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Impact of Heavy Metals Consumption on Human Health: A Literature Review

Yaser Qureshi^{1*}

¹Department of Zoology, Government College Khertha, Balod, Chhattisgarh, India.

Author's contribution

The sole author designed, analyzed, interpreted and prepared the manuscript.

Article Information

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Review Article

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ABSTRACT

While some heavy metals are essential trace components, many are bio toxic in human biochemistry. As a result, a full grasp of underlying systems is required. For supporting life and minimizing environmental damage, we must grasp their sources, liquidation techniques, chemical modifications, and deposition patterns These metals are discharged into the environment by both natural and human activity, including mining, industrial operations, and vehicular emissions. Soils and groundwater are contaminated when they leak into subsurface fluids and eventually into the aquifer. The world's commerce and coordinating systems frequently generate environmental toxicity and poisoning. Swallowed, they generate bio toxic compounds, lose structural integrity, and block bio reactions. This study's goal is to learn more about heavy metals and their bio toxic effects on humans.

Keywords: Heavy metal; environment; human health; illness.

1. INTRODUCTION

Environmentally important metallic elements in the environment, they are tough to eradicate.

Metal is an important class of harmful chemicals in various occupational and environmental circumstances. The ubiquity of exposure today affects these harmful compounds to human

^{*}Corresponding author: E-mail: yaserqureshi@rediffimail.com;

health. The increased use of the wide range of metals in business and our daily lives has resulted in serious worries due to dangerous metal contamination in our environment.

Metals are a natural component of the highly conductive ecosystem. They are substances that voluntarily release their electrons into cations. In biodiversity, metals such as air, crusts, water bodies, including plants and animals, can also develop worldwide. 23 of the present 35 natural metals contain high specifications and atomic densities above 5 g/cm3, commonly referred to as heavy metals [1-2]. Heavy metals include antimony, tellurium, steel, platinum, silver, manganese, cobalt, cadmium, steel, platinum, and zinc. The heavymetal high-density class is known not only for its negative impact on ecosystems and organisms [3]. Heavy metals which may produce inappropriate diseases and syndromes, if inappropriate, but which are of acute or chronic toxicity at high doses.

The Heavy Metals can be distributed by various natural processes including volcanic eruptions, spring water, erotic and bacterial activity as well as by the use of fossil fuels, industrial processes, agriculture and feed [4]. These heavy metals have diverse effects on living species and humans. Metallic macromocules bind and hinder cell function. Thus, heavy metal poisoning in humans has numerous effects. The CNS can cause harmful blood molecules in the lungs, liver, and kidneys [5]. Physical, musculoskeletal, and neurological functions are slowing down, mimicking Parkinson's and Alzheimer's [6]. Acids, mutations, hormone disorders, and cancer may ultimately be damaged by long-term contact or by heavy metal compounds [5].

2. MECHANISM OF HEAVY METAL TOXICITY

Some heavy metals release free radicals that can harm other cells or induce oxidative stress. The free radical mechanism for generating heavy metals is particular (Engwa et al., 2019).

Arsenic: Bacteria, algae, fungi, and humans use methyl-hazardous compounds containing MMA and DMA (DMA). It's the end product of persistent arsenic poisoning.

iAs (V) \rightarrow iAs (III) \rightarrow MMA (V) \rightarrow MMA (III) \rightarrow DMA (V)

Inorganic arsenic methylation eliminates urine as a bioindication of chronic arsenic exposure via MMA (V) and DMA end products (V). However, MMA (III) remains inside the cell as an intermediary product.

MMA III is a hazardous intermediate product of arsenic that may be responsible for arsenic-induced cancer [7].

Iron: It has biological components like haemoglobin and physiological activities. The human body needs iron. However, as the Fenton reaction illustrates, iron is one of the heavy metals commonly known as radical hydroxyl [8].

 $Fe3++O2-\rightarrow Fe2++O2Fe3++O2-\rightarrow Fe2++O2$ Fe2++H2O2 \rightarrow Fe3++OH·+OH-(Fenton reaction)Fe2++H2O2 \rightarrow Fe3++OH•+OH-Fenton reaction

Net reaction (Haber-Weiss reaction):

02-+H2O2→OH-+OH·+O2O2-+H2O2→OH-+ OH•+O2

Besides the aforementioned reactions, the following reactions can occur:

 $OH \cdot H2O2 \rightarrow H2O + H + + O2 \cdot - OH \cdot H2O2 \rightarrow H2O + H + + O2 \cdot -$

 $OH \cdot + Fe2 + \rightarrow Fe3 + + OH - OH \cdot + Fe2 + \rightarrow Fe3 + + OH - LOOH + Fe2 + \rightarrow Fe3 + + LO - + OH \cdot LOOH + Fe2 + \rightarrow Fe3 + + LO - + OH \cdot$

Oxidative iron oxidation occurs frequently. OH• can oxidise proteins, lipids, or DNA. FAPy-G is formed when OH• interacts with guanine [9].

MOX can harm PUPL. Inculcated. They found OH•iron can oxidise lipid membranes (lipid peroxidation).

He hypothesised: Lipoperoxidase:

Initiation:Lipid+R·/OH· \rightarrow Lipid·Initiation:Lipid+R•/OH• \rightarrow Lipid•

 $\label{eq:lipid-OO+Lipid-OO+$

Termination:

 $\label{eq:Lipid-Lipid-Lipid-LipidTermination:Lipid+Lipid + Lipid + L$

 $\label{eq:lipid-OO-LipidLipid-OO-LipidLipid-OO+Lipid-OO-LipidLipid-OO+Lipid-OO-Lipid$

Early phase radical (R•)/OH• impacts lipid membrane to form radial lipid. This radical lipid promotes radical peroxyl lipid formation via dioxygen or lipid reactions. This process also breaks down lipid molecules. Finally, two radical lipid molecules or a radical peroxyl lipid molecule engage a stable lipid molecule. Malondialdehyde is the major lipid peroxidation aldehyde and an indication [10]. Proteolytic enzymes require transition metals to break down proteins. This leads to the formation of R•, alcohoxyle (RO•), alkyl peroxyle (ROO•), protein-centred alkaline radicals (PCARs), oxidation, loss of itstidin residue, introduction and development of R• [8].

Copper: For cupric (Cu2+) and cupric (Cu1+) reactive oxygen (ROS) forms that may lead to oxidation and reduction processes were identified. CU2+ can be reduced to Cu+ by accessible biological reducers such as Glutathione (GSH) and ascorbic acid which can catalyse H2O2 in OH• through the Fenton reaction [11].

 $Cu++H2O2 \rightarrow Cu2++OH+OH-Cu++H2O2 \rightarrow Cu2 ++OH+OH-$

The radical OH• generated might react with different biomolecules. Experimental studies have shown that copper can also promote DNA rupture and base oxidation with oxygen-free radicals [5]. Although in vivo study has demonstrated that copper-induced low-density lipoprotein (LDL), in vitro research has demonstrated a definite lack of copper-induced LDL oxidation [12].

Chromium: Free H2O2 radicals are produced by chromium (Cr), particularly Cr4+ [13]. Chromium has also been demonstrated to identify free radicals in the liver and blood of animals. One electron was reduced to find the intermediates of Cr5+.

Cobalt: As a result of the H2O2 collapse, Cobalt (Co), in particular Co2+ has been found to create superoxide (-O2-) [14].

 $\begin{array}{c} Co2++O2 \rightarrow Co++O2 \cdot - \\ \rightarrow Co+-OO \cdot Co2++O2 \rightarrow Co++O2 \bullet - \rightarrow Co+-OO \bullet \end{array}$

• Vanadium

Vanadium is a heavy metal that produces free radical compounds in various oxidation states. NADPH and ascorbic vanadium (IV) antioxidants diminish vanadium (V) in plasma binding plasma proteins [15].

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 $V5++NADPH \rightarrow V4++NADP++H+V5++NADPH \rightarrow V4++NADP++H+$ $V4++O2 \rightarrow V5++O2 \cdot -V4++O2 \rightarrow V5++O2 \cdot -V5++O2 \cdot -V5++O2 \cdot -V5++O2 \cdot -O4$

V(IV) may also form OH• from the breakdown of H2O2 under physiological conditions at around 7 pH in accordance with the Fenton reaction.

 $V4++H2O2\rightarrow V5++OH-+\cdot OHV4++H2O2\rightarrow V5++OH-+\bullet OH$

3. EFFECTS OF HEAVY METAL ON HUMAN HEALTH

Metal, methane, gold, iron, plaster, manganese, mercury, and zinc are heavy metals [16]. A frequent environmental and food heavy metal. Small amounts are necessary for healthy health, while large amounts can be poisonous or hazardous. Intoxication by heavy metals can affect the brain and lungs. Long-term disease exposure, such as MS, Parkinson's, Alzheimer's, and Muscle Dystrophies, may cause physical, muscle, and neurological alterations. Long-term exposure to several metals and chemicals can cause cancer [17]. Some heavy metals are naturallv hazardous in the environment. Thorough awareness of heavy metals is essential to avoid excessive interaction [18].

Arsenic: Arsenic contamination happened owing to both natural and human geological processes. Anthropogenic sources of arsenic include mining and processing. Smelting can produce arsenic from both old and new air and soil [19]. These sources may discharge or runoff into surface waters. Groundwater can also be contaminated by arsenic minerals. The sedimentary and metasedimentary basis [20]. The element is found in nearly every type of chemical and medication. Some insecticides, fertilisers, and feeds can leach arsenic into the environment. Human health is harmed by inorganic arsenic forms like arsenite and arsenate. It can cause lung, liver, bladder, and skin cancer. Arsenic is found in the air, food, and water. Arsenic is a major source of toxicity in over 30 nations [21]. Where arsenic concentrations in groundwater are above the WHO standard (10 g/L) [22]. Misuse of arsenic compounds. pesticides, or minerals can contaminate water. Chronic toxicity refers to arsenic toxicity. It is based on skin disease diagnosis. Keratosis and pigmentation are distinct skin disorders implying arsenic exposure [23].

Name	Description
Arsenic	Arsenic is a major heavy metal for the environment and humans. It is available as oxides or sulphides of iron, sodium, calcium, copper, etc. Inorganic forms of arsenic, Arsenite and arsenate are toxic to the environment and living things. Natural, industrial, and accidental sources of arsenic in humans. Arsenic insecticides, natural mineral reserves, and inappropriate chemical disposal can contaminate drinking water. Suicidal or accidental intake of arsenic can cause acute poisoning in youngsters. Arsenic is a protoplastic toxin that targets the sulfuryl group, enzymes, and mitosis.
Lead	Lead is a particularly hazardous metal that has been widely employed in a variety of parts of the world, causing significant environmental and health hazards. Lead is a somewhat blue silver metal in a dry atmosphere. It begins to tarnish upon contact with air and so forms a variable chemical mix depending on the conditions. Industrial processes, food and tobacco consumption, as well as water and household use, are primarily helpful. Petrol and house paint were created by combining tanks, battery storage devices, toys, and mowers.
Mercury	Metallic mercury is a naturally occurring metal that is capable of warming colourless and odourless gas, as well as bright white silver and odourless liquid. Mercury is a highly bio accumulative and toxic substance. Mercury's presence has a detrimental effect on the marine environment, which is why numerous studies focus on the dispersion of mercury in the ocean. Mercury is mostly produced by human activities such as agriculture, municipal wastewater disposal, mining, and cremation.
Cadmium	Cadmium is an ATSDR-category 6 heavy metal. It is a by-product of zinc production that can be consumed by humans and animals. This metal develops in the body following human absorption. Initially, during WWI, the metal was used to replace pigment and tin in paint. It is also used in rechargeable batteries, metal manufacturing, and smoke production. In alkaline batteries, cadmium is utilised for electrode coating, coloration, location, and even plastic stability. This metal is usually inhaled and consumed, causing chronic and acute exposure. In the ecosystem, cadmium stays in soil and sediment for decades. These metals are progressively taken into the human body by plants.
Chromium	The tenth biggest element is chromium. The most common Cr-6 is trivalent Cr-3. Combining oil and coal, ferrochrome oil refractory, pigment oxidants, catalysts, chromium stainless steel, fertilisers, oil wells, and boiling metal tannery. Wastewater and fertiliser discharge chromium into the environment.
Copper	It's a heavy metal used to build copper pipes, wires, and other products. It is also used for making copper and birth control pills intrauterine. Copper sulphate is added to drinking water and pools Because of anthropogenic and industrial activity it can colonise and absorb soils. Copper is found in almonds, avocados, sprouts and bran.
Manganese	This metal is added to gasoline in the form of Methylcyclopentadienyl manganese tricarbonyl (MMT), and as a result, the petroleum vapours contain a manganese compound that is extremely hazardous.
Nickel	Applied in battery production, nickel plating, machine components, metal placement, steel production, smoking, wire, electric parts, etc. Nickel can cause contact dermatitis in certain persons. Although working with nickel alloys, like stainless steel is completely safe. But nickel compounds and even metallic nickel must be handled with extreme care as they may cause cancer.
Aluminium	Aluminium is the world's third-largest crust element. It is found in the environment. Aluminium mining and processing is more eco-friendly. Aluminium may be a major cause of human, animal, and plant ailments.
Iron	The second richest metal is Iron. He's the twenty-sixth leader. Iron is crucial to the growth and survival of all living things. It is found in algae, cytochromes, catalases, and oxygen proteins including haemoglobin and myoglobin.

Chart 1. Description of heavy metals

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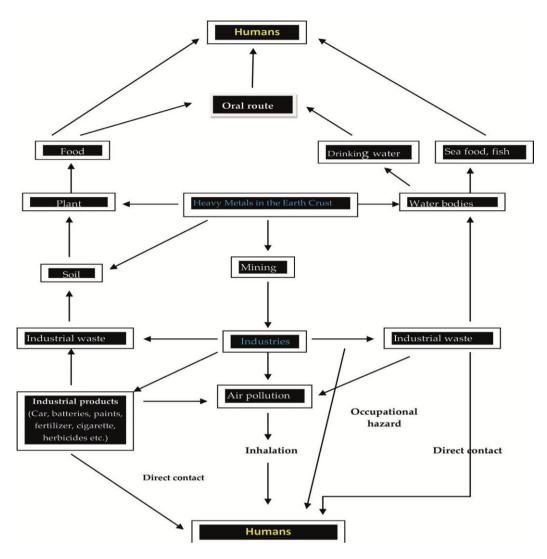


Fig. 1. Heavy metal intoxication mechanisms in humans (source: Engwa et al., 2019)

Blood vessel damage, nose and vomiting, reduced erythrocytes and leucocytes, irregular heartbeat, pricking hands and legs. Long-term contact can cause skin lesions, internal malignancies, neurological difficulties, lung, peripheral vascular, cardiovascular, and diabetes issues [24]. Chronic arsenic poisoning alters permanent organs and increases mortality. While this condition is dangerous, there is no effective cure [25].

Lead: Fossil fuel mining, production, and use have exacerbated air, water, and soil pollution. Batteries, cosmetics, metals, solders, pipelines, etc [23]. Sadly, due to its toxicity, plum is used in paints, gasoline, and other products only to a limited PVC pipes were exposed to purple paint, polluted soil, and industrial [26] Toxic lead poisoning caused symptoms in the CNS and GI tracts of children and adults [27]. Plum water toxicity Components of plumbing and water discharge [28]. Lead is toxic (EPA). The body has a huge impact on numerous parts. Feathers are deposited as insoluble phosphate into the skeleton bone by blood flow [29]. Acute or chronic lead toxicity Acute exposure can cause nausea, vomiting, diarrhoea, renal failure, fatigue, insomnia, arthritis, and vertigo. Acute exposure occurs in various workplaces. Feather exposure causes mental retardation and neurodegeneration (brain and kidney damage) [23]. Plum intoxication is dangerous for most organs. When the blood brain block is exposed to more fluid [30]. The main cause is feather ions from the environment and household, although appropriate avoidance may lessen the threat of toxicity [31].

Mercury: Mercury's heaviest. It's a poisoning of mercury. Many industries are damaging the

environment with mercury [32]. Organic and inorganic mercury can be generated by metals. Quecksilver toxicity can harm the foetus [33]. Methyl mercury is high in seafood from 1 to 50 g/. Lipophilicity of fatty and maize liver [34]. Methylene mercury is microbial. Mercury Chloride and Methyl Mercury Carcinogenicity Mercury produces disaster in addition to these symptoms, mercury poisoning causes fright and loss of memory. Inflammation of the lung and heart may occur. Organic mercury causes tiredness, depression and loss of memory.

Cadmium: Cadmium and its compounds affect human health in numerous ways. Caution should be taken when handling cadmium due to its toxicity. Cadmium is reabsorbed by the kidneys. Consumption of cadmium can cause vomiting and GID, while current exposure can cause substantial lung damage and respiratory pain. Causing bone and lung deposition, long-term cadmium exposure Lead exposure causes bone and lung damage. According to studies on both animals and humans, cadmium can cause osteoporosis (skeletal deterioration). There is a bone fracture outbreak in Japan because of the "Itai-itai" disease [35]. Women had more bone fractures, had poorer bone density, and lost less height than males, hence their cadmium toxicity was higher. Exposure to cadmium can cause renal failure. Exposure to cadmium may disrupt calcium metabolism, the production of kidney stones and hypercalciuria. Cadmium is a human category 1 carcinogen in toxicology. Smokers absorb cadmium more than non-smokers since the major source is tobacco [36]. Cadmium may cause atrophy of the testicles and raise prostate cancer risk.

Chromium: Chemists use chromium to make dyes, pigments, It is solid, liquid, or gaseous. Chromium compounds are very stable in water. It can be divalent. 4-valent. 5-valent. or hexavalent. The most stable forms are Cr(VI) and Cr(III), and only human exposure matters [37]. Like calcium chromate, zinc, strontium, and feather chromate, chromium (VI) is a carcinogen. Conversely, chromium (III), an essential dietary mineral for both animals and humans, aids glucose metabolism. Hexavalent chromium compounds are absorbed faster than trivalent chromium compounds. A wide variety of chromium products are available [23]. Schroeder et al. (1970) found 390 g/kg Cr in cigarettes, but no data on chromium inhalation. When chromium compounds encounter broken skin, they create a deep penetrating hole. Exposure to chromium

compounds can cause and treat monthly ulcers. Erythrocyte glutathione reductase inhibitors limit the ability to convert methemoglobin to haemoglobin [38]. Many in vitro and in vivo studies have shown that chromato chemicals can induce DNA damage including DNA adducts, chromosome abnormalities, chromatid exchange for sisters, replication alterations, and DNA transcriptions.

Aluminium: Aluminum is the third most abundant element on Earth. Inhalation, ingestion, and skin contact are all present in one oxidation (3+). Aluminium is found in water, food, drinks, and medications. Of course, food contains aluminium. Aluminium and its compounds are slightly absorbed in humans, however the rate is unknown. The symptoms of a high aluminium content in the body are nausea, mouth ulcers, skin ulcers and arthritic pain. But these are mild and transient effects [39]. The WHO hypothesised in 1997 that aluminium exposure increases the risk of Alzheimer's disease in people. Contact dermatitis and irritating dermatitis have been reported in workers exposed to aluminium. Aluminum has harmed the brain, causing memory loss, balance issues, and coordination issues [40]. Aluminum is difficult to eliminate from the body and might cause bone or brain damage. Aluminum poisoning can be dusty caused by conditions, long-term intravenous feeding, impaired renal function, hemodialysis, or ingestion of high-aluminum compounds. Aluminum can be found in polluted dialysates and phosphate binders. Aluminum can cause exposure secondary hyperparathyroidism, adynamic bone disorder, and osteomalacia [41]. Aluminum toxicity is linked to respiratory issues, anaemia, poor iron absorption, and neurological issues.

Iron: Iron is the most plentiful transition metal. Many essential proteins and enzymes in living beings require a biological cofactor. It aids most aerobic species' breathing. Radiation can interact with biomolecules, cells, tissues, and the entire body if not appropriately segregated. Doctors have long been fascinated by iron toxicity. Many iron-containing products are used on children, causing iron poisoning [42]. Cyclisme de l'ironThe initial stage of iron therapy involves gastrointestinal symptoms like vomiting and diarrhoea [43]. А six-to-twenty-four-hour overdose is termed latent. Between 12 and 96 hours follow the initial clinical manifestation. Lethargy, tachycardia, liver necrosis, improper metabolism, and mortality [44]. Stages 4 and 5 have iron overload. Ulcers and constipation are prevalent. Excess iron consumption boosts cancer risk in wealthy meat-eating cultures. Workers at risk of asbestosis are the second leading cause of lung cancer [45]. Asbestosrelated cancer is linked to free radicals. Iron can harm a cell's DNA. Iron oxidises DNA, causing cancer [46]. Iron sulphate, monohydrate, and heptahydrate cause no immediate harm whether consumed orally, cutaneously, or inhaled. The FDA deems iron salts safe, with little negative effects. Iron toxicity [47]. Free radicals create friends like hydrogen peroxide and superoxide in pathological metabolism [48]. Surplus superoxides and hydrogen peroxides react aggressively with free iron, causing oxidative damage [49]. Hydroxyl radicals can destroy enzymes, damage DNA, and oxidise lipids and polysaccharides. It may cause cell death [50-51].

4. CONCLUSION

Heavy metals enter the body via food, water, air pollution, skin contact, and work. Heavy metals like iron and manganese are essential for specialised biochemistry and physiology, but too much can be harmful. The majority of other heavy metals have little to no effect on the body. Heavy metals cause oxidative stress, biomolycle damage (e.g., enzymes, proteins, lipids, and nucleic acids), cancer-causing DNA, and Toxicology neurotoxicity. advances have improved our understanding of the medical consequences of hazardous chemical exposure Developmental in humans. reversals. malignancies. kidney damage. endocrine. immunological, neurological, and other illnesses discovered through research are examples. The current focus of research is on the unique biochemical and molecular processes that contribute to human illness. We looked at how heavy metals like arsenic, lead, and mercury affect the environment and living things like humans. Metals studied included cadmium, chromium, aluminium, and iron. Clear rules, identification of high-concentration heavy metal locations, and adequate laws and regulations are required to protect public health. Heavy metal exposure must be managed to avoid future issues. Technical methods can help limit heavy metal exposure. Keeping track of your exposure to heavy metals in the environment and in vourself can help prevent exposure. Preventing heavy metal toxicity requires international and national cooperation.

CONSENT

It is not applicable.

ETHICALAPPROVAL

It is not applicable.

COMPETING INTERESTS

Author has declared that no competing interests exist.

REFERENCES

- 1. Duffus JH. Heavy metals a meaningless term?(IUPAC Technical Report). Pure and applied chemistry. 2002;74(5):793-807.
- Li F, Qiu Z, Zhang J, Liu W, Liu C, Zeng G. Investigation, pollution mapping and simulative leakage health risk assessment for heavy metals and metalloids in groundwater from a typical brownfield, middle China. International Journal of environmental research and public health. 2017;14(7):768.
- 3. Bradl H. (Ed.). Heavy metals in the environment: origin, interaction and remediation. Elsevier; 2005.
- Levander OA, Whanger PD. Deliberations and evaluations of the approaches, endpoints and paradigms for selenium and iodine dietary recommendations. The Journal of nutrition. 1996;126(suppl_9):2427S-2434S.
- 5. Engwa GA, Ferdinand PU, Nwalo FN, Unachukwu MN. Mechanism and health effects of heavy metal toxicity in humans. Poisoning in the modern world-new tricks for an old dog. 2019;10.
- Ramírez-García R, Gohil N, Singh V. Recent advances, challenges, and opportunities in bioremediation of hazardous materials. In Phytomanagement of Polluted Sites Elsevier. 2019;517-568.
- Bhowmick S, Pramanik S, Singh P, Mondal P, Chatterjee D, Nriagu J. Arsenic in groundwater of West Bengal, India: A Review of human health risks and assessment of possible intervention options. Science of the Total Environment. 2018;612:148-169.

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- Phippen B, Horvath C, Nordin R, Nagpal N. Ambient water quality guide-lines for iron: overview. Ministry of Environment Province of British Columbia; 2008.
- 9. Nimse SB, Pal D. Free radicals, natural antioxidants, and their reaction mechanisms. RSC advances. 2015; 5(35):27986-28006.
- Parra-Ortiz E, Browning KL, Damgaard LS, Nordström R, Micciulla S, Bucciarelli S, Malmsten M. Effects of oxidation on the physicochemical properties of polyunsaturated lipid membranes. Journal of colloid and interface science. 2019;538:404-419.
- 11. Ranji-Burachaloo H, Gurr PA, Dunstan DE, Qiao GG. Cancer treatment through nanoparticle-facilitated fenton reaction. Acs Nano. 2018;12(12):11819-11837.
- Burkitt MJ. A critical overview of the chemistry of copper-dependent low density lipoprotein oxidation: roles of lipid hydroperoxides, α-tocopherol, thiols, and ceruloplasmin. Archives of biochemistry and biophysics. 2001;394(1):117-135.
- 13. Katz AJ, Chiu A, Beaubier J, Shi X. Combining Drosophila melanogaster somatic-mutation-recombination and electron-spin-resonance-spectroscopy epidemiologic data to interpret observations on chromium carcinogenicity. Molecular and cellular biochemistry. 2001;222(1):61-68.
- 14. Zhang Z, Chen Z, Pan D, Chen L. Fentonlike reaction-mediated etching of gold nanorods for visual detection of Co2+. Langmuir. 2015;31(1);643-650.
- Treviño S, Díaz A, Sánchez-Lara E, Sanchez-Gaytan BL, Perez-Aguilar JM, González-Vergara E. Vanadium in biological action: chemical, pharmacological aspects, and metabolic implications in diabetes mellitus. Biological trace element research 2019;188(1):68-98.
- Mosby CV, Glanze WD, Anderson KN. St. Louis; 1996. Mosby Medical Encyclopedia, The Signet: Revised Edition. [Google Scholar]; 1996.
- Järup L. Hazards of heavy metal contamination. Br Med Bull. 2003;68(1):167–182. [PubMed] [Google Scholar]
- 18. Ferner DJ. Toxicity, heavy metals. eMed J. 2001;2(5):1. [Google Scholar]

- Matschullat J. Arsenic in the geosphere a review. Sci Total Environ. 2000;249(1– 3):297–312.
- 20. Smedley PL, Kinniburgh DG. A Review of the Source, behavior and distribution of arsenic in natural waters. Appl Geochem. 2002;17:517–568.
- Chowdhury UK, Biswas BK, Chowdhury TR, Samanta G, Mandal BK, Basu GC, Chakraborti D. Groundwater arsenic contamination in Bangladesh and West Bengal, India. Environ Health Perspect. 2000;108(5):393–397.
- 22. Hoque MA, Burgess WG, Shamsudduha M, Ahmed KM. Delineating low-arsenic groundwater environments in the Bengal Aquifer System, Bangladesh. Appl Geochem. 2011;26(4):614–623.
- Martin S, Griswold W. Human health effects of heavy metals. Environmental Science and Technology Briefs for Citizens. 2009;(15):1–6.
- Smith AH, Lingas EO, Rahman M. Contamination of drinking-water by arsenic in Bangladesh: a public health emergency. Bull World Health Organ. 2000;78(9):1093–1103.
- 25. Mazumder G. Chronic arsenic toxicity & human health. Indian J Med Res. 2008;128(4):436–447.
- Gerhardsson L, Dahlin L, Knebel R, Schütz A. Blood lead concentration after a shotgun accident. Environ Health Perspect. 2002;110(1):115–117.
- 27. Hauptman M, Bruccoleri R, Woolf AD. An update on childhood lead poisoning. Clinical pediatric emergency medicine. 2017;18(3):181-192.
- Katner A, Pieper KJ, Lambrinidou Y, Brown K, Hu CY, Mielke HW, Edwards MA. Weaknesses in federal drinking water regulations and public health policies that impede lead poisoning prevention and environmental justice. Environmental Justice. 2016;9(4):109-117.
- 29. French AD, Conway WC, Cañas-Carrell JE, Klein DM. Exposure, effects and absorption of lead in American woodcock (Scolopax minor): A Review. Bulletin of environmental contamination and toxicology. 2017;99(3):287-296.
- Dasarathy S, Mookerjee RP, Rackayova V, Thrane VR, Vairappan B, Ott P, Rose CF. Ammonia toxicity: from head to toe?.

Metabolic brain disease. 2017;32(2):529-538.

- Brochin R, Leone S, Phillips D, Shepard N, Zisa D, Angerio A. The cellular effect of lead poisoning and its clinical picture. GUJHS. 2008;5(2):1–8.
- 32. Morais S, Costa FG, Pereira ML. Heavy metals and human health, in Environmental health – emerging issues and practice (Oosthuizen J ed). 2012;227– 246, In Tech.
- Alina M, Azrina A, MohdYunus AS, MohdZakiuddin S, MohdIzuan Eff endi H, Muhammad Rizal R. Heavy metals (mercury, arsenic, cadmium, plumbum) in selected marine fish and shellfish along the Straits of Malacca. Int Food Res J. 2012;19(1):135–140.
- Reilly C. Pollutants in Food Metals and Metalloids, in Mineral Components in Foods, (Szefer P, Nriagu JO eds), Taylor & Francis Group, Boca Raton, FL; 2007;363-388.
- Nishijo M, Nakagawa H, Suwazono Y, Nogawa K, Kido T. Causes of death in patients with Itai-itai disease suffering from severe chronic cadmium poisoning: a nested case–control analysis of a follow-up study in Japan. BMJ open. 2017;7(7):e015694.
- 36. Mishra S, Dwivedi SP, Singh RB. A Review on Epigenetic effect of heavy metal carcinogens on human health. The open Nutraceuticals Journal. 2010;3(1).
- Zhitkovich A. Importance of chromium-DNA adducts in mutagenicity and toxicity of chromium (VI). Chem Res Toxicol. 2005;18(1):3–11.
- Koutras GA, Schneider AS, Hattori M, Valentine WN. Studies on chromated erythrocytes. Mechanisms of chromate inhibition of glutathione reductase. Br J Haematol. 1965;11(3):360–369.
- 39. Clayton DB. Water pollution at Lowermoore North Cornwall: Report of the Lowermoore incident health advisory committee. Truro, Cornwall District Health Authority. 1989;22.
- 40. Krewski D, Yokel RA, Nieboer E, Borchelt D, Cohen J, Harry J, Rondeau V. Human health risk assessment for aluminium, aluminium oxide, and aluminium hydroxide. JJ Toxicol Environ Health B Crit Rev. 2007;10(S1):1–269.

- 41. Andia JB. Aluminum toxicity: Its relationship with bone and iron metabolism. Nephrol Dial Transplant 11 Suppl. 1996;3:69–73.
- 42. Girelli D, Ugolini S, Busti F, Marchi G, Castagna A. Modern iron replacement therapy: clinical and pathophysiological insights. International Journal of Hematology. 2018;107(1):16-30.
- 43. Campione E, Cosio T, Rosa L, Lanna C, Di Girolamo S, Gaziano R, Bianchi L. Lactoferrin as protective natural barrier of respiratory and intestinal mucosa against coronavirus infection and inflammation. International Journal of Molecular Sciences. 2020;21(14):4903.
- 44. Hillman RS. Chapter 54. Hematopoietic agents: Growth factors, minerals, and vitamins, in Goodman & Gilman's The Pharmacological Basis of Therapeutics, 10th Edition (Hardman JG, Limbird LE, Gilman AG eds), New York: McGraw-Hill. 2001;1487-1518.
- 45. Duda TA. Review of natural health philosophy in support of understanding optimal health. unpublished thesis, University of Natural Medicine, Santa Fe, New Mexico; 2010.
- 46. Sharma GN, Gupta G, Sharma P. A comprehensive review of free radicals, antioxidants, and their relationship with human ailments. Critical Reviews[™] in Eukaryotic Gene Expression. 2018;28(2).
- Macdougall IC, Bircher AJ, Eckardt KU, Obrador GT, Pollock CA, et al. Iron management in chronic kidney disease: conclusions from a "kidney disease: Improving Global Outcomes" (KDIGO) Controversies Conference. Kidney international. 2016;89(1):28-39.
- 48. Di Marzo N, Chisci E, Giovannoni R. The role of hydrogen peroxide in redoxdependent signaling: homeostatic and pathological responses in mammalian cells. Cells. 2018;7(10):156.
- 49. Berdoukas V, Coates TD, Cabantchik ZI. Iron and oxidative stress in cardiomyopathy in thalassemia. Free Radical Biology and Medicine. 2015;88:3-9.
- 50. Ahmad A, Ahsan H. Biomarkers of inflammation and oxidative stress in ophthalmic disorders. Journal of Immunoassay and Immunochemistry. 2020;41(3):257-271.

51. Bucher JR, Tien M, Aust SD. The requirement for ferric in the initiation of lipid peroxidation by chelated ferrous iron. Biochemical and biophysical research communications. 1983; 111(3):777-784.

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