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The Impact of Heavy Metals on Human Health: A Biochemical Perspective

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Annotation: Heavy metals (HMs) have become a major environmental issue because contamination of the ambient environment with HMs and other pollutants is continuously increasing due to the increasing progress in industrialization, urbanization and agricultural practices, which brings serious environmental threat to human health and ecosystem. Anthropogenic activities include mining, smelting, oil refining, landfill sites, the use of fossil fuels, industrial effluents, application of fertilizers, pesticides, herbicides, waste from chemical factories, and automotive, as well as the use of unlicensed land and groundwater. Accumulation of one or more HMs in an ecosystem, far beyond natural threshold limits, causes environmental pollution; this is of significance primarily because it leads to the degradation of air, water, and soil quality. With growing population, urbanization, and industrialization, increased undesirable exposure of human populations to HMs has been reported.

Major industries contributing HMs pollution include mining, steel production, sludge from sewage treatment plants, oil refining, electroplating, fertilizer manufacturing, battery manufacturing, textile dyeing and finishing, wood preservation, leather industries, and glass manufacturing.

Mercury (Hg), followed by arsenic (As), lead (Pb), chrome (Cr), and cadmium (Cd), was reported to be the most prevalent HMs causing toxicity in human biological systems today. These toxicants are widespread in air, drinking water, food, and soil. Non-essential HMs are toxic in extremely low concentrations and are shown to induce various deleterious alterations in tissues and organ systems. Poisonings of very broad spectrum can be acute (usually high exposure over a short period of time) or chronic (low exposure over an extended period of time), resulting in more subtle, long-term health effects. There may also be regional differences in types of poisoning, with endemic exposure from natural occurrences; these high exposures are often more easily quantifiable, even with ecological or soil data, and these models of exposure may also be used to predict health effects in similar populations quantitatively. In acute poisonings, HMs may cause direct toxicity in the tissues with extensive tissue damage.

1. Introduction

There is an increasing and notable interest in understanding individuals' exposure to heavy metals, primarily due to the rising concerns regarding human toxicity, the alarming rates of environmental pollution, and the associated risks of various metabolic disorders. Heavy metals, which include substances like mercury (Hg), cadmium (Cd), lead (Pb), chromium (Cr), and aluminum (Al), are unfortunately abundant in many sources including fresh food, packaged food items, beverages, a wide range of medicines, various personal care products, and even common home products. The presence of these heavy metals is linked to several detrimental health effects, as they contribute significantly to indicators of lipid peroxidation products, genetic mutations, and have the potential to interact with numerous different proteins found within the human body. In particular, heavy metals such as cadmium, chromium, iron, lead, and zinc have been identified as major contributors to human toxicity. They are associated with serious health conditions, including infertility, chronic diseases, immune system malfunctions, and alterations in DNA, along with a host of other health-related issues that can significantly impact individuals' lives. Given these serious implications, continuous screening and vigilant monitoring of environmental toxicity, especially regarding the presence of heavy metals in the human body, are considered absolutely vital in our health assessments. Therefore, exploring the presence of heavy metals—including chromium, aluminum, cadmium, lead, iron, zinc, copper, and manganese—in the hair, nails, and serum of females with varied dietary habits represents a novel and important area of investigation that holds promise for further understanding health risks associated with these toxic elements. [1] [2][3][4][5][6]

Mineral trace elements in hair, nails, and serum can significantly predict nutritional valued, risk of malnutrition, and predisposition to certain illnesses. An analysis of metals in hair can reflect the level of metals in the serum at the time the hair was grown. Hair and nails are long-term loaded with heavy metals and minerals. Human nails also reflect concentrations of the end productivity of metals and minerals in the metabolism that could lead to illness and risk of toxicity. Heavy metals, such as chromium, aluminum, cadmium, and lead, enter the human body in different ways, such as soil, water, fresh and manufactured food, fish, and beverages. Heavy metals react biologically in vivo with metal cations after losing electrons. Heavy metals cause acute or chronic diseases of different organ systems in the body. The highest exposure to heavy metals can result in fluoride-related gastrointestinal illness, nephrotoxicity, and carcinogenicity. The lowest exposure can result in neuropsychiatric issues, such as anxiety and chronic fatigue. [7][8][6][9]

2. Overview of Heavy Metals

Heavy metal (HM) ions output into the ecosystem from numerous natural and anthropogenic sources are being more and more prevalent and are a persistent environmental issue. Typically, heavy metals exist as metal ions which possess high atomic mass (and, hence, high density relative to other substances) and represent significant chemical elements in one or more oxidation states. Although many metals, among them essential trace elements such as Cu, Co, Zn and Fe, are necessary for the health of living organisms, they can be harmful to health once accumulated in excess due to their prolonged persistence in the body. In fact, many heavy metals have been noted to have toxic effects on organisms, most significantly on human health, following anthropogenic activities including agricultural and industrial practices as well as mining activities. Nowadays, due to the large-scale mechanization of the agriculture, mining and construction industries, as well as the economic development accompanied by the rapid urbanization and industrialization of cities, the industries generally release large quantities of toxic and recalcitrant wastes containing heavy metals into water, air, and soils, posing a hazard to human health and hence increasing the health concerns [10]. [7][11][12][13]

After release into the body, heavy metals can accumulate in various organs (e.g., the liver, kidney, brain, and hair) and interfere with cellular functions. The exact mechanisms on the toxicity of heavy metals vary with their characteristics and oxidation states. This review hence deals with the uptake and toxicity mechanisms associated with commonly encountered heavy metals that are believed to be ecotoxicologically important and known to elicit biological effects on a variety of organisms, especially humans. Heavy metals typically enter living organisms via three major routes: dermal, intravenous injection, inhalation and ingestion. Ingested heavy metals can be absorbed into the blood in the gastrointestinal tract along the mucosa and transported into systemic circulation. In metals enter the systemic circulation, they can be distributed to various organs (e.g., the bile, liver, kidney, hair, and bone tissue) via both the blood and lymphatic system. The metals are then excreted from the body into bile or urine. They can also accumulate within tissues due to gene mutations, which can induce neoplastic transformation and tumorigenicity in the long term. [7][8][13][9]

2.1. Definition and Classification

Heavy metals, which are defined as metals with a high atomic weight and a density greater than 5 g/cm^3, include many transitional metals and metalloids such as mercury (Hg), cadmium (Cd), lead (Pb), chromium (Cr), and arsenic (As) that lead to toxicity to living organisms. These metals are categorized into essential and non-essential heavy metals . Essential metals, which are utilized in various biochemical pathways through metallation resulting in functional proteins, include iron (Fe), cobalt (Co), zinc (Zn), copper (Cu), nickel (Ni), and manganese (Mn). These metals are of prime importance for human health owing to the biological role they perform. They exist in a non-toxic form in living organisms. However, higher concentrations due to anthropogenic activities lock these essential metals in bio-geochemical cycles leading to harmful effects on living systems. On the other hand, metals like lead, cadmium, aluminium, chromium, and mercury, which are non-essential metals for living organisms, are toxic in nature. These metals are released into the environment as the result of natural processes and anthropogenic activities such as petrifaction of metals, oxidation of ores, corrosion of metal usage, industrial waste disposal, mining activities, and application of metallic contaminants onto agricultural fields. Heavy metals tend to accumulate in the organism through inhalation, ingestion, and dermal routes leading to a myriad of pathological effects including carcinogenicity, teratogenicity, mutagenicity, immunotoxicity, and neurotoxicity. [14][8][11][12]

In higher doses, heavy metals induce cell death via apoptosis and necrosis. The impact of heavy metals varies between species and based on the form and route of exposure. Studies show that exposure to heavy metals often leads to the inhibition of protein and enzyme synthesis, denaturation of cellular proteins, gene mutations, lipid peroxidation of membranes, and inhibition of glucose uptake in the liver. The symptoms and effects are from the surface exposure and contain local skin irritation, dermatitis, burns, etc. Transportation to the bloodstream contains irritation of target organs—liver, kidney, brain, and irritation of respiratory systems, reproductive system (major cause of infertility), and immune system. These effects are both reliable and specific. Detection of heavy metal-induced pathogenesis markers is very crucial in terms of preventive health management. Metabolomics dietetic consideration allows identification of the impaired metabolic effect of excessive heavy metal exposure and predicts the possible actions of its heavy metal-induced pathogenesis. [15][9][13][7]

2.2. Sources of Heavy Metals

Heavy metals, which are biologically important elements, are often present in trace amounts in living organisms. Some of them, such as iron, copper, manganese, zinc, molybdenum, and vanadate, have been regarded as essential nutrients. However, some other non-essential metals like chromium and lead can cause toxic effects when their body burden exceeds a certain threshold [10]. Metallic and metalloid elements that exhibit metallic properties include heavy metals, which have a density of over 5 g cm-3. Several elements are recognized as heavy metals, with the most common being manganese, copper, zinc, nickel, cadmium, arsenic, chromium, mercury, and lead. Heavy metals are principally derived from terrestrial and geological sources, but their concentrations have spurred several anthropogenic activities, including mining, industrialization, urbanization, land reclamation, and agricultural runoff. Increased anthropogenic activities in and around mining sites have led to the concentration of heavy metals in the soil. [12][7][8]

Human beings can be exposed to heavy metals from air, water, food, soil, and recreational activities [1]. Heavy metals are transferred through the food web and have acute and chronic effects on human health. The extent of the effect depends on the metal's route of entry into the body, its bio-accessibility, and the environmental conditions governing its absorption, distribution, biotransformation, interaction, and elimination by the physiological systems. Heavy metals have a damaging effect on the central nervous system, liver, kidney, lung, and cardiovascular system, leading to associated diseases. Excess levels of heavy metals lead to possible morbidities and mortality. Genotoxic lesions caused by the activation of heavy metals involve various processes, among them, lipid peroxidation products such as malonyl dialdehyde, hydroxynonenal, and DNA-reactive aldehydes are generated, which can give rise to basic DNA damage leading to strand breaks. Heavy metals may also evoke genetic mutation by increasing the frequency of chromosomal aberrations and other cellular injuries. Interaction with different body proteins may lead to protein denaturation and damage, alteration of cellular morphology, and inhibition of enzymatic activities. [16][17]

3. Biochemical Mechanisms of Heavy Metal Toxicity

Heavy metals are of great public health concern because of their high toxicity, persistence in the food chain, accumulation in human tissues, and potential to cause cancer. As free-cations, metal ions acquire a net positive charge that allows them to interact with negatively charged functional groups (such as –COO, –OH, –NH) of large biological macromolecules, such as proteins, nucleic acids, and polysaccharides. This leads to the premature malfunctioning of biomolecules, inhibition of essential bioreactions, and apoptosis. As a result, it is possible to consider that metal cations are brought in contact with target biomolecules by diffusion and/or electroosmotic transport on cellular membranes [10]. When cadmium, lead, and mercury salts enter cells, they are taken up and transported through the cytoplasm in intracellular compartments, i.e., cytoplasmic vesicles, organelles. Following this transport, toxic effects gradually build up, often with a threshold, over time. [6]

The toxicity of metals is due to a biochemical mechanism of action that occurs at the discount of cellular redox state in a decreasing order of potency as follows: (i) binding to intracellular free thiols. A specific binding site for compounds such as heparin and polyphosphoinositides (PPIs) has not been elucidated yet. (ii) Blocking and inhibiting metallothionein activity. (iii) Inhibition and malfunctioning of enzymes containing a thiol cofactor. (iv) Oxidative stress, which in turn causes a secondary deregulation of protein sulphydryl status, etc. Each cation has a unique structural property and so different ligand interactions [18]. Cations with somewhat similar properties will have similar toxicity in a rank order that depends on their common properties. [19]

3.1. Cellular Uptake Mechanisms

Cellular uptake mechanisms of heavy metals influencing intracellular accumulation are reviewed for non-ionic, glutathione (GSH)-binding metals such as mercury, gold, and silver, as well as the ionic metals cadmium, zinc, lead, chromium, and copper. Globally, industrial production and use of metals are continuously rising at a notable pace, with per capita production double that of the past fifty years for cadmium, gold, lead, and silver, while the rate for mercury is even higher. GSH-binding metals operate on various cellular uptake mechanisms, depending on their physicochemical characteristics and cellular GSH levels. Diverse uptake routes, from bilayer diffusion to GSH transporters, are discussed. Besides, interactions of the acquired metals with cellular components and the resulting adverse effects are briefly examined [18].

Heavy metals, defined as metals with relatively high density, high atomic weight, or high atomic number, have been widely applied for industrial, domestic, agricultural, medical, and technological purposes. However, their applications can give rise to worrying environmental impacts, putting human health at risk. Human exposure routes of metals include inhalation, ingestion, and dermal contact through different environmental sources. Exposure to metals can cause various adverse health effects, including cancers, neurodegenerative diseases, reproductive and developmental disorders, and endocrine disruption. As a result, metals such as arsenic, cadmium, chromium, and nickel have been classified as Group 1 carcinogens by the International Agency for Research on Cancer [20].

Chromium (Cr) is a naturally occurring metal on the earth's crust that exists in various chemical states, including trivalent Cr (Cr) and hexavalent Cr (Cr). Trivalent Cr is an important micronutrient involved in carbohydrate, lipid, and protein metabolism, and Cr is used for producing various goods, including pigment manufacturing, painting, metal plating, wood treating, leather tanning, metallurgy, and refractory materials. However, toxicity of Cr depends on its chemical state; while Cr mainly originates from the earth's crust, it is mostly non-toxic. Nevertheless, salt form of trivalent and hexavalent Cr compounds may generate toxic dust upon the manufacture of Cr products. Hexavalent Cr is environmentally persistent and thus comes in contact with living systems through various exposure paths, inducing severe toxic effects such as carcinogenicity. [21][22]

3.2. Oxidative Stress Induction

Oxidative stress is loosely defined as a condition of impaired physiological balance between oxidative metabolism, oxygen supply to the cells, and the concentrations of antioxidant compounds. At the biochemical level, it reflects an imbalance of the dynamic physiological ratio of “oxidizing” and “reducing” processes related to low-molecular-weight cellular metabolites such as: (a) reactive oxygen species (ROS), by-products of oxidative metabolism derived mostly from the mitochondrial electron transport chain; (b) reduced and oxidized forms of nucleotide cofactors such as NADP(H) and NAD(H) which are involved in the redox cycling of water-soluble species; (c) soluble thiols such as GSH and cysteine, and thioredoxins and their disulfide derivatives, which are involved in the redox cycling of protein thiol groups; and (d) a few additional underinvestigated small molecules including α-tocopherol, ubiquinone, ascorbate, and metallothioneins [18].

Ion homeostasis is essential in living systems, as it ensures the activity of the metalloenzymes and the correct values of the ionic cellular potentials. Gold, cobalt, mercury, copper, iron, manganese, nickel, palladium, platinum, silver, and zinc are redox active; i.e., they can access at least two different charges in the physiological pH range and have the ability to bind, exchange electrons with, or activate the reaction of some biological co-factors. Manganese, iron, cobalt, nickel, and copper can generate ROS starting from molecular oxygen at physiological pH [23]. Fe(II) and/or Cu(I)-dependent Fenton chemistry is responsible for the formation of hydroxyl radicals also in endogenous physicochemical conditions. It has to be stressed that hydroxyl radicals produced by Fenton’s reaction can react with almost all biological molecules, yielding damage whose secondary products can propagate the attack through reaction chains. Cellular macromolecules whose structure and function can be substantially altered from ROS include purine and pyrimidine bases, ribose and deoxyribose moieties of nucleotides, GSH and protein thiols, amino acid side chains, fatty acids, nucleotides and dinucleotides, and also structural components of the cells such as membranes. [24][25]

3.3. Enzyme Inhibition

Various metals are naturally occurring elements of the earth’s crust, which constitute low-percentage traces in environmental samples. At elevated exposures, metals cause toxic effects to living organisms, including fauna and flora. Though aquatic systems are considered as more selective compared to terrestrial environments, water chemistry of cooler climates has proved to be more conducive to the biogeochemical cycling of heavy metals. Once introduced into aquatic systems, metals undergo transformations among solid, colloidal and soluble phases. Such cycle controls transport and bioavailability of metals to aquatic organisms such as phytoplankton, zooplankton, mollusks and fish. However, many heavy metals are toxic even at trace levels and are known to interfere with cellular components such as lipids, proteins and nucleic acids. Despite toxic accumulation of metal salts in various living systems, detoxification occurs by bio-sequestration in a relatively inert form, which are then excreted [26]. The body gives scant attention to small organic pollutants but acts vigorously to excrete heavy metals. Enzyme inhibition strategies are one of the most successful approaches for combating diseases. It is being tried approaches of biocatalyst immobilization in solids and liquids with efficiency to develop an environmentally benign lay cat. CAD is a biocatalyst with the capability of converting organic materials to gaseous by-product. This biocatalyst was immobilized in a) 1% polyvinyl alcohol beads, and b) sponge with scaffolds made from alginate for the catalyzation of degradation of heavy metals. It is subsequently sequenced through illumina genome seq. platform. Most effluent samples exhibited staining effects. The diameter of the decolorized halos ranged from 5.0-20.0 mm. Absorbance values ranging from 0.077-0.181 with a high degree of R2 values confirmed the order of effectiveness. It was observed that, heavy metals such as As, Cd, Cr exhibit max inhibition pattern with .1mM concentrations. Kinetics of inhibition was suggested competitive with the value of Ki as 0.068,0.095,0.167mM respectively [18]. The study suggests a sustainable and economic model for bioengineering approach for combatting water/waste water pollution. [7][13]

4. Health Effects of Specific Heavy Metals

The health effects of heavy metals have been meticulously reviewed in a wide array of studies from diverse perspectives and frameworks. Most of this extensive work highlights the various routes of heavy metal exposure and the health effects that manifest once toxicity begins to take hold within the body. In this chapter, we will present a detailed examination of the health effects associated with six specific heavy metals in relation to their biochemical functions and mechanisms of action. These metals are grouped into two primary categories: essential and toxic, as well as being classified based on their intracellular or extracellular roles and impacts within biological systems. [27][18]

Copper (Cu) is a transition metal of difficulty that is an essential micronutrient for man and animals. It is involved in electron transport in mitochondria and cytochrome c oxidase, catecholamine biosynthesis by tyrosinase, oxygen transport by hemocyanins, synthesis of the connective prefibroin protein by the copper peptide, and phosphoinositides-PKNO kinase regulation of phosphoinositides. In ongoing processing, absorbed copper is distributed to the liver for storage, where it is bound to longer-term storage metal-binding protein and currently stored until the excess is biomarked by ceruloplasmin and exported. The health risks of copper exposure vary from growth retardation to liver damage and diabetes or death. Very early effects (0.5 h after contamination) lead to biochemical changes (for instance, elevating lactate dehydrogenase or reducing glutathione levels), followed by physiological and pathological changes that take time (for example, alanine aminotransferase elevation, 4 h after poisoning; abnormal spheroid hepatocytes, 12 h or more after poisoning). [28][29]

Arsenic (As) is associated with different environmental exposures, but most studies on As's health effects focus on its organic forms associated with seafood consumption and some drinking waters. There are a great variety of effects, often dependent on exposure and its valorized form. Toxic effects of dimethyl As include cardio-vascular damage (especially apoptosis of endothelial cells). Dimethyl As also exerts developmental neurotoxicity and is thought to hinder metal metabolizing and export proteins, leading to copper retention. Other studies focus on the carcinogenicity of tetra-organic Arses, but these have seldom been examined from the perspective of the heavily studied methyl cycle. The mechanism(s) by which inorganic As causes cancer has also rarely been described. [30]

4.1. Lead Toxicity

Exposure to lead occurs in a variety of fashions that include food, water, air, and various consumer products, which is often referred to as the four pathways of lead exposure. These pathways have distinct human health impacts, including predilection for accumulation in the bones, its role as a teratogen in the development of the fetus, and socio-political economic impacts, especially on the poor. Over the past 30 years, relatively early and successful elimination of leaded gasoline, ban of lead-containing paints, lead-acid batteries, and some consumer goods such as toys containing lead, has shifted the current burden of lead exposure onto the poor and 3rd world countries [31].

Lead (Pb) is an environmental pollutant that negatively affects human health, ecological balance, and socioeconomic development. Lead accumulates primarily in bone, liver, kidney, lung, and brain. Lead-induced toxicity operates through increased production of reactive oxygen species, alterations of microtubule integrity, mitochondrial impairment, and interference with neuronal signaling. Lead adversely affects male fertility through dysregulation of spermatozoa morphology, motility, and capacitation. Additionally, through increased production of peroxynitrite and increased ascorbic acid utilization, Pb exhausts the antioxidant reserves of testis and epididymis. Non-receptor mediated intracellular signaling pathways are important in the coordination of spermatozoa motility-associated hyperphosphorylation of proteins. These signaling pathways are involved in cGMP-production, calcium uptake by intracellular stores resulting in mitochondrial changes, phosphorylation of threonine residues, and the activation of several phospholipases in mouse spermatozoa. Lead-based urban infrastructures are detrimental to human health, and Pb-accumulating plants and aqueous solutions should be pitched in polluted regions. [32][33]

4.2. Mercury Toxicity

Mercury, which is involved in a variety of human activities, is among the most toxic heavy metals. Mercury (Hg) is a heavy metal widely present in nature and among the most toxic elements to human beings [34]. Mercury has no known physiological role in human beings. Its toxicity is related to its ability to bind to thiol and seleno groups, thereby affecting the redox status of the cells and altering intracellular signaling pathways. Additionally, mercury has been shown to alter gene expression and protein interactions.

Mercury exists in several chemical forms: elemental mercury (Hg0), inorganic salts (Hg2+, Hg2Cl2, and CH3HgCl), and organic forms (alkyl, aryl, and methyl mercury). In the environment, elemental mercury can be oxidized to inorganic forms, which can be transformed by microbes to organic forms in anoxic conditions. Mercury is released into the environment by multiple human activities, such as mining, burning fossil fuels, and the use of mercury in amalgams and some cosmetics. As a consequence, and due to its persistence in the environment, mercury is widely distributed and easily accessible to humans. The mercury bioaccumulates in the food chain, and some species of fish can amass significant amounts of mercury, most of which in the toxic organic methylmercury form. Fish consumption is one of the major sources of exposure to mercury, especially in populations where diet is based mainly on fish.

The metabolism of mercury is particularly complex, and the existence of different intake pathways accounts for its easy accessibility to humans. Exposures exist by ingestion (water, food, drugs, cosmetics, and dental amalgams), inhalation (Hg0 vapors from dental amalgams and some cosmetics), transdermal absorption of organic mercury compounds (drugs and cosmetics), and subcutaneous accumulation of mercury-containing vaccines. Curiously, as with other toxic heavy metals, mercury is able to cross biological barriers, reaching the brain, fetus, and testis.

4.3. Cadmium Toxicity

Cadmium is an extremely toxic heavy metal that is widely recognized for causing a multitude of detrimental effects on various organisms, ranging from microorganisms to humans. This hazardous metal accumulates in nearly every organ and tissue within living beings, which poses significant health risks. Interestingly, even in cases where individuals do not display any clinically apparent symptoms, the accumulation of cadmium in the body can lead to adverse effects on essential biological functions. These functions include hormone homeostasis, cellular signaling, oxidative stress management, and the integrity of mitochondria, all of which are crucial for maintaining health. Cadmium is commonly utilized in several applications, most notably in the production of cadmium-cadmium-nickel rechargeable batteries. Additionally, it is found in pigments, coatings, and in processes related to metal plating. The extensive and pervasive use of cadmium, combined with its extraordinarily long half-life—lasting several decades in humans—renders cadmium a significant public health hazard. The improper and careless disposal of waste materials, alongside the operations of plants that involve cadmium in their manufacturing processes, mining activities, smelting, and the incineration of cadmium-cadmium-nickel batteries, contribute to the release of cadmium into the surrounding environment. Consequently, cadmium becomes a substance that bioaccumulates in various ecological components such as soil, crops, groundwater, and vegetation. With the increasing recognition of the highly hazardous effects of cadmium throughout the global environment, it has become imperative for researchers, public health officials, and policymakers to study its toxicological effects in greater detail and to address this growing concern. Understanding this metal's interaction with biological systems is crucial for developing effective strategies to mitigate its harmful impact and protect public health. [35][36]

Acute high-dose exposure to cadmium vapor in workplaces has been reported to cause pulmonary damage. However, in the general population, low-dose exposure to cadmium through the diet, air, and tobacco smoke is most significant. Tobacco contains approximately 1 μg of cadmium per cigarette. As a matter of fact, Europeans are estimated to be exposed to an average of 0.32-0.74 μg of cadmium daily, virtually all from dietary sources. Shellfish, liver, kidneys, mushrooms, bamboo shoots, and raw cocoa beans are suggested as major sources of cadmium exposure in humans. In spite of extensive public health measures aimed at reducing human exposure to this heavy metal, the need to continually remain vigilant over such exposure seems paramount due to its insidious and long-lasting effects in living organisms. [37][38]

4.4. Arsenic Toxicity

Arsenic (As) is a toxic metalloid with a wide range of oxidation states, and its most stable forms in the environment and human bodies are the trivalent and pentavalent As (As(III) and As(V)) states. It presents in both inorganic and organic forms in nature, and the inorganic As is the most toxic form which may cause human diseases. As is a wellknown carcinogen and OEM Genotoxic. Researches revealed that more than 300 species of illnesses including cancers, skin lesions, vascular, respiratory, neurological and reproductive diseases may be related to inorganic As exposure although the exact mechanisms still remain to be studied . Further, recent epidemiological studies also showed that chronic As exposure may cause developmental adverse health effects in children . [39][40]

As a result, a large amount of toxicological studies on As have been carried out in the past decades. However, some old issues, e.g. the cut-off dose, the toxicities and biomarker predictions of the organic species, the effects and biotransformation of the methylated As, etc., still remain unresolved due to the complicated As biochemistries and the diverse toxicological actions of the different species. A summary of some information related to the As toxicity may be helpful for understanding the mechanisms underpinning the toxic actions of As and the future investigations. [41]

Arsenic is a metalloid with an atomic number of 33 that is widely distributed in the environment. Arsenic is assigned to the class of chemicals that is “known to be human carcinogens” by the US Environmental Protection Agency. High arsenic levels are found in some regions of Bangladesh, India, Mexico, Chile, Hungary, and Argentina. Its source is drinking water / dug wells and tube wells contaminated by naturally occurring arsenic. Four As metalloids with oxidation states of +3 and +5, i.e. As(III), As(V), methylarsenic acid (MMAA, CH3 As(III)O3), and dimethylarsinic acid (DMAA, (CH3)2 AsO2H), exist in the groundwater after dissolution and may cause diseases in exposed human beings. Arsenic is a notorious environmental pollutant and a serious chemical hazard for humans and wildlife due to its relentless toxicological effects. RSS exposure has been implicated in multiple biological effects. It exhibits carcinogenic, mutagenic, pro-inflammatory, neurotoxic, hepato-toxic, cytotoxic, reproductive, immunotoxic, and developmental toxic effects. It is an IARC Group A1 human carcinogen. Translational studies in both laboratory animals and human populations have confirmed its toxic potential through oxidative and nitrosative stress-associated mitogen-activated protein kinase and NF-κB pathways. [42][43]

4.5. Chromium Toxicity

Chromium is a common element found abundantly within the Earth's crust, ranking as the 20th most prevalent element, and it serves as an essential micronutrient that plays a significant role in various metabolic processes involving carbohydrates, lipids, and proteins. The compounds known as chromate and dichromate salts, which fall under the category of Cr(VI) species, are generated in substantial quantities from chromite ore extraction and have widespread applications across many industrial sectors. However, these Cr(VI) species are not without their dangers; they are considered toxic chemicals that can cause severe irritation and corrosion to the eyes and skin upon contact. Moreover, exposure to these compounds is linked to various serious health issues, including genetic damage, an increased risk of developing lung cancers, and the occurrence of chromosomal aberrations, which can have grave implications for human health. [44]The general population often encounters chromium via Cr-contaminated food or drinking water sources. Potential food sources rich in chromium include items such as cheese, onions, garlic, and various wheat products. When it comes to drinking water, groundwater can be a significant source of contamination, along with treated water that may include byproducts from food processing waste. Additionally, occupational exposure to chromium occurs primarily in several industries such as aerospace, metalworking, tanneries, and lumber processing. In these workplaces, individuals may face risks stemming from dermal contact and the inhalation of dust particles containing Cr(VI) or from accidental splashes of solutions containing Cr(VI) in open-air environments. [45][46]While the toxic effects and cancer-causing potential of inhaling Cr(VI) compounds have been extensively studied and documented in the past, recent research has begun to uncover alarming new evidence indicating that chromium may also pose significant risks for skin and oral carcinogenicity. This emerging understanding underscores the need for vigilant monitoring and control measures in both environmental and occupational settings to mitigate the risks associated with chromium exposure and to protect public health effectively. [20][47]

Toxic effects of Cr exposure via dermal contact from Cr-contaminated dust or swimming pool water are still poorly understood. Dermal contact with Cr(VI) increases the intrinsic cytotoxicity of Cr, resulting in anti-apoptotic mechanisms, including down-regulation of pro-apoptotic protein expression, suggesting that Cr may contribute to skin carcinogenicity. Toxicity from oral exposure to Cr(VI) species from Cr-contaminated drinking water also remains poorly understood. Cr(VI) uptake in the digestive tract can produce oxidative damage in the nucleus and mitochondria, hyperproliferative and hyperplastic lesions in glands, and carcinogenic effects within the esophagus or stomach microbes. Toxicity due to oral exposure is thought to be low, however Cr(VI) is poorly absorbed via the gastrointestinal tract. Thus, toxic effects and carcinogenicity from oral exposure remain a controversial issue. [48]

5. Biomarkers of Heavy Metal Exposure

Metalloproteins as Biomarkers of Exposure and Effect. Transport and storage proteins as biomarkers of exposure to heavy metals. Any non-essential metal with a partition coefficient greater than 1, metallothionein, equivalent transport and/or storage proteins with a different structural fold (e.g. appendage). Rather than relying on the measurement of total metal concentrations this ought to be the ideal approach to biomonitor exposure to relatively toxic metals or metalloids such as as, Pb, Cd, and Hg. For a number of non-essential metals and metalloproteins candidates are provided, which are available for further research and can readily be converted into analytically viable assays. The key challenge, and one which is generally applicable for biometrics of toxicant exposure or effect, is ensuring that the necessary sampling methodology, minute as the amounts of biological material needed for bioanalysis, in concert with sample handling, transport, storage and processing methods, is achieved concurrently and treating the biota bank as a single timepoint-based snapshot analogue of an exposure history is avoided [49]. This has been acutely appreciated and state-of-the-art methods exist to mitigate/characterize these issues for most widely used biomatrices blood and urine, but have received little relevant attention across dispersed biological matrices, such as hair/tissue, which are typically locked in amber by means of internal safeguards and preservation properties. Deliberation on these characteristics, analyses with respect to their biometrics (exposure, effect) and the dangers associated with interpretation of biomarker data and selection of analysis methods are warranted. [50]

Regarding biomarkers of the effect of exposure to heavy metals, non-essential metals with high affinity for cysteine-containing proteins are most toxic. Such proteins are most abundant in tissues experiencing the clearest adverse biological effect (Kidneys: Metallothioneins and meaderine kidney disease; Brain: Amyloid- proteins associated with Alzheimer's disease; and Testes: Meiotic arrest associated with elevation in free intracellular zinc). Little headway has been made in biomonitoring these proteins in blood or urine, notwithstanding the development of urinalysis methods, and practical breaches. The metals of concern are not systematically identified within some of these proteins. Moreover, it will be noted the body of research underpinning such links is co-evolutionary analysis-based and identification of predictive epitope exposures has yet to be completed. The lack of coordination across these research fields has obscured opportunities for joint progress. [51]

5.1. Blood and Urine Testing

Standard methods for heavy metals testing include blood and urine testing. Urinalysis relates to exposure to acute heavy metal toxicity, while blood sampling shows chronic or prolonged exposure to these metals. Blood testing is the preferred test due to its more progressive nature, but the concentration of metals or salts in the blood is usually low. Therefore, when analyzing blood, sample preparation procedures such as microwaving, ultrasound, and heating with appropriate digests like nitric acid or hydrogen peroxide are crucial. After sample digestion, the solution is filtered through a 0.45 μm filter to remove particulate debris [1].

When exposing heavy metals to the human body, the levels of oxides and salts of metals are generally low. Consequently, the metals move towards the excretion step. If a person is exposed to heavy metal toxicity recently, metals can be removed from the body through urine testing. In this way, metals must be accessible through the bloodstream, so the kidneys can filter and excrete them in urine. When analyzing urine for heavy metal concentration, the urine sample is directly tested without sample preparation procedures; however, it is advised to keep in mind that a small urinary volume of 20-24 mL is suggested for the best results. [52]

On the other hand, hair and fingernails represent the fetal exposure assessment conducted with minimal invasiveness. Hair grows at an average growth rate of 1 cm per month, which provides a time line for toxicant exposure history. Therefore, both hair and fingernails act as storage pool matrices integrating all previous exposures and are capable of analyzing levels of exposures over a long period of time. Hair protection from numerous environmental toxicants is accomplished in part through the actions of the sebum. This barrier is effective in retarding the passage of lipophilic substances. Furthermore, hair is a thermally good insulator and this property may contribute to slow degradation of retained toxic substances. Similarly, fingernails grow continuously from the skin of the pad at an average growth rate of 0.1 mm/day. Unlike hair, there is no melanin or sebaceous oil in fingernails. Therefore, fingernails are excellent matrices for the monitoring and assessing of several metal exposures. The long-term integration is based on hard keratinization, of which cross-linked intermediate filaments regulate their structure and biochemical characteristics. [53]

5.2. Tissue Biopsies

With the advancement of commercial products, the human body continuously interacts with various toxic species. Regular exposure to numerous toxic heavy metals, such as chromium, aluminum, cadmium, lead, mercury, and silver, poses serious health risks such as infertility, chronic and immune diseases, cardiovascular problems, DNA alterations, behavioral problems, and many others. These toxic species enter the body through the soil, dust, water, and varieties of food and commercial products such as canned foods, colored foods, manufactured drinks, makeup products, cosmeceuticals, and other products used daily. Exposure to notable levels of heavy metals leads to lipid peroxidation product indications in the urine, DNA alterations in the blood, and parabens in hair and nails-exacted protein reaction relevance. Certain heavy metals react biologically in vivo and cause acute diseases, affecting the gastrointestinal system with unsteadiness, vomiting, colic pain, and intestinal hemorrhage within hours [1]. Toxic heavy metals ingested from the environment or food products have chronic effects, including nephrotoxicity, hepatotoxicity, and carcinogenicity, affecting the kidney, liver, and blood. Continuous screening and monitoring of environmental toxicity in the human body, including heavy metals, are vital. This pilot study aims to screen selected heavy metals in female hair, nails, and serum from the lifestyle cosmetics, dyed canned food, and colored manufactured drinks ingested daily. This pilot study focused on analyzing mineral trace elements and heavy metals in hair, nails, and serum taken from females using colored food, drinks, and cosmetic products. Mineral trace elements and heavy metals in hair nails and serum were predicted to significantly notify metal nutritional value, risk of malnutrition, and predisposition to specific illnesses. Hair sampling: hair samples were collected from the temporal region, while nail clippings and small blood samples were collected from the inner part of the finger. The analysis of metals in hair was generally believed to reflect serum levels at the time the hair was grown. This method of analysis could not give useful estimates of the current serum levels of the metals if the hair was older than 2 to 3 months (for children) or up to 1 year (for adults) and had not changed significantly in hair cosmetics. Hair is an indicator of forensic pollution and hair identifying characteristics in chronic toxicological assessment screening for the exposure to heavy metal contamination. Hair samples indicated that environmental pollution, racial distribution, and daily habits are all thought to play a role. Hair and nails are considered end-fate metabolic products; therefore, they are largely consisted of keratin matrix, long-term loaded with heavy metals and minerals reflecting concentrations of metals in metabolism and hence in the risk of illness and toxicity. [54][9]

5.3. Hair Analysis

Hair is one of the most important biological matrices for health assessment, intoxications and mineral values. Its mineral content is around 0.25–0.95%, while its weight is made of about 80% protein. The hair follicle, surrounded by a dermal papilla, is strongly vascularized. These blood vessels make contact with the most superficial level of the skin in the papillary layer. The anatomy and physiology of the hair follicles have a direct connection with the mineral content of the hair. As the hair grows, the hair bulb (which has a specific architecture) is injected with blood that fixed traces of toxic and/or essential elements into the protein structure of hair [55]. For a successful hair analysis, it is important that the samples be of good quality, i.e., clean, free of chemicals and not contaminated, which may affect the interpretation of results. The hair analysis for heavy metals is part of a complete evaluation of the subject's health status. Identifying accumulated metals in hair relates to their intake from various sources, thus, sources, gastric absorption and intensity of incorporation are assessed with respect to toxicity. The method could be simple, quick, and low cost. In general, HMs are higher in hair than in serum and most other tissues; hence, the concentration of HMs from hair is in direct correlation with a variety of diseases, being in direct relation of proportionality to the severity of the pathology. When the hair is not analyzed and possible intoxications are ignored, simultaneously with a series of tiresome, aggressive and expensive tests, classical external medicine proposed and, often tried to institute as mandatory tests, in order to establish a health status, this society is facing a criminal health assessment. The most recent views maintaining the exclusion of hair analysis are solely based on rough or erroneous misinterpretations of results. But if hair is blamed for exposing it to non-biologically relevant high concentrations of environmental metals, teeth, nails, skin, CNS, serum, immune cells and urine retain too. Except for soft tissue, where a local) or systemic) distribution is observed, excretion is high immediately after exposure or even during exposure (unless some intoxications need advanced geriatric age). Other routines proposed costly and aggressive tests for assessing internal exposure are either inactive or the bodily fluid samples are totally unsuitable. Very rarely, blood mercapturinate paracetamol gives concomitantly substance administered and its retention time in blood is exactly the opposite of that of the author (in skin, brain, peripheral nerves, normal plasma, in urine and but not in blood secreted acetaminophen is detected and remain detectable for many years). [56][57]

6. Risk Assessment of Heavy Metal Exposure

Ever since mankind has existed, heavy metals are a common occurrence in the environment and have resulted in human exposure. Heavy metals enter the human body through lungs, skin and ingestion (consume food and water) [58]. They are considered toxic elements of concern and there is increasing public fear of their health impacts. As a result, regulatory agencies have set human health standards of permissible levels for numerous heavy metals in soils, sediments, air pollutants, food and foodstuffs. Tight regulations are also in place to control their release into the environment. The regulations are based on scientific assessments of anthropogenic heavy metal emissions, environmental fate and transport, exposure routes and concentrations, toxicology, risk and biomarkers [59]. The levels and extent of monitoring of metals of concern and the consumption of locally grown food products are inescapably different in developed and developing countries. In developing countries, there is significant likelihood of heavy metal food contamination and human exposure and there is very little reliable information about human health risk assessment of heavy metals. [8][15]

In order to assess the long-term health risks associated with exposure to As, Pb, Hg, Cd, Cr, Co, Ni, Cu and Zn, soil samples were extracted from the Witwatersrand Gold Mining Basin and subjected to a health risk assessment of their concentrations. Locally available food uptake of metals was also investigated by means of feeding trials. This information is important in helping the South African authorities to develop policies to monitor, manage and mitigate heavy metal contamination of soil to protect the health and safety of the public. [60]

6.1. Population Vulnerability

Vulnerability involves the exposure of a particular area to hazardous properties of certain chemicals, ecological situations in its community, and its general state of emergency preparedness at a particular point of time. Approaches to assess environmental health vulnerability with regard to general properties of the community and its natural environment were reviewed. For risk management of environmental health, vulnerability originated from uncertainties and inaccuracy in the deterministic problem and susceptibility to the stressors were also reviewed. A more definite description and framework of vulnerability were presented in terms of threat, hazardous properties of the stressors, and physical and/or social vulnerabilities of the receiving community. Integrated population environmental health vulnerability is involved, which includes assessment of vulnerability with regard to both heavy metal exposure and possible health of the communities or population, namely, physical vulnerability; and comprehensive measurement of sensitivity, coping ability, adaptability, and resilience of the communities before and in the face of the threats, namely, social vulnerability. Deterministically understood physical population vulnerability makes no sense for public health partly because of recognizing it as low. This in turn provides the defense against liability. Thus, social vulnerability and its assessment with/on bioremediation strongly emerge [61]. Social vulnerability refers to the comprehensive measurement of sensitivity, coping capability, adaptability, resilience, and susceptibility to stressors, situations and environments of the communities and societies facing possible threats. There have been attempts to identify social vulnerabilities with respect to adverse environmental threats like heavy metal contamination, water contamination, floods, earthquakes, and other phenomenon. [62]

6.2. Environmental Risk Factors

Heavy metals, such as Aluminum (Al), Cadmium (Cd), Cobalt (Co), Copper (Cu), Chromium (Cr), Lead (Pb), and Manganese (Mn), provide idiosyncratic hazards to human health and cause toxicity due to their environmental persistence [1]. Sources of heavy metals include soil, water, food such as fresh and canned fish, manufactured drinks, and cosmetics' products. Different metals possess unique toxicological properties. Heavy metals lead to an indication of lipid peroxidation products, genetic mutation, and interaction with many different body proteins, such as albumin, and cell receptors. Heavy metals are considered a major cause of human toxicity, infertility, chronic and immune disease, hormonal changes, emotional disorders, growth impairment, developmental delay, blocking movement for the main liquids within the body, and DNA alterations. As non-biodegradable pollutants, heavy metals accumulate throughout the food chain, with no ecological protective mechanisms. Adverse reactions can be acute or chronic. Continuous screening and monitoring the environmental toxicity in the human body as heavy metals is vital. Mineral trace elements and heavy metals in hair, nails, and serum significantly predict nutritional value, risk of malnutrition, and predisposition to certain illnesses. An analysis of metals in hair reveals the genuine concentration over the growth period and reflects the level of metals in the serum at the time the hair was grown. Hair and nails are considered end-fate metabolic products, and they are long-term loaded with heavy metals and minerals. Human nails also reflect concentrations of the end-productivity of metals and minerals in the metabolism to lead to illness and toxicity risk. [7]

Heavy metals are defined as elements with an atomic number greater than 20. Toxicity occurs when a heavy metal exceeds the bio-availability limit. The most prevalent heavy metals are Copper (Cu), Zinc (Zn), Cadmium (Cd), Lead (Pb), Arsenic (As), Nickel (Ni), Mercury (Hg), and Chromium (Cr). They enter the human body in several ways, such as soil, water, fresh and manufactured food, fish, beverages, paint, detergents, cosmetics products, and dairy products. Bioavailability approaches blood flow circulation to the site of action, where the metals react biochemically. After losing electrons, heavy metals react biologically in vivo with metal cations and persist in human tissue, causing acute or chronic diseases in different organs of the body. The highest exposure to heavy metals leads to severe complications in many organs, including gastrointestinal illness, nephrotoxicity, cardiac toxicity, CHE toxicity, hepatotoxicity, and carcinogenicity. Otherwise, the lowest exposure leads to neuropsychiatric issues, such as anxiety, chronic fatigue, irritability, and mood swings. The use of hair analysis for toxic element testing is controversial. Heavy metals, such as aluminum (AL), chromium (Cr), cadmium (Cd), nickel (Ni), and lead (Pb), continuously contaminate human bodies like water and food. The different ranges of contamination with heavy metals that affect the human body consisted Health Effect Division. [6][13]

7. Regulatory Standards and Guidelines

When describing standards and measurement methods, it is essential to define the scope, including target analytes and materials, in such a way that existing knowledge of the subject is not lost. [63]

Existing standards already consider these parameters. As an example, the VDI 2950 guideline specifies general measurement and evaluation methods to assess the state of preservation of surface waters or sediments, its variability and implications for the ecological state, the effects of sediment removal measures and the effectiveness of water quality improvement measures and, indirectly, adherence to regulatory standards for sediment-related contaminants. However, since the subject is not yet widely understood, inflated expectations regarding the general applicability of certain standards and instruments should be avoided. This is particularly relevant when it comes to understanding the measurements and models analytically. [64][65]

Guidelines for Statistical Evaluations of Detection Limits address aspects related to data evaluation, data quality assessment and graphical comparison of data from different sources. The latter topic is of growing importance as public demand for local transparency by publication of data increases. Measurements of biota and sediment contaminants are often covert, which means that they are not availed for use in regional differences or time series analysis. Needs for an interdisciplinary consensus on the relative merits of covert vs overt studies, background data and data on prevalence of effects arise, along with a philosophy of data provenance and quality assessment guidelines that promote rather than avoid meta-analyses and information integration from different domains. [66]

Relevant fields of research are broad, ranging from evidence assembly, exposure study and source characterization methodology to regulatory science. Regulatory steps from concern science to a list of hazardous substances and which substances are assigned to pragmatic vs non-pragmatic classes, need further improvement, notably for non-pragmatic. Discussions on unconventional policy aspects and additional discussion questions are welcome. Influence of burial depth, sediment remobilization and other transport processes on the general scientific applicability of dredging as a sediment management strategy, needs more research. Reasoning and sites have been described where higher considerations regarding dredging were voiced. Further such knowledge integration is essential in preparing for a future with ever-elaborate plume contaminations on seafloors arising from river- and estuary-based usage of affordable marine resources [27].

7.1. Global Regulatory Frameworks

Globally, the significant adverse health impacts which can arise from anthropogenic pollutants have been a topic of much recent discussion. A recent global burden of disease study estimated that the emission of pollutants caused 9 million deaths in 2015 [49]. This estimate highlights the substantial burden that pollutants incur on the global economy which is estimated to be US$4.6 trillion per year or 6.2% of global GDP. Understanding complex systems and gaining insight into the environment–bloodstream–organ system; a gateway to human organs, is critical from both a basic science and translational research perspective. Following exposure to toxic metals, events which unfold in the bloodstream play an important role in determining the onset of organ damage and may be implicated in human diseases of unknown etiology. There is growing recognition that toxic metals are inadvertently introduced into the food chain by anthropogenic activities. Anthropogenic environmental chemical exposures impact health through many pathways, including through the food chain. It is well established that human exposure to toxic metals, such as cadmium, lead and mercury adversely affects the structure and function of internal organs, results in poor pregnancy outcomes, and adversely impacts neurodevelopment in children. These toxic metals are bioaccumulative and persistent in the environment and food chain. Cadmium is widely recognized as a priority substance by numerous international regulatory frameworks due to human health concerns. Plasma is a valuable matrix to analyze tissue specific biomarkers, since it reflects injuries not detectable in other commonly analyzed non-invasive matrices such as urine, and shed light on human exposure and the effect of pollutants. Exogenous exposure to toxic metals will induce complex and species-dependent responses in tissues, including the production of endogenous metalloproteins which change in response to experience either homeostatic or dyshomeostatic states. The analysis of plasma for endogenous metalloproteins represents a feasible approach to gain insight into both homeostasis and changes in metal dyshomeostasis or excess. Furthermore, exogenous exposures to toxic metals such as exposure to cadmium can result in the induction of metal-containing biomarkers such as metallothionein to better assess health status. Understanding biomolecular events which link exposure to disease is a critical prerequisite before tightening environmental regulations to reduce the emission of toxic metals and metalloids. [7][9][8]

8. Prevention and Mitigation Strategies

Heavy metals are chemically defined as metals in which atomic weight is more than 20 that subsequently can produce dense metallic oxides. It consists of metals that exhibit high toxic properties, minimum or no use in biological systems, high electro positivity and oxidation state with consequent evolution of free radicals and generation of reactive oxygen species that result in excess toxicity and imbalance in the internal cellular dynamics. Heavy metals undergo bio-accumulation and hence transfer up the food chain, leading to serious health hazards [10]. These metals are pollutants in nature due to their toxicity, carcinogenicity and radioactivity properties. Contamination of heavy metals in soil and subsequent leaching into the ground water is a global environmental problem, posing a serious threat to the human health [67]. Both chemical and physical decontamination strategies have been used to alleviate this health hazard. Heavy metal exposure damages a number of organs, and especially during the prenatal stage when neural development proceeds critically. The toxicity of heavy metals depends on absorbed doses, routes of exposure and duration of exposure (acute or chronic). [68]

Heavy metals can induce free radical formation, which leads to oxidation of macromolecules, such as lipids, proteins and nucleic acids. The reactive radical species generated by heavy metal exposure have been shown to be effective in producing excessive oxidative stress resulting in cellular and organ damage. The prion-like proteins misfolding, aggregates and toxicity are provoked by elevated level of heavy metals. Mechanisms that underlie the cytotoxicity of heavy metals involve the development of oxidative stress, apoptosis and changes in the cellular dynamics. As scientists develop more effective strategies to slow down aging and age-related diseases, the mechanisms through which heavy metals induce cellular damage will unveil the underlying pathways of aging. Cellular damage induced by heavy metals is multiogeneous and multi-organ, such as those in the central nervous system (brain), hearing organs (inner ear), digestive organs (liver and pancreas), kidneys and respiratory organs (nose and lung). The damage to central nervous system including both peripheral (e.g., craniofacial) and central (e.g., neocortex) neurological functions, behavior and pathology underlying neurodegenerative diseases has been extensively studied, and heavy metal-induced cellular damage in the ear and liver have also been reported. [69]

9. Future Research Directions

Even though a variety of efforts are underway to reduce human exposure to toxic metal species, their inadvertent introduction into the food chain is being increasingly recognized. Exposure to different species and chelation environments determines the fate and toxicity of metals inside the body. There are countries where ingesting “freshwater fish” in certain conditions is more dangerous than consuming the same amount of air pollution. The health effects arising from exposure to toxic metals often manifest with several decades of delay. Despite taking preventive action, several toxic metal species can still inadvertently enter the body. To gain insight into the environment–bloodstream–organ system is critical [49].

There is direct experimental evidence that human exposure to toxic metals adversely affects organs and pregnancy outcomes. The cardiovascular system is often the primary target of environmental pollutants. Physico–chemical properties of metals and chelation conditions may determine the risks that toxic metals pose. Hence, in addition to the necessity to reduce direct environmental release and exposure, there is a pressing need for new bio-analytical approaches that provide insight into the dynamics of the bloodborne toxic metal species. [70]

Events that unfold in the bloodstream play an important role in determining the onset of organ damage and may also be implicated in human diseases of unknown etiology. Some environmental bloodborne pollutants induce biochemical events that remain hidden in organs for decades after withdrawal of initial exposure. Moreover, circulating biomarkers of exposure to cardiovascular damaging toxic metal species are currently lacking. Taken together, there exists considerable knowledge gaps, which will need to be bridged by a multidisciplinary effort, to gain insight into the environmental–bloodstream–organ systems. [71]

9.1. Innovative Detection Methods

The potential of heavy metals (HMs) to damage DNA and membranes has demonstrated that they represent a significant risk to human health. Heavy metal contamination is unnecessary and, by choice, does not occur in terms of the environment, food, and water in any measure. Because humans cannot deliberately ingest HMs, their presence in either the environment or a suspicious analytical sample must be due to industrial, analytical, or medical errors. At present, the dominant analytical technique for the detection of trace elements in the human body is indeed atomic absorption spectrometry (AAS). The importance of this method has determined a shift to inductively coupled plasma mass spectrometry (ICP-MS), a more modern method, with the possibility of determining multiple elements simultaneously, of greater performance and dexterity. The choice of the analytical method used for detection will remain at the discretion of the toxicologist/chemist. The proposed method will depend on the metals to be detected, the number of metals to be detected, the analyzed matrix (blood, urine, hair, etc.), and the intended purpose of the analysis (clinical, screening, or forensic) [55].

Another analytical method with greater practical importance, for monitoring population health with the determination of both nontoxic and toxic minerals, is the so-called toxicological hair mineral analysis (TMA). The importance of this method cannot be denied, although some criticize this way of detecting metals. Forensic medicine considers the analysis of biological fluids and tissues and the toxicological analysis of these with modern equipment in order to establish the cause of death and the diagnosis for a particular pathology, whether it is criminal or civil. Biology is the most used discipline for detecting traces of criminal actions, given the ability to locate, preserve, and analyze biological fluid traces [49]. There by discovering traces of substances or elements, several speculations about the person in question can be drawn. Materials can reveal whether they have unique properties and can be thus characterized or linked to an origin, whether it is natural or anthropogenic. [72]

10. Conclusion

The effect of heavy metals arises from the structural and functional influence of their excessive accumulation in living organisms—even those previously considered trace or essential elements. As a highly discussed topic, heavy metal toxicity includes biochemical investigations and in vivo animal and human studies . Heavy metals leak from manufacturing plants, smelters, battery recycling, sewage disposal sites, and incineration, affecting the air and thrifting into water systems. These consecutive events leave heavy metal stains unreachable by considering famous food brands legally tasked with food safety. Water plants normally remove most colloidal heavy metals, yet small fractions, from ionic symmetry entering surfaces of cell units and wine membrane filtration, are impossible to handle. As no prior investigations been undertaken, the toxicity of five heavy metals (cadmium, lead, mercury, chromium, and arsenic) suspected to be accumulated from the four beverages was detected biochemically. The biochemistry approach—labeled blue, cholinesterases (ChE) inhibition—selectively points out their accumulation and relative toxicity.

Biochemical investigations had broadly addressed “why?” but not “how?”, where questioned heavy metals produced toxic effects. The methodology utilized limited contexts from few case studies or from certain opinions, referrals, or speculations. The study began bioinformatics assessments disguised within mutant energies, defects at cellular levels, or receptor mischiefs, predicted by accurately calibrated and accepted protocols amid light biases but without sole alternatives—both reflective of academic omissions. The investigated heavy metal effects at gene and protein structural and functional aberration levels were reported. Inhibition of bioinformatics cleavage points at five proteins explains the highly selective, the one closest to the intake pathway with the most pivotal roles, cholinesterase (ChE) enzyme, with expected lower inhibitions in DNA and absorbed organ systems. Biochemical evaluations of genetic mutations or stability via methylated presentation were normally edge cases for certain human organs or cases; heavy metals were often not assessed as co-causative agents.

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