy metal pollution in the environment. Different animal species have also been suggested as bioindicators of heavy metal pollution. For example, the date mussel (*Lithophaga lithophaga*) has been suggested as a valid bioindicator of marine pollution [69].

Bioaccumulation of heavy metals in biota is important from environmental, ecological, and human health point of view and has important implications for wildlife and human health. Contamination of aquatic and terrestrial food chains with potentially toxic heavy metals poses a threat to the health of consumer organisms including humans. In aquatic ecosystems, organisms are simultaneously exposed to different metals, which may have additive, synergistic, or antagonistic interactions [70]. The topic of bioaccumulation of heavy metals in biota is a very broad topic. Here, the discussion of the topic will be limited to bioaccumulation of heavy metals in fish and rice, which serve as the major dietary sources of heavy metal exposure for the general human population. Additionally, bioaccumulation of heavy metals in cigarette tobacco will also be discussed as tobacco smoke acts as an additional source of heavy metal exposure for the smoking human population.

9. Bioaccumulation of Heavy Metals in Freshwater Fish

Aquatic biota is exposed to heavy metals through different routes such as water, sediments, and food [71]. Freshwater fish are exposed to different toxic heavy metals released to freshwater bodies from different natural and anthropogenic sources. Contamination of fish by heavy metals has become an important global issue because it presents a threat to fish and poses health risks to fish consumers [72]. Assessment of heavy metal bioaccumulation in fish species of different aquatic habitats is very important [73]. Assessment of heavy metal levels in fish tissues is essential for aquatic ecosystem management and human consumption of fish [74]. Fish have high levels of unsaturated fatty acids and low levels of cholesterol. They are an important source of proteins [75]. Use of an edible fish in human diet is beneficial and therefore recommended in balanced diet. However, contamination of fish by toxic heavy metals is considered as a risk for human health and has raised concerns about their consumption especially in more sensitive groups of human population such as women, children, and people at risk of diseases from other causes.

The bioaccumulation of heavy metals in freshwater fish depends on various factors, both fish characteristics and external environmental factors. Factors related to fish include fish age, size (weight and length), feeding habits, and body physiology, while external environmental factors include concentration and bioavailability of metals in the water column, physicochemical properties of water, and other climatic factors. The degree of accumulation of heavy metals in different tissues of fish is generally different depending on the structure and function of tissues. Generally, metabolically active tissues such as gills, liver, and kidneys have higher accumulations of heavy metals than other tissues such as skin and muscles. The comparatively higher heavy metal accumulation in metabolically active tissues of fish is generally explained by the induction/occurrence of metal-binding proteins called metallothioneins (MTs) in these tissues upon exposure to heavy metals. Fish gills have been found as the target tissue for accumulation and elimination of heavy metals such as Ni [76]. Although fish muscles are the tissue of poor heavy metal accumulation [77], they are important from the view point of consumption by humans. Bioaccumulation of trace metals in muscles of fish is generally species specific [78]. Most studies on bioaccumulation of heavy metals in fish have investigated metal concentrations in fish muscles because this tissue is edible and is the most relevant regarding human health.

Bioaccumulation of toxic heavy metals in freshwater fish has important environmental, ecological, and social consequences; it has implications for humans and other fish consuming carnivorous wildlife [79–83]. Waterborne heavy metals are incorporated in fish and enter the human body through the food chain and therefore have impact on human health [84]. Furthermore, toxic heavy metals also affect fish health and well-being. It has been reported that pollution of river with heavy metals-containing wastewater induced stress in the freshwater fish *Channa punctatus*, making it weak and more vulnerable to diseases [85]. Heavy metal pollution is regarded as one of the possible causes for population declines of freshwater fish and other aquatic species in freshwater ecosystems. It has been reported that increased contamination in River Indus, Pakistan, has caused decline in the number and diversity of freshwater fish and other aquatic species in this river [86].

10. Bioaccumulation of Heavy Metals in Rice (*Oryza sativa*)

Rice is a very important human food and is the staple food in Asian countries especially in South Asia and China. Contamination of rice fields with toxic heavy metals leads to bioaccumulation of these elements in the rice plant. The translocation of heavy metals from roots of the rice plant to stem, leaves, and rice grains is of human health concern. Rice crop is especially susceptible to heavy metal contamination because it needs water during most of its growth period. The trace elements, Cd, Pb, Hg and As, are ubiquitous in the environment with harmful effects on human health. Regarding their presence in rice as a public health concern, As is on top followed by Cd [87]. Human intake of Cd has been reported to be highest through consumption of rice [88]. Contamination of rice with toxic heavy metals is especially a health concern in developing countries [89].

Irrigation of agricultural soils with wastewater is a widespread practice in developing countries, which results in elevated uptake of metals in crops. Elevated levels of heavy metals in crops affect food quality and pose health risks to the consumers [90]. Application of phosphate fertilizers rich in Cd can also lead to Cd contamination in rice fields [91]. For the general population, consumption of rice may be a potential exposure source of toxic heavy metals, particularly Cd, Pb, and As [92]. Long-term consumption of rice grown on polluted areas may cause potential health hazards to the consumers [93]. Efforts are being made to minimize uptake through roots and translocation to grains of toxic heavy metals especially Cd in rice. Genetic engineering is used as an approach to achieve this goal, and some transgenic rice varieties have been developed to meet the challenge.

11. Bioaccumulation of Heavy Metals in Tobacco (*Nicotiana tabacum*)

Bioaccumulation of toxic heavy metals in cigarette tobacco is a human health concern because tobacco leaves are used for making cigarettes. Tobacco plants naturally accumulate relatively high concentrations of heavy metals in their leaves, and the metal bioaccumulation in tobacco leaves varies with the geographical origin of the tobacco plants [94]. Tobacco crop is grown with application of commercial inorganic fertilizers especially phosphate fertilizers, which contain considerable concentrations of some toxic heavy metals. During growth, uptake of heavy metals by tobacco roots is considerable and the same are translocated from soil to leaves. During cigarette smoking, a fraction of heavy metals is inhaled in the smoke and thus reaches the lungs of the smoker. Tobacco smoke, both mainstream and side stream, is an important source of environmental metal exposure. Passive smoking has an important contribution in the exposure of children to Pb [95]. Heavy metals inhaled during tobacco smoking are easily absorbed in the body from the lungs and reach the blood from where they may reach other parts of the body. Higher levels of toxic heavy metals have been reported in blood of cigarette smokers compared to that of nonsmokers.

As stated by Dissanayake and Chandrajith [29], the application of inorganic fertilizers in agriculture has unfortunately become a "necessary evil." Since commercial chemical fertilizers are usually not purified enough during the manufacturing processes, they usually contain heavy metals as impurities [96]. Much of the phosphate fertilizers in the world are commercially produced from phosphate rocks that contain the mineral apatite [$Ca_5(PO_4)_3OH$,F,Cl]. Due to their geological and mineralogical nature, phosphate rocks contain different environmentally hazardous elements including Cr, Cd, Pb, Hg, As, and U. Application of chemical fertilizers leads to increase in the concentrations of these potentially toxic heavy metals in agricultural soils [97]. A high correlation has been reported between concentrations of metals, i.e., Cr, Ni, Cd, and Pb and content of phosphate in fertilizers [98]. A study investigating concentrations of Cr, Mn, Fe, Ni, Cu, Zn, Sn, Cd, Pb, and As in tobacco products in the UK has concluded that overapplication of phosphate/nitrate fertilizers is the most likely cause of their transfer to these products [99]. However, Bozhinova [100] reported a limited impact of application of phosphate fertilizers on accumulation of Ni, Cu, Cd, and Pb in soil and tobacco plants. In summary, the addition of toxic heavy metals from long-term application of phosphate fertilizers to agricultural soils and their subsequent transfer to the human food chain is a matter of great concern with respect to human health, especially in case of low-quality phosphate fertilizers containing elevated levels of heavy metals.

12. Human Exposure to Heavy Metals

Humans are exposed to toxic heavy metals in the environment through different routes including ingestion, inhalation, and dermal absorption. People are more exposed to toxic metals in developing countries [101]. Generally, people have no awareness and knowledge about exposure to heavy metals and its consequences for human health, especially in the developing countries [102]. People may be exposed to heavy metals in the work place and in the environment. Human exposure to toxic chemicals in the work place is called occupational exposure while exposure to such chemicals in the general environment is called non-occupational or environmental exposure. Workers are exposed to heavy metals in mining and industrial operations where they may inhale dust and particulate matter-containing metal particles. People extracting gold through the amalgamation process are exposed to Hg vapors. It has been reported that welders with occupational prolonged exposure to welding fumes had significantly higher levels of the heavy metals Cr, Ni, Cd, and Pb in blood than the control and showed increased oxidative stress [103]. Cigarette smoking is also a principal source of human exposure to Cd [104] and other toxic heavy metals present in the tobacco leaves.

Ingestion of heavy metals through food and drinking water is a major exposure source for the general human population. Industrialization, urbanization, and the rapid economic development around the globe have led to intensification in industrial and agricultural activities. Such activities may cause contamination of water, air, and soils with toxic heavy metals. Growing human foods in heavy metal-contaminated media lead to bioaccumulation of these elements in the human food chains from where these elements ultimately reach the human body.

13. Bioaccumulation and Biomagnification of Heavy Metals in the Human Food Chains

Humans are omnivorous. They may be exposed to toxic heavy metals through different food items such as fish, cereals, and vegetables. Heavy metal contamination in freshwater bodies such as rivers, lakes, and streams leads to bioaccumulation of these elements in freshwater fish, while such contamination in agricultural lands leads to bioaccumulation of these elements in agricultural crops. Contamination of the human food chains with toxic heavy metals poses a threat to human health. Certain examples from the twentieth century have shown that such contamination is a serious human health issue. Minamata disease (MD) and *itai-itai* disease both in Japan were caused by consumption of Hg-contaminated fish and Cd-contaminated rice, respectively. Figure 4 depicts the transfer of heavy metals from contaminated fish to humans.

Although biomagnification of heavy metals is a controversial issue in metal ecotoxicology, numerous studies have reported biomagnification of heavy metals in certain food chains. In case of biomagnification of these metals in food chains, organisms at higher trophic levels in the food chains are at greater risk. Higher concentrations of trace metals in organisms of higher trophic levels as a result of biomagnification can pose health risk to these organisms or to their human consumers [105]. To protect human health from the harmful effects of toxic heavy metals, the human food chains should be constantly monitored for bioaccumulation and biomagnification of heavy metals. However, nondestructive sampling techniques and use of environmental biomarkers should be opted to avoid loss of biota due to analysis. Furthermore, in order to avoid contamination of food chains with heavy metals, untreated municipal and industrial wastewaters should not be drained into natural ecosystems such as rivers and farmlands [106].

14. Heavy Metal Toxicity

Although some heavy metals, called essential heavy metals, play important roles in biological systems, they are generally toxic to living organisms depending on dose and duration of exposure. It is a well-known fact in toxicology that "excess of everything is bad." Nonessential heavy metals (Cd, Pb, and Hg) and metalloids (As, etc.) may be toxic even at quite low concentrations. Essential heavy metals are required in trace quantities in the body but become toxic beyond certain limits or threshold concentrations. For some elements, the window of essentiality and toxicity is narrow. Heavy metals have been reported to be carcinogenic, mutagenic, and teratogenic. They cause generation of reactive oxygenic species (ROS) and thus induce oxidative stress. Oxidative stress in organisms leads to the development of various diseases and abnormal conditions. Heavy metals also act as metabolic poisons. Heavy metal toxicity is primarily due to their reaction with sulfhydryl (SH) enzyme systems and their subsequent inhibition, e.g., those enzymes involved in cellular energy production [16]. Figure 5 shows the reaction of a heavy metal (M) with glutathione (GSH), an important antioxidant in the body. Here, the metal replaces H atoms from SH groups on two adjacent glutathione molecules. The engagement of the two glutathione molecules in formation of strong bond with the metal deactivates them for further reactions:

$$2\ \text{glutathione} + \text{metal ion}\left(M^{2+}\right) \longrightarrow M\,(\text{glutathione})_2 + 2H^{+} \quad (3)$$

15. Effects of Toxic Heavy Metals on Human Health

The heavy metals Cd, Pb, Hg, and As deplete the major antioxidants of cells, particularly antioxidants and enzymes having the thiol group (—SH). Such metals may increase the generation of reactive oxygen species (ROS) like hydroxyl radical ($HO^{\cdot}$), superoxide radical ($O_2^{\cdot -}$), and hydrogen peroxide (H_2O_2). Increased generation of ROS can devastate the inherent antioxidant defenses of cells and lead to a condition called "oxidative stress" [108]. Heavy metals, including Cd, Pb, and Hg, are nephrotoxic, especially in the renal cortex [109]. The chemical form of the heavy metals is important in toxicity. Mercury toxicity largely depends on Hg speciation [110]. Relatively higher concentrations of toxic heavy metals, i.e., Cr, Cd, and Pb, and relatively lower concentrations of the antioxidant element Se have been found in patients of cancer and diabetes compared to those in the normal subjects in Lahore city, Pakistan [111].

16. Monitoring and Analysis of Heavy Metals in the Environment

Monitoring and analysis of heavy metal concentrations in the environment are necessary for pollution assessment and control [112]. The levels/concentrations of potentially toxic metals and metalloids should be regularly monitored in the different environmental media such as water, sediments, and soils as well as in the resident biota. Such environmental analysis will provide useful information about distribution, principal sources, and fate of these elements in the environment and their bioaccumulation in the food chains. Such analysis is also used to assess the risk posed by these elements to wildlife and human health.

17. Use of Bioindicators and Biomarkers for Assessment of Heavy Metal Pollution

Regarding the use of bioindicators for monitoring and assessment of heavy metal pollution, Morgan [113] summarizes that "a more meaningful assessment of the impact of metal pollution may be obtained by measuring metal concentrations in selected species of the resident biota." Different plant and animal species have been used as biological indicators or bioindicators to assess and monitor heavy metal contamination and pollution in the environment. Different environmental biomarkers are also used to assess and monitor pollution pertaining to heavy metals in the environment.

18. The Nature and Scope of Studies on Heavy Metals in the Environment

Environmental studies on different aspects of heavy metals and metalloids are interdisciplinary in nature and require background knowledge in environmental chemistry, ecotoxicology, and ecology. Analysis of xenobiotics such as

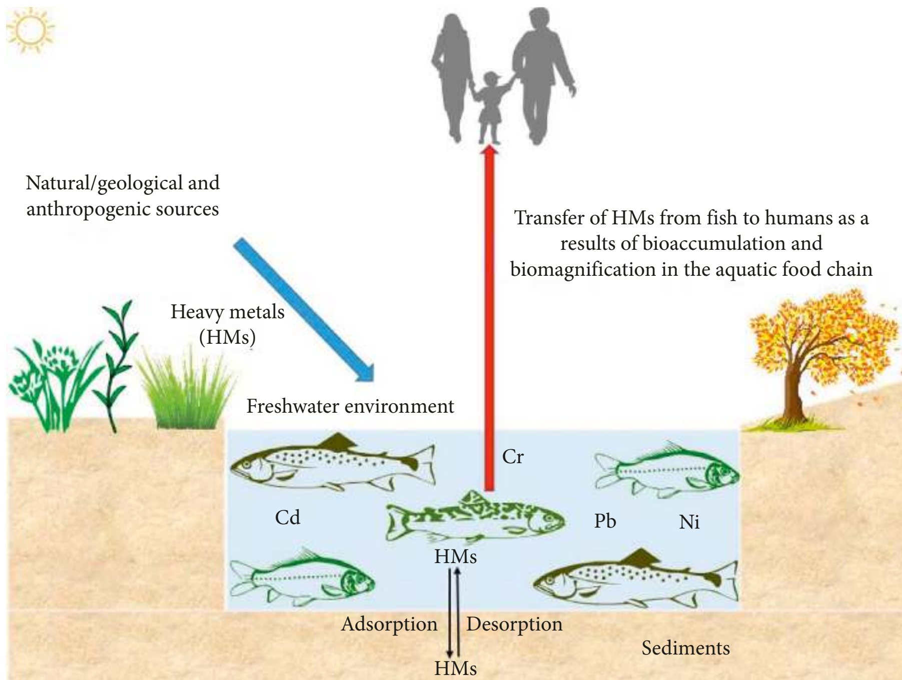
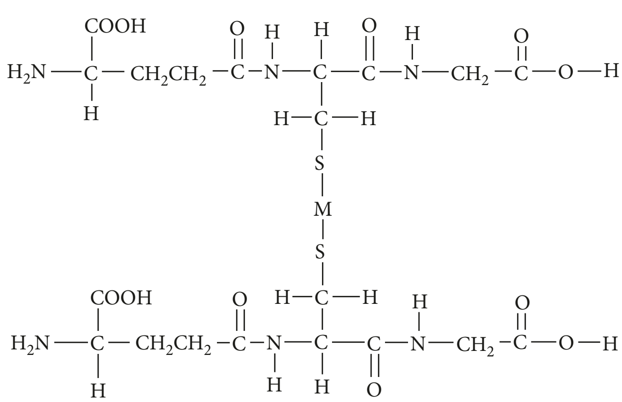


FIGURE 4: Trophic transfer of heavy metals from freshwater fish to humans in the human food chain.



Metal-glutathione complex

FIGURE 5: Reaction of a metal with glutathione (adapted from [107]).

toxic heavy metals in food chains is an important study area and has environmental, ecological, and economic importance. It has a scope for public health. Such studies involve aquatic chemistry, which has a scope for public health as remarked by Johnston [114]: "aquatic chemistry is a fundamental element of public health." Bioaccumulation data of toxic heavy metals in different biota such as fish and rice can be used for health risk assessment for the general human population.

19. Conclusions and Recommendations

Heavy metals and metalloids are ubiquitous environmental pollutants in both aquatic and terrestrial ecosystems. The hazard of an environmental chemical is a function of its environmental persistence, toxicity, and bioaccumulative potential. Toxic environmental chemicals which are persistent and bioaccumulative are more hazardous. Heavy metals are considered hazardous due to these three characteristics: persistence, bioaccumulation, and toxicity (PBT). Environmentally relevant most hazardous heavy metals and metalloids include Cr, Ni, Cu, Zn, Cd, Pb, Hg, and As. The trophic transfer of these elements in aquatic and terrestrial food chains/webs has important implications for wildlife and human health. It is very important to assess and monitor the concentrations of potentially toxic heavy metals and metalloids in different environmental segments as well as in the resident biota. A comprehensive study of the environmental chemistry and ecotoxicology of hazardous heavy metals and metalloids shows that steps should be taken to minimize the impact of these elements on human health and the environment. The following recommendations are made:

(i) Background concentrations of heavy metals and metalloids should be documented in the different environmental media around the world, for later use as a reference.

(ii) The levels of potentially toxic heavy metals and metalloids in water, sediments, soils, and the resident biota should be assessed and monitored regularly.

(iii) Regular surveys should be conducted to record the per capita daily consumption of freshwater fish and other food items such as rice by the resident population around the world. Such data will be valuable for a more accurate and reliable human and ecological risk assessment.

(iv) Efforts should be made to minimize heavy metal contamination in aquatic and terrestrial ecosystems to safeguard the biota and the health of their consumers.

(v) The public should be educated about the harmful effects of toxic heavy metals on human health and the environment.

(vi) Wastewaters from industries should be treated effectively before their discharge into the natural water bodies.

(vii) Scientific research on environmental assessment of toxic chemicals including toxic heavy metals and metalloids should be encouraged and promoted through allocation of appropriate funds for protecting human health and the environment.

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

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