Pure Appl. Biol., 12(2):835-847, June, 2023
http://dx.doi.org/10.19045/bspab.2023.120083

Review Article

Essential and non-essential heavy metals sources and impacts on human health and plants

Maria Bibi[1], Samiullah[1*], Farida Behlil[2], Saba Afzal[2] and Sahifa[1]
1. Department of Chemistry, University of Balochistan, Quetta, Balochistan, Pakistan
2. Department of Chemistry, SBK Women's University, Quetta, Balochistan, Pakistan
**Corresponding author's email:* sami435889@gmail.com

Citation
Maria Bibi, Samiullah, Farida Behlil, Saba Afzal and Sahifa. Essential and non-essential heavy metals sources and impacts on human health and plants. Pure and Applied Biology. Vol. 12, Issue 2, pp835-847.
http://dx.doi.org/10.19045/bspab.2023.120083

Received: 04/12/2022 Revised: 11/01/2023 Accepted: 18/02/2023 Online First: 24/02/2023

Abstract

Contamination of heavy metals occurs in environment due to natural sources and human activities. Some heavy metals including copper, cobalt, chromium, manganese, zinc, nickel, iron are essential for living organisms and play vital role in various processes, while others are non-essential for living organisms including arsenic, cadmium, lead, mercury, and have acute to chronic toxic effects. Exposure of arsenic, cadmium, chromium, mercury and lead beyond permissible limits is lethal for human health and are classified as carcinogenic as per report of the U.S. Environmental Protection Agency (U.S. EPA) and International Agency for Research on Cancer (IARC). Current review provides an analysis of essential and non-essential metals sources, their impacts on human health and plants, recommended dietary allowance (RDA) and world health organization (WHO) maximum permissible limits (MPL). This review study provides insight about beneficial and lethal impacts of heavy metals on living organisms and also emphasizes on peer metal analysis of each product utilized by living organisms to enhance the nutritional factors and reduce the toxicity.

Keywords: Essential heavy metals; Heavy metals; Human health; Impacts of heavy metals; Non-essential heavy metals; Plants; Sources of heavy metal

Introduction

Heavy metals are group of specific elements (metalloids and metals) with relatively high density and are also known as trace metals, as they are toxic even in small amount. They are naturally occurring components on earth crust and are non-biodegradable therefore it is easier to find out their concentration [1]. Some heavy metals are essential nutrients in trace amount for various biochemical and physiological functions and humans accumulate them through air, drinking water and food, while elevated levels of them can be poisonous for human health. They are lethal for human health as they tend to bio-accumulate in human body. In bioaccumulation process, chemical concentration elevates in living organism with time as compare to chemical concentration in environment. In living organism compounds stored faster in comparison of metabolism (broken down) or excretion [2]. In developing era uncontrolled and rapid urbanization and industrialization have elevated the levels of contamination in ecosystem. Contamination of ecosystem and human exposure to heavy metals mainly occurs due to anthropogenic activities including fertilizers, various industries, waste used to fertilize soil, municipal waste, dumping sites, waste management, transport and agricultural activities [3]. Industrial sources of heavy metals are coal burning in power plants, pharmaceuticals, metal processing in refineries, textiles, petroleum combustion, high tension lines and nuclear power stations, microelectronics, plastics, paper processing plants and wood preservation. Whereas heavy metals immigration in environment take place due to number of different natural activities including; vaporization of oceans, volcanic eruptions, rock degradation, metal corrosion, soil erosion of metal ions, sediment re-suspension and heavy metals leaching, forest fires and soil formation [4].

These heavy metals also found in plants and various products (drinking water, food, cosmetics, commercial products) utilized by humans. Among these heavy metals some are essential (Cr^{+3}, Cu^{+2}, Co^{+3}, Fe^{+3}, Ni^{+3}, Mn^{+2}, Zn^{+2}) for plants and humans, while others are non-essential (As^{+3}, Cd^{+2}, Hg^{+2}, Pb^{+2}) and have toxic effects on both. They play essential role in different oxidation-reduction reactions and are important constituent of various enzymes. Bioavailability of heavy metals is influenced by various physical factors including phase association, temperature, sequestration, adsorption and chemical factors including complexation kinetics, octanol/water partition coefficients, lipid solubility and thermodynamic equilibrium. Toxicity of heavy metals affects biological system including cellular organelles and its components. When metal ion interacts with components of cell like Deoxyribose Nucleic Acid (DNA) and proteins; result in damage of DNA and conformational changes leading to carcinogenesis, apoptosis and cycle modulation. As per report of United States Environmental Protection Agency (U.S. EPA) and International Agency for Research on Cancer (IARC), some heavy metals are classified as carcinogenic. Each metal has unique physiochemical properties that define its specific toxicological mechanisms of action [2]. Current review on heavy metals provides various sources, effects on humans and plants of essential and non-essential heavy metals. RDA and MPL of essential and non-essential heavy metals are shown in Table 1 and 2 respectively.

Essential heavy metals

Chromium (Cr)

On earth crust chromium is naturally found 7th most abundant element [5].

Chromium sources

Chromium naturally occurs in pigments, coal burning and oil, petroleum, well drilling of oil, oxidants, catalyst, fertilizers and steel [6, 7]. It is consumed in different industries such as; tanning, metallurgy, electroplating, wood preservation, synthesis of chemicals, paints and pigments, pulp and paper, welding of stainless steel, production of chromate [2, 8] and these industries are causing increase in the concentration of chromium in environment and exhibit toxic impacts on living species and agriculture [7]. Development in industrial, agricultural and anthropogenic activities results in chromium contamination in air, soil and water [9].

Chromium impacts on humans

In human body trace amount of chromium is found and is essential for several processes such as; cholesterol synthesis, simulation of fatty acid and carbohydrate metabolism [10]. Chromium is present in various oxidation states including (Cr^{+2} to Cr^{+6}) [8, 11]; among which Cr (III) is essential nutrient for humans and exhibit less toxic impacts [2]. However, hexavalent chromium is the most toxic specie of chromium [7]; inhaling of Cr (VI) compounds results in nose ulcer, nose lining irritation, allergic reactions, anemia, stomach and small intestine ulcer [2, 7] and its high exposure causes severe diseases including; cardiovascular, neurological, respiratory, hepatic renal, hematological, gastrointestinal, inhibition of erythrocyte glutathione reduction. Compounds of chromium damaging DNA causes; alternation in replication (exchange of sister chromatid), transformation of DNA, emergence of DNA adducts, chromosomal aberrations [7]. As per IARC exposure of Cr (VI) can increases the rate of carcinogenicity in humans [2, 12].

Chromium impacts on plants

Chromium is known to have potential effects on development and growth of plants however there is no proof that chromium is necessary for plant metabolism. High levels of chromium compounds are lethal for plants and in higher plants it affects seed germination [13] and in terrestrial plants inhibits biosynthesis of chlorophyll [14]. Chromium phytotoxic effects include; leaf chlorosis, inhibits seed germination, depress biomass and root growth reduction. Toxicity of chromium affects the biological processes of various plants (maize, barley, wheat, cauliflower, citrullus) [8] and also impacts the number of enzymes including peroxidase, catalase and cytochrome oxidase [15].

Oxidative state and solubility are the major factors of chromium toxicity [16]. Interaction of chromium with cell causes cellular integrity disrupter, metabolism of lipid and protein and function through DNA attacking [17]. Toxicity of chromium in tomato results in plant nutrition reduction [18] and in onion inhibits germination process and reduces plant biomass [17, 19].

Cobalt (Co)

On earth crust cobalt is a naturally occurring metal present in the state of cobaltite, smaltite and erythrite [13].

Cobalt sources

Cobalt sources in environment include cobalt containing alloys, guardian rock, sewage sludge and burning of fossil fuels [12, 20, 21].

Cobalt impacts on humans

In trace amount cobalt is necessary for humans such as; essential component of vitamin B12 and as cofactor for various enzymes in DNA synthesis [22]. Exposure of cobalt may result in many diseases including; cancer, immunological, respiratory, cardiac, hepatic, hematological, dermal, lung parendemic and renal [23, 24].

Cobalt impacts on plants

Plants are able to accumulate cobalt in low concentration, taken from soil [25-27]. However, outcomes of elevated concentration of cobalt include; limiting the levels of chlorophyll, protein, iron and activity of catalase in leaves; reduces water potential and rate of transpiration; hazardous impacts on shoot growth and biomass; influence Zn, P, Mn, S, Cu translocation [12, 13, 28].

Copper (Cu)

Copper is naturally existing metal and in small amount is essential for living creatures [29].

Copper sources

Naturally it is present in coca nuts, beans, wheat grain, bran, avocado and organ meat. On industrial level it is utilized in making of cables, wires, pipes, sheet metal and cookware [7, 29]. Levels of copper are elevating in environment because of anthropogenic and industrial activities including; copper containing ores smelting, mining and copper refining [13, 29].

Copper impacts on humans

For health of human small amount of copper is essential and plays vital role in different functions like; human growth, iron absorption, bone formation, crucial part of several enzymes, normal metabolic functions, energy provider [30, 31]. Copper deficiency results in anemia, skeletal problems, osteoporosis and reduction in number of white blood cells (WBC). However surplus of copper can cause short term acute effects (abdominal pain, nausea, vomiting, liver toxicity, red blood cells (RBC) destruction) and long term chronic effects (group D carcinogenic, Wilson's disease, kidney and liver damage) [29].

Copper impacts on plants

In plants copper is found as micronutrient [13] and in trace amount plays vital role like; formulation of CO_2, construction of different proteins, synthesis of Adenosine triphosphate (ATP). Whereas in soil exceeded levels of copper results in cytotoxicity (leaf chlorosis, induce stress, growth hindrance and injury to plants), oxidative stress (metabolic pathway disturbance) and reactive oxygen species (ROS) generation [12, 32, 33].

Iron (Fe)

Iron is the 2nd most abundantly found element on earth crust [8] and is vital metal for all living species [34].

Iron sources

Surface water contamination with iron occurs due to anthropogenic and mining activities [8].

Iron impacts on humans

Iron is key constituent of myoglobin, cytochrome and hemoglobin and is required for oxidative energy production in human body [35]. In the form of iron sulfates, it has low acute toxicity, while it's other forms exhibit toxic health effects. Iron toxicity takes place in 4 different stages: first stage take place after 6hrs characterized by vomiting, diarrhea, gastrointestinal bleeding; second stage take place after 6 to 24hrs and is named as apparent therapeutic recovery inactive period; third stage take place after 12 to 96hrs marked by lethargy, metabolic acidosis, hypotension, tachycardia, shocks, hepatic necrosis and fourth stage take place after 2 to 6 weeks marked by development of ulcer in gastro-intestine. Iron high exposure creates free radicals, give rise to asbestos and lead to cancer of lung [7].

Iron impacts on plants

In suitable quantity iron is vital for various processes of plants including plant metabolism, transformation of energy needed for synthesis and different life processes of cell. Concentration of iron in plants depends upon several factors such as; stages of plant growth, genotype properties of plants, climate and condition of soil. Deficiency of iron cause roots of plants to develop various mechanisms which cause increase in iron solubility [13]. However, on plants high levels of iron could have adverse impacts [8]. Toxicity of iron in rice plants could be remarked by yield loss, leaves bronzing, roots high uptake of iron, acropetal translocation into leaves [36] and in plants of tobacco causes reduction of photosynthesis, ascorbate peroxidase activity, impact yield of plant, oxidative stress [37].

Manganese (Mn)

Manganese is the 5th common metal on earth crust [38].

Manganese sources

Manganese sources involve food (meat, tea leaves, nuts, cereal, green vegetables and grapes), ceramics, batteries, air, colors and methylcyclopentadienyl manganese tricarbonyl (MMT) used in gasoline [7, 39].

Manganese impacts on humans

Trace amount of manganese is vital for humans [40]. In humans it serves as a cofactor in physiological processes and reactions of enzymes [35, 41]. It is necessary in the synthesis of urea, glycoprotein, proteoglycan and metabolism of pyruvate [35]. Manganese deficiency usually not occurs in humans [40], while manganese toxicity has been became global issue because of utilization of MMT as gasoline additive. MMT is responsible for causing various diseases such as; postural instability, tremor syndrome, gait and cognitive disease [7]. High levels of manganese cause its accumulation in Central Nervous System (CNS), resulting in neurotoxicity [42, 43].

Manganese impacts on plants

Manganese is essential in plants for oxidation–reduction process and its levels in plants depend upon characteristics of plants, manganese concentration in soil and metabolic system. Manganese deficiency is not noticed in plants. However, its toxicity in plants takes place because of highly alkaline (pH-8) soil. For healthy plants manganese and iron are interconnected in metabolic functions, their suitable levels and ratio [13].

Nickel (Ni)

Nickel is a naturally occurring transition metal found in trace amount [12].

Nickel sources

There are various sources of nickel. Food sources of nickel include; unrefined grains and cereals, commercial peanut butter, imitation whip cream, chocolates, beverages and hydrogenated vegetables [7, 29]. Contamination of nickel because of human activities include coal and oil burning, sewage, mining works, smelters emission, fertilizers, pesticides [12, 44] and because of industrial production include machine parts, batteries, wires, electrical parts, cigarettes, manufacturing of steal [7].

Nickel impacts on humans

Trace amount of nickel is vital for humans [29]. It plays vital role in metabolism of nucleic acid and serves as cofactor of enzyme in enzymatic reactions [45]. However, high levels of nickel may have hazardous impacts on human health. Exposure of nickel to humans takes place due to different sources like; air, smoking, drinking water and food. High exposure of nickel causes various diseases in humans including asthma, respiratory failure, lung embolism, chronic bronchitis, sickness, dizziness, dermatitis (nickel itch), allergies, pneumonitis, disturbance in kidney, birth defects, heart disorders, cancer (lung, larynx and nose cancer) [29, 46].

Nickel impacts on plants

Nickel contamination in soil results in different toxic effects (chlorosis and necrosis) and physiological alternations [47-49]. In plants elevated concentration of nickel causes; cell membrane function disorders, impartment of nutrient balance, affects composition of lipid, affects activity of plasma membrane, changes in water balance, ion balance disturbance [50-53].

Zinc (Zn)

Zinc is essential bluish-white metal [54] and is 23rd most abundant element on earth crust [55].

Zinc sources

Richest food sources of zinc include meat and organs of mammals, fish, fowl, crustaceans, eggs and dairy products. However, plants, cereals and legumes have zinc, but their high phytate (myoinositol hexaphosphate) content inhibit the zinc absorption. And some fruits, green leafy vegetables (spinach), rice possesses small amount of zinc [55]. Zinc contamination also occurs in soil due to fertilizers, sewage sludge, mining, emissions from municipal waste incinerators and industry of metal smelting [12].

Zinc impacts on humans

Zinc is essential nutrient for humans and its function can be classified into three group's namely catalytic, structural and regulatory functions [56]. Zinc has ability to create strong, flexible and exchangeable, complexes with organic molecules, which makes it possible to alter three-dimensional (3D) structure of nucleic acids, cellular membranes, specific proteins, intracellular signaling and impacts the catalytic properties of several enzymes. It is associated with various metalloenzymes, useful for synthesis of specific proteins (hormones and their receptors) and nucleic acids. Therefor zinc is essential for cellular growth, metabolism, neurobehavioral development, susceptibility to infection and differentiation [55]. Deficiency of zinc influences various organ systems including epidermal, gastrointestinal, skeletal, immune, CNS and reproductive systems [56]. Zinc deficiency can be mild to severe. Mild deficiency of zinc causes male hypogonadism in adolescents, growth retardation, poor appetite, slow wound healing, rough skin, mental lethargy, abnormal neurosensory changes and cell mediated immune dysfunctions. Whereas severe deficiency of zinc results in alopecia, emotional disorder, bullous pustular dermatitis, diarrhea, inter-current infections, weight loss, hypogonadism, difficulty in healing of ulcers, neurosensory disorders [57].

Zinc impacts on plants

Zinc is essential for plants and act as plant nutrient [54]. It is essential for plant growth, gene expression, function, photosynthesis, sugar transformation, structures of enzymes, pollen development, protein synthesis, the synthesis of nucleic acid, signal transduction, membrane permeability, auxin metabolism, regulating the nitrogen metabolism, cell multiplication and cofactor for several enzymes (dehydrogenases, anhydrases, peroxidases, oxidases) [54, 58]. Zinc deficiency in plants affects plant growth, small leaves, leaf chlorosis, delayed maturity, short internodes and necrotic tissue death [58]. While zinc toxicity in plant results in limiting root and shoot growth, younger leaves chlorosis, leaves purplish-red color, young leaves curling and rolling and leaf tips death [12, 54].

Non-essential heavy metals

Arsenic (As)

On earth crust arsenic is the 20th most abundantly found element. It is available in the forms of arsenate and arsenite compounds are hazardous for living organisms and environment [7].

Arsenic sources

Contamination of arsenic in environment and human toxicity occurs due to natural means (soil erosion, volcanic eruptions, and anthropogenic activities) and industrial sources (microelectronic, smelting) [2, 8]. Drinking water contamination occurs due to herbicides, fungicides, pesticides, wood preservatives and paints [7].

Arsenic impacts on humans

Arsenic is lethal for human health [29] and is carcinogenic [8]. Its toxicity is affected by its solubility and oxidation state. Toxicity level of arsenic depends upon several factors including dose (exposure, frequency and duration), gender, age, individual susceptibilities, nutrition and genetics. Human encounter to arsenic can occurs through inhalation, ingestion, dermal contact and parenteral route. Arsenic exposure almost influences all organ systems including nervous, dermatologic, cardiovascular, renal, gastro-intestinal, hepatobiliary and respiratory systems [2]. Toxicity of arsenic can be acute to chronic for humans. Acute toxicity of arsenic affects brain, heart, gastrointestinal tissue and blood vessels, while chronic arsenic toxicity causes number of cancers (colon, kidney, bladder, liver, lung, skin) and affects skin (pigmentation and keratosis). Short term arsenic exposure results in vomiting, nausea, reduction in production of leukocytes and erythrocytes, pricking sensation in legs and hands, abnormal heart beat and blood vessels damage, while long term arsenic exposure results in neurological disorders, vascular disease, pulmonary disease, hypertension, diabetes, cardiovascular disease and skin lesions [7].

Arsenic impacts on plants

Arsenic is non-essential and toxic element for plants. Arsenates are less toxic as compare to arsenites; symptoms of arsenate toxicity are chlorosis but not turgor in early expression of toxicity, like arsenites [59]. In plants roots are first tissue that is affected by arsenic toxicity, where root extension and proliferation is inhibited. And when it transfers to shoot it causes growth inhibition through slowing expansion and biomass accumulation, also compromises reproductive capacity of plant by losing fertility, yield, and fruit production. And when it interacts with critical metabolic processes, it causes death of plant [60]. It produces ROS that causes damage of lipids, proteins and DNA and it also disturbs central cellular functions of plants [61].

Cadmium (Cd)

Cadmium is 7th most toxic heavy metal according to Agency for Toxic Substances and Disease Registry (ATSDR) ranking [8] and is classified as Group-I carcinogenic according to IARC [7].

Cadmium sources

There are various cadmium sources in environment such as; cement plants, sewage sludge, fossil fuels, uncontrolled drainage, tobacco smoke, paints, pigments, plastic stabilizer, rechargeable batteries, electrode in alkaline batteries, production of alloys, plating's [8, 29, 62].

Cadmium impacts on humans

Cadmium can have acute to chronic intoxications for humans health either inhaled or ingested [29]. The adverse impacts of cadmium on humans are because of inability of human being to excrete cadmium instead kidney inhibits its excretion by reabsorbing cadmium. By inhalation short term exposure of cadmium can cause respiratory system damage; however, ingestion can result in stomach problems including vomiting, irritation of stomach and diarrhea. Whereas cadmium long term exposure causes its accumulation into lungs and bones. Cadmium toxicity also results in various diseases including osteoporosis, decreases bone density, bone fractures in women, testicular degeneration, hypercalciuria, renal dysfunction, renal stone formation, influence calcium metabolism, height loss [8].

Cadmium impacts on plants

Cadmium remains in soil and sediments for number of decades. From soil plants grasp cadmium, collect it and through food chain transit it to further living species [8]. Toxicity of cadmium in plants results in deficiency of nutrition's, oxidative stress and influence enzymatic cells [63].

Lead (Pb)

Lead is naturally occurring metal on earth crust in trace amount [8] and it begins to tarnish and forms complex compounds when it come in contact with air [64].

Lead sources

Lead exposure in environment occurs due to various sources including industrial processes, anthropogenic activities, agricultural activities, domestic sources, mining, burning of fossil fuels, vehicle exhausts, smoking, drinking water, food [2, 8]. Sources of lead from industrial means include paint used for house, plumbing pipes, gasoline, house paint, pewter pitchers, storage batteries, faucets, toys, lead bullets [8, 65].

Lead impacts on humans

Lead is extremely toxic metal and even small amount of it could be toxic for health of humans [66]. Lead inhalation in humans occurs because of aerosols, dust particles and lead ingestion occurs because of drinking water and food (children absorbs 50% of lead and adults absorbs 35 to 50% of lead). Lead absorption in humans depends upon different features (physiological status and age) [2] and affects different tissues and organs in human body like brain, CNS, heart, kidney, liver, gastro intestine, hematopoietic, reproductive and endocrine system [67, 68]. CNS is most endangered target of lead and symptoms include dullness, poor attentiveness, headache, loss of memory, irritability [2]. Lead poisoning can be acute to chronic; acute exposure of lead causes sleeplessness, headache, fatigue, appetite loss, vertigo, abdominal pain, arthritis, hypertension, dysfunction of renal and chronic exposure of lead causes muscle weakness, paralysis, weight loss, allergies, dyslexia, autism, kidney destruction, birth defects, psychosis, hyperactivity, mental retardation, coma, destruction of brain and may lead to death [7]. High exposure of lead can be responsible for various kinds of cancer (stomach, rectum, colon, bladder, kidney, lung, brain) [29] and can transfer to developing fetus from pregnant mothers [2].

Lead impacts on plants

In plants there is no reported biological function of lead. It is highly toxic for plants and disturbs various processes including physiological processes, morphology, photosynthesis, growth, damage lipid membrane and increases production of ROS [12, 69]. Excessive exposure of lead in plants causes enzymatic activity inhibition, water imbalance, mineral nutrition disturbance, alternation in permeability of membrane [12, 64] and lead toxicity impacts shoots, roots, seeding, concentration of chlorophyll, nitrogen and protein in rice plants [17, 70].

Mercury (Hg)

Mercury is naturally occurring shiny silver-white metal and is available in three various forms including inorganic salts, organic compounds and metallic elements [2].

Mercury sources

Anthropogenic activities including discharge of municipal wastewater, incineration, agriculture, mining, industrial wastewater discharge are the major source of pollution of mercury. Water resources of mercury include oceans, rivers and lakes, which is taken up by aquatic organisms and converted into methyl mercury. Consumption of these contaminated aquatic organisms by humans is the major source of exposure of mercury [8]. On industrial level it is utilized in dentistry (dental amalgams), electrical industry (switches, thermostats, batteries) and in the production of several materials like; caustic soda, barometers, thermometers, hydrometers, pyrometers, fluorescent lamps, mercury arc lamps, batteries, nuclear reactors, pulp and paper, as antifungal agents for wood processing and as catalyst [7, 8].

Mercury impacts on humans

Mercury is toxic for human health and its toxicity depends upon the form of mercury (elemental, inorganic, organic). Elementary mercury vapors inhalation causes emotional lability, memory loss, insomnia, tremors, headaches, neuromuscular changes, lungs, thyroid and kidney problems and ingestion may cause death. Inorganic mercury exposure can occur through dietary sources and various products including soaps, skin lightening creams, traditional medicine and can be hazardous for humans [29]. Organic mercury exposure usually occurs due to dietary ingestion (seafood) and is lipophilic in nature (penetrate cell membranes) [7] such as; methylmercury is neurotoxin (affects developing human brain) and according to IARC is carcinogenic [29] and dimethylmercury can penetrate the skin and even its low dose can degenerate CNS lead to death. Short term exposure of mercury can cause vomiting, nausea, diarrhea, skin rashes, high blood pressure, lung damage, tremors, fatigue, depression, headache, hair loss, memory problems. While long term exposure can cause memory loss, tremor of the hands, excitability, insomnia, timidity. Exposure of mercury to pregnant women can affects fetus results in cerebellar symptoms, mental retardation, retention of primitive reflexes and malformation [7].

Mercury impacts on plants

Mercury is nonessential for plants and does not have any beneficial effects on plants. Even trace amount of mercury can be toxic for plants and causes growth retardation. Elevated levels of mercury in soil have adverse effects on plant metabolism, growth, water uptake, transpiration, chlorophyll synthesis, photosynthesis and increased lipid peroxidation [71]. Toxicity of mercury causes damages and physiological disorders in plants such as; mercury causes physical obstruction of water flow through binding with water channel proteins and forces leaf stomata to close [12]. High levels of mercury in plants causes seed injuries, reduces seed viability, disruption of cellular metabolism and bio-membrane lipids, generation of ROS (H_2O_2, hydroxyl radicals, anion radicals, superoxide), loss of potassium, manganese and magnesium, influence the activity of enzymes [12, 71, 72].

Table 1. Recommended dietary allowance (RDA) and Maximum permissible limit (MPL) of medicinal plants, edible plants and drinking water of essential heavy metals

Essential Heavy Metals	RDA (mg/day)	WHO MPL (Medicinal Plants) (mg/kg)	WHO MPL (Edible Plants) (mg/kg)	WHO MPL (Drinking Water) (mg/L)
Chromium	35 (men) 25 (women)	1.5	1.3	0.05
Cobalt	0.005-0.04	---	0.01	0.08
Copper	2-5	10	10	2.00
Iron	8 (men) 18 (women)	15	20	0.3
Manganese	2.3 (men) 1.8 (women)	200	2	0.4
Nickel	0.08-0.13	1.5	1.63	0.07
Zinc	11 (men) 8(women)	50	50	3.0

(RDA) [10, 73, 74]
(MPL) of medicinal plants [75-81]
(MPL) of edible plants [74, 78, 81-83]
(MPL) of drinking water [80, 84-88]

Table 2. Recommended dietary allowance (RDA) and Maximum permissible limit (MPL) of medicinal plants, edible plants and drinking water of non-essential heavy metals

Non-essential Heavy Metals	RDA (mg/day)	WHO MPL (Medicinal Plants) (mg/kg)	WHO MPL (Edible Plants) (mg/kg)	WHO MPL (Drinking Water) (mg/L)
Arsenic	---	1.0	0.5	0.01
Cadmium	---	0.3	0.02	0.003
Lead	---	10	0.43	0.010
Mercury	---	1.0	0.03	0.006

(RDA) [10, 73, 74]
(MPL) of medicinal plants [75-78, 80, 81]
(MPL) of edible plants [74, 78, 81-83]
(MPL) of drinking water [80, 85-88]

Conclusion

Heavy metal contamination is increasing day by day due to various sources and influencing the human health and production of plants. Some heavy metals including cobalt, copper, chromium, iron, zinc, nickel, manganese are essential for living organisms and play vital role in various processes, while others are non-essential for living organisms including arsenic, cadmium, lead, mercury, and have acute to chronic toxic effects. It is necessary to diagnose the sources of heavy metals sources and their impacts on health of humans and plants. This review demonstrates the sources of heavy metals, symptoms of various diseases caused by heavy metal interaction in humans, impacts of heavy metals on plants, RDA and WHO permissible limits of heavy metals.

Authors' contributions

Conceived and designed the experiments: M Bibi & Samiullah, Analyzed the data: M Bibi, F Behlil & Sahifa, Contributed materials/ analysis/ tools: M Bibi & S Afzal, Wrote the paper: M Bibi & Samiullah

References

1. Kiazai I, Samiullah, NK, Attiq-Ur-Rehman, AG & Baqi A (2019). Determination of heavy metals concentration in Astragalus anisacanthus and Ebenus stellata of Balochistan, Pakistan. *Pure and Appl Biol* 8(3): 2028-2035.
2. Tchounwou PB, Yedjou CG, Patlolla AK & Sutton DJ (2012). Heavy metal toxicity and the environment. *Mol, Cli and Environ Toxicol* 133-164.
3. Bibi M, Khan S, Khan N, Tareen AH, Bibi S & Taj H (2021). Determination of essential and non-essential elements in Xylanthemum macropodum of Balochistan, Pakistan. *Bag J of Biochem and ApplBiol Sci* 2(02): 94-103.
4. Dogan Y, Baslar S & Ugulu I (2014). A study on detecting heavy metal accumulation through biomonitoring: content of trace elements in plants at Mount Kazdagi in Turkey. *Appl Ecol Environ Res* 12(3): 627-636.
5. Monalisa M & Kumar PH (2013). Effect of ionic and chelate assisted hexavalent chromium on mung bean seedlings (Vigna radiata L. wilczek. var k-851) during seedling growth. *J of Str Physiol & Biochem* 9(2).
6. Ghani A & Ghani A (2011). Effect of chromium toxicity on growth, chlorophyll and some mineral nutrients of brassica juncea L. *Egy Aca J of Biol Sci, H Bot* 2(1): 9-15.
7. Engwa GA, Ferdinand PU, Nwalo FN & Unachukwu MN (2019). Mechanism and health effects of heavy metal toxicity in humans. Poisoning in the modern world-new tricks for an old dog. pp. 10.
8. Jaishankar M, Tseten T, Anbalagan N, Mathew BB & Beeregowda KN (2014). Toxicity, mechanism and health effects of some heavy metals. *Interd Toxicol* 7(2): 60.
9. Zayed AM & Terry N (2003). Chromium in the environment: factors affecting biological remediation. *Plant and Soil* 249(1): 139-156.
10. Al-Fartusie FS & Mohssan SN (2017). Essential trace elements and their vital roles in human body. *Indian J Adv Chem Sci* 5(3): 127-136.
11. Rodríguez MC, Barsanti L, Passarelli V, Evangelista V, Conforti V & Gualtieri P (2007). Effects of chromium on photosynthetic and photoreceptive apparatus of the alga Chlamydomonas reinhardtii. *Environ Res* 105(2): 234-239.
12. Yadav S (2010). Heavy metals toxicity in plants: an overview on the role of glutathione and phytochelatins in heavy metal stress tolerance of plants. *South Afr J of Bot* 76(2): 167-179.
13. Janadeleh H, Kardani M, Rad MK & Salemi M (2015). Study of heavy metals effects on plants. Third International Symposium On Environmental and Water Resources Engineering.
14. Vajpayee P, Tripathi R, Rai U, Ali M & Singh S (2000). Chromium (VI) accumulation reduces chlorophyll biosynthesis, nitrate reductase activity and protein content in Nymphaea alba L. *Chemosphere* 41(7): 1075-1082.
15. Nath K, Singh D, Shyam S & Sharma YK (2008). Effect of chromium and tannery effluent toxicity on metabolism and growth in cowpea (Vigna sinensis L. Saviex Hassk) seedling. *Res in Environ and Life Sci* 1(3): 91-94.
16. Connett PH & Wetterhahn KE (1983). Metabolism of the carcinogen chromate by cellular constituents. *Inorg Ele in Biochem* 93-124.
17. Syed R, Kapoor D & Bhat AA (2018). Heavy metal toxicity in plants: a review. *Plant Arch* 18(2): 1229-1238.
18. Shanker AK, Cervantes C, Loza-Tavera H & Avudainayagam S (2005). Chromium toxicity in plants. *Environ Inter* 31(5): 739-753.
19. Nematshahi N, Lahouti M & Ganjeali A (2012). Accumulation of chromium and its effect on growth of (Allium cepa cv.

Hybrid). *Eur J of Exper Biol* 2(4): 969-974.
20. Barceloux DG & Barceloux D (1999). Cobalt. *J of Toxicol: Cli Toxicol* 37(2): 201-216.
21. Chatterjee J & Chatterjee C (2000). Phytotoxicity of cobalt, chromium and copper in cauliflower. *Environ Poll* 109(1): 69-74.
22. Czarnek K, Terpiłowska S & Siwicki AK (2015). Selected aspects of the action of cobalt ions in the human body. *Central-Eur J of Immunol* 40(2): 236.
23. Bibi S, Fatima N, Syed M, Shah W, Naz A & Rizwan M (2017). A review on the heavy metal cobalt: source, environmental impact, effect on human health and remediation. 4th International Water Conference Climate Change & Disaster Risk Management for sustainable development & Businesses.
24. Lison D (1996). Human toxicity of cobalt-containing dust and experimental studies on the mechanism of interstitial lung disease (hard metal disease). *Crit Rev in Toxicol* 26(6): 585-616.
25. Bakkaus E, Gouget B, Gallien JP, Khodja H, Carrot F, Morel J & Collins R (2005). Concentration and distribution of cobalt in higher plants: the use of micro-PIXE spectroscopy. *Nuclear Instruments and Methods in Physics Research Section B: Beam Interactions with Materials and Atoms* 231(1-4): 350-356.
26. Kukier U, Peters CA, Chaney RL, Angle JS & Roseberg RJ (2004). The effect of pH on metal accumulation in two Alyssum species. *J of Environ Qual* 33(6): 2090-2102.
27. Li Z, McLaren R & Metherell A (2004). The availability of native and applied soil cobalt to ryegrass in relation to soil cobalt and manganese status and other soil properties. *New Zealand J of Agric Res* 47(1): 33-43.
28. Li HF, Gray C, Mico C, Zhao FJ & McGrath SP (2009). Phytotoxicity and bioavailability of cobalt to plants in a range of soils. *Chemosphere* 75(7): 979-986.
29. Mahurpawar M (2015). Effects of heavy metals on human health. *Inter J of Res-Granthaalayah* 2394-3629.
30. Chandra RK (1990). Micronutrients and immune functions: an overview. *Annals of the New York Acad of Sci* 587(1): 9-16.
31. Tan JC, Burns DL & Jones HR (2006). Severe ataxia, myelopathy, and peripheral neuropathy due to acquired copper deficiency in a patient with history of gastrectomy. *J of Pare and Enter Nutr* 30(5): 446-450.
32. Hegedüs A, Erdei S & Horváth G (2001). Comparative studies of H_2O_2 detoxifying enzymes in green and greening barley seedlings under cadmium stress. *Plant Sci* 160(6): 1085-1093.
33. Stadtman ER & Oliver CN (1991). Metal-catalyzed oxidation of proteins: physiological consequences. *The J of Biol Chem* 266(4): 2005-2008.
34. Valko M, Morris H & Cronin M (2005). Metals, toxicity and oxidative stress. *Curr Med Chem* 12(10): 1161-1208.
35. Soetan K, Olaiya C & Oyewole O (2010). The importance of mineral elements for humans, domestic animals and plants-A review. *Afri J of Food Sci* 4(5): 200-222.
36. Becker M & Asch F (2005). Iron toxicity in rice—conditions and management concepts. *J of Plant Nutr and Soil Sci* 168(4): 558-573.
37. Sinha S, Gupta M & Chandra P (1997). Oxidative stress induced by iron in Hydrilla verticillata (lf) Royle: Response of antioxidants. *Ecotoxicol and Environ safety* 38(3): 286-291.
38. Tanaka S & Lieben J (1969). Manganese poisoning and exposure in Pennsylvania. *Arch of Environ Health: An Inter J* 19(5): 674-684.
39. Levy BS & Nassetta WJ (2003). Neurologic effects of manganese in humans: a review. *Inter J of Occupa and Environ Health* 9(2): 153-163.
40. Zayed J, Vyskocil A & Kennedy G (1999). Environmental contamination and human exposure to manganese–contribution of methylcyclopentadienyl manganese tricarbonyl in unleaded gasoline. *Inter Arch of Occupa and Environ Health* 72(1): 7-13.

41. Soldin O & Aschner M (2007). Effects of manganese on thyroid hormone homeostasis: potential links. *Neurotoxicol* 28(5): 951-956.
42. Cawte J (1985). Psychoactive substances of the South Seas: betel, kava and pituri. *Australian and New Zealand J of Psy* 19(1): 83-87.
43. Menezes-Filho JA, Bouchard M, Sarcinelli PN & Moreira JC (2009). Manganese exposure and the neuropsychological effect on children and adolescents: a review. *Revi Panamer de Salud Púb* 26: 541-548.
44. Gimeno-García E, Andreu V & Boluda R (1996). Heavy metals incidence in the application of inorganic fertilizers and pesticides to rice farming soils. *Environ Poll* 92(1): 19-25.
45. Hurley L (1976). Manganese and other trace elements. Present Knowledge in Nutrition (Nutrition Reviews'), Fourth Edition. The Nutrition Foundation, Inc. New York, Washington.
46. Duda-Chodak A & Blaszczyk U (2008). The impact of nickel on human health. *J of Elementol* 13(4): 685-693.
47. Pandey N & Sharma CP (2002). Effect of heavy metals Co^{2+}, Ni^{2+} and Cd^{2+} on growth and metabolism of cabbage. *Plant Sci* 163(4): 753-758.
48. Rahman H, Sabreen S, Alam S & Kawai S (2005). Effects of nickel on growth and composition of metal micronutrients in barley plants grown in nutrient solution. *J of Plant Nutr* 28(3): 393-404.
49. Zornoza P, Robles S & Martin N (1999). Alleviation of nickel toxicity by ammonium supply to sunflower plants. *Plant and Soil* 208(2): 221-226.
50. Gajewska E, Skłodowska M, Słaba M & Mazur J (2006). Effect of nickel on antioxidative enzyme activities, proline and chlorophyll contents in wheat shoots. *Biol Planta* 50(4): 653-659.
51. Gonnelli C, Galardi F & Gabbrielli R (2001). Nickel and copper tolerance and toxicity in three Tuscan populations of Silene paradoxa. *Physiol Planta* 113(4): 507-514.
52. Pandolfini T, Gabbrielli R & Comparini C (1992). Nickel toxicity and peroxidase activity in seedlings of Triticum aestivum L. *Plant, Cell & Environ* 15(6): 719-725.
53. Ros R, Cook DT, Martinez-Cortina C & Picazo I (1992). Nickel and cadmium-related changes in growth, plasma membrane lipid composition, ATPase hydrolytic activity and proton-pumping of rice (Oryza sativa L. cv. Bahia) shoots. *J of Exper Bot* 43(11): 1475-1481.
54. Rout GR & Das P (2009). Effect of metal toxicity on plant growth and metabolism: I. Zinc *Sust Agri* 873-884.
55. Brown KH, Wuehler SE & Peerson JM (2001). The importance of zinc in human nutrition and estimation of the global prevalence of zinc deficiency. *Food and Nutr Bull* 22(2): 113-125.
56. Roohani N, Hurrell R, Kelishadi R & Schulin R (2013). Zinc and its importance for human health: An integrative review. *J of Res in Med Sci: the Offl J of Isfahan Uni of Med Sci* 18(2): 144.
57. Prasad AS (2008). Zinc in human health: effect of zinc on immune cells. *Mol Med* 14(5): 353-357.
58. Hacisalihoglu G (2020). Zinc (Zn): The last nutrient in the alphabet and shedding light on Zn efficiency for the future of crop production under suboptimal Zn. *Plants* 9(11): 1471.
59. Council NR (1977). Biologic Effects of Arsenic on Plants and Animals. In: Arsenic: Medical and Biologic Effects of Environmental Pollutants. US: National Academies Press.
60. Finnegan PM & Chen W (2012). Arsenic toxicity: the effects on plant metabolism. *Frontiers in physiology* 3: 182.
61. Bergqvist C (2011). Arsenic accumulation in various plant types. PhD. Thesis. Deptt. of Botany., Univ. Stockholm., Sweden.
62. Singh BR, Gupta SK, Azaizeh H, Shilev S, Sudre D, Song WY, Martinoia E & Mench M (2011). Safety of food crops on land contaminated with trace elements. *J of the Sci of Food and Agric* 91(8): 1349-1366.
63. Irfan M, Hayat S, Ahmad A & Alyemeni MN (2013). Soil cadmium enrichment: Allocation and plant physiological

manifestations. *Saudi J of Biol Sci* 20(1): 1-10.

64. Sharma P & Dubey RS (2005). Lead toxicity in plants. *Brazil J of Plant Physiol* 17(1): 35-52.
65. Thürmer K, Williams E & Reutt-Robey J (2002). Autocatalytic oxidation of lead crystallite surfaces. *Sci* 297(5589): 2033-2035.
66. Pirkle JL, Kaufmann RB, Brody DJ, Hickman T, Gunter EW & Paschal DC (1998). Exposure of the US population to lead, 1991-1994. *Environ Health Persp* 106(11): 745-750.
67. Abadin H, Ashizawa A, Llados F & Stevens YW (2007). Toxicological profile for lead.
68. Matović V, Buha A, Đukić-Ćosić D & Bulat Z (2015). Insight into the oxidative stress induced by lead and/or cadmium in blood, liver and kidneys. *Food and Chem Toxicol* 78: 130-140.
69. Najeeb U, Ahmad W, Zia MH, Zaffar M & Zhou W (2017). Enhancing the lead phytostabilization in wetland plant Juncus effusus L. through somaclonal manipulation and EDTA enrichment. *Arab J of Chem* 10: S3310-S3317.
70. Kibria M, Maniruzzaman M, Islam M & Osman K (2010). Effects of soil-applied lead on growth and partitioning of ion concentration in Spinacea oleracea L. tissues. *Soil Environ* 29(1): 1-6.
71. Gworek B, Dmuchowski W & Baczewska-Dąbrowska AH (2020). Mercury in the terrestrial environment: a review. *Environ Sci Europe* 32(1): 1-19.
72. Azevedo R & Rodriguez E (2012). Phytotoxicity of mercury in plants: a review. *J of Bot*.
73. Khan H, Khan MA, Tariq SA, Saeed M, Muhammad N, Gul F & Inayat H (2012). Analysis of metal content of samples of Gloriosa Superba L (Colchicaceae) collected from two different locations in Pakistan. *Trop J of Pharma Res* 11(4): 631-636.
74. Karpiuk UV, Al Azzam KM, Abudayeh ZHM, Kislichenko V, Naddaf A, Cholak I & Yemelianova O (2016). Qualitative and quantitative content determination of macro-minor elements in Bryonia alba L. roots using flame atomic absorption spectroscopy technique. *Adva Pharma Bull* 6(2): 285.
75. Shah A, Niaz A, Ullah N, Rehman A, Akhlaq M, Zakir M & Khan MS (2013). Comparative study of heavy metals in soil and selected medicinal plants. *J of Chem*.
76. Akram S, Najam R, Rizwani GH & Abbas SA (2015). Determination of heavy metal contents by atomic absorption spectroscopy (AAS) in some medicinal plants from Pakistani and Malaysian origin. *Pak J of Pharma Sci* 28(5).
77. Nkansah MA, Hayford ST, Borquaye LS & Ephraim JH (2016). Heavy metal contents of some medicinal herbs from Kumasi, Ghana. *Cogent Environ Sci* 2(1): 1234660.
78. Parveen R, Abbasi AM, Shaheen N & Shah MH (2020). Accumulation of selected metals in the fruits of medicinal plants grown in urban environment of Islamabad, Pakistan. *Arab J of Chem* 13(1): 308-317.
79. Baba H & Mohammed M (2021). Determination of Some Essential Metals in Selected Medicinal Plants. *Chem Res J* 12(1): 15-20.
80. Dinu C, Gheorghe S, Tenea AG, Stoica C, Vasile GG, Popescu RL & Pascu LF (2021). Toxic Metals (As, Cd, Ni, Pb) impact in the most common medicinal plant (Mentha piperita). *Inter J of Environ Res and Pub Health* 18(8): 3904.
81. Popovici V, Bucur L, Calcan SI, Cucolea EI, Costache T, Rambu D, Schröder V, Gîrd CE, Gherghel D, Vochita G, Caraiane A & Badea V (2021). Elemental Analysis and In Vitro Evaluation of Antibacterial and Antifungal Activities of Usnea barbata (L.) Weber ex FH Wigg from Călimani Mountains, Romania. *Plants* 11(1): 32.
82. Jabeen S, Shah MT, Khan S & Hayat MQ (2010). Determination of major and trace elements in ten important folk therapeutic plants of Haripur basin, Pakistan. *J of Med Plants Res* 4(7): 559-566.
83. Mekassa B & Chandravanshi BS (2015). Levels of selected essential and non-

essential metals in seeds of korarima (Aframomum corrorima) cultivated in Ethiopia. *Brazil J of Food Technol* 18(2): 102-111.

84. Ljung K & Vahter M (2007). Time to re-evaluate the guideline value for manganese in drinking water? *Environ Health Persp* 115(11): 1533-1538.
85. Arain MA, Haque Z, Badar N & Mughal N (2009). Drinking water contamination by chromium and lead in industrial lands of Karachi. *JPMA. The J of the Pak Med Assoc* 59(5): 270.
86. Cobbina SJ, Duwiejuah AB, Quansah R, Obiri S & Bakobie N (2015). Comparative assessment of heavy metals in drinking water sources in two small-scale mining communities in northern Ghana. *Inter J of Environ Res and Pub Health* 12(9): 10620-10634.
87. Shirkhanloo H, Mirzahosseini SAH, Shirkhanloo N, Moussavi-Najarkola SA & Farahani H (2015). The evaluation and determination of heavy metals pollution in edible vegetables, water and soil in the south of Tehran province by GIS. *Arch of Environ Prot* 41(2).
88. Mahugija JA (2018). Levels of heavy metals in drinking water, cosmetics and fruit juices from selected areas in Dar es salaam. *Tanza J of Sci* 44(1): 1-11.