HANG TUAH MEDICAL JOURNAL

www.journal-medical.hangtuah.ac.id

Literature Review

Heavy Metals Excessive Intake in Humans: Implications for Brain Cognition and Selected Dietary Essential Micronutrients

Aminu Umar Imam[1]; Yusuf Sarkingobir[2*]

[1]Department of Biochemistry and Molecular Biology, Sokoto State University, Sokoto, Nigeria

[2]Department of Environmental Education, Shehu Shagari University of Education Sokoto, Nigeria

Email correspondence: superoxidedismutase594@gmail.com

Abstract:

Heavy metals are metallic or relative elements described based on characteristics such as higher density, toxicity, and likes. They are present ideally in the natural environment and, therefore, have to be expunged through human activities which are currently excessive in nature. This article aims to deliver a conceptual review of the implications of heavy metals intake for brains and certain dietary nutrients such as copper, zinc, etc. Humans take in heavy metals because of the excessiveness of human activities, thereby causing detrimental effects on the body, brain, development, and nutritional growth. On the brain, heavy metals improvised ways to circumvent the wall of the bilayer and exert harm on certain areas of the brain. This leads to poor functioning of the brain, as well as the body. Similarly, the heavy metals utilized efforts such as molecular mimicry or chelation to outcompete or impede the functions of essential micronutrients required for body functioning. Cd^{2+} impedes Cu^{2+}, Ca^{2+}, and Zn^{2+}; Pb^{2+} also can impede essential elements. Other heavy metals, such as chromium and arsenic, exert similar approaches. This review elucidated the following themes: Meaning of heavy metals, dietary sources of heavy metals, non-dietary sources of heavy metals, dietary nutrients for learning/cognition, implications of heavy metals to the Brian or quasi, and effects of heavy metals on micronutrients. Food materials and water should be safeguarded from heavy metals through disparate methods. Curative heavy metal removal methods (remediation) should be accessible to all.

Keywords: *Heavy metals, dietary, lead, non-dietary, brain development, cognition*

INTRODUCTION

A heavy metal (HM) is a metalloid or metal with an atomic density above 4g/cm3 or an element that is 5 times heavier than water. Examples of heavy metals include zinc, lead, and copper (Vyas *et al*., 2017). Mahanty (2021) submitted that heavy metals (HMs) include a subset of elements having metallic features and are located in polluted sites or events, including metalloids, transition metals, lanthanides, and actinides such as cadmium, copper, zinc, nickel, lead, chromium, etc. Heavy metals heterogeneously form a group of elements with various properties and biological activities (beneficial or harmful). Heavy metals, on many occasions, elicit pollution effects due to their ability to exert toxicity on plants, animals, and humans. Heavy metals cause toxicity even at minute concentrations (Tahir & Alkheraije, 2023). Upon the inception of anthropogenic processes such as mining, smelting, consumer products synthesis, agriculture, construction, etc, heavy metals have been polluting the environment, resulting in abnormal levels of heavy metals (such as cadmium, arsenic, lead, mercury, nickel, etc) in our midst and the environment (Bhattacharjee & Goswami, 2018). Opoku *et al*. (2024) submitted that heavy metals such as zinc, copper, manganese, iron, etc., are essential for their various biochemical roles in the human body and plants. These elements elicit effects at higher doses (Thomas, 2019). Likewise, some elements such as lead, arsenic, and cadmium have no known roles in the body and elicit toxicity when present even in minute amounts (Opoku *et al*., 2024).

Heavy metals enter the body through air, food, and water (Lawal *et al*., 2021). The effects or adverse events elicited by HMs are diverse and dangerous. Parable cadmium toxicity cases include hematoxicity, disturbed calcium metabolism, hepatoxicity, reproductive abnormalities, immunotoxicity, etc. (Bhattacharjee & Goswami, 2018). Lead can cause toxicity in neurons, blood, bone, cardiovascular, and reproductive systems. Arsenic elicits cardiovascular dysfunction, carcinogenesis, diabetes, oxidative stress, etc (Bhattacharjee & Goswami, 2018). Mercury toxicity leads to spontaneous abortion, gingivitis, neurological defects, brain damage, etc (Vjas *et al*., 2017). Chromium has a strong ability to oxidize biological membranes. Similarly, other heavy metals have their damaging effects (Vyas *et al*., 2017).

Heavy metals are many, densely harmful, bioaccumulative, and threatening. Numerous processes expunge heavy metals embedded in the ecosystem components. This expunge releases metals to the human and other biological systems contact, and possible threats are imminent. Human foods (diets) become polluted several times with toxic heavy metals, amounting to harm to the body (Radu-Rusu *et al*., 2013; Dauda *et al*., 2021). Upon entering the body, heavy metals can transgress to invade the brain and affect cognition and learning, among other functions. Similarly, metals tend to cause nutritional problems due to their ability to inhibit essential nutrients (Narwal *et al*., 2017; Rahman *et al*., 2019). This article aims to deliver a conceptual review of the implications of heavy metals intake for brains and certain dietary nutrients such as copper, zinc, etc.

RESEARCH METHOD

An adapted review is a scholarly review to inform the public and fellow scholars about the effects of HMs on nutrition, cognition, and other related effects (Snyder, 2019). Additionally, a review and correlational analysis are formed through the utilization of other related literature to describe insights and possible research directions of the effects of HMs on nutrition and cognition to pave the way for improving public health. Knowledge production is accelerating at a tremendous speed while remaining fragmented and interdisciplinary. This is why the literature review as a research method is more relevant than ever. An effective and well-conducted review as a research method creates a firm foundation for advancing knowledge and facilitating theory development. By integrating findings and perspectives from many empirical findings, a literature review can address research questions with a power that no single study has. It can also help provide an overview of areas where the research is disparate and interdisciplinary. In addition, a literature review is an excellent way of synthesizing research findings to show evidence on a meta-level and to uncover areas in which more research is needed, which is a critical component of creating theoretical frameworks and building conceptual models (Palmatier *et al*., 2018; Snyder, 2019).

RESULT AND DISCUSSION

Heavy Metals

Heavy metals are classified metals and metalloids that are believed to be generally of high density (of more than 5g/cm^3), bioaccumulative in nature (especially in the biological system or diet), and ideally toxic or poisonous to living organisms (Witkowska *et al*., 2021).

Dietary Sources of Heavy Metals to Human Biological System

Heavy metals get their way into foods through numerous pathways, such as pollution of the environment where foods are raised, made, stored, prepared, transported, and dissipated into the environmental components. Weathering, agriculture, industrial processes, etc., strongly pollute water, air, and soil with chemicals, including heavy metals. Therefore, humans or animals can take heavy metals directly from contaminated food and water (Faizal *et al*., 2021). Plants can absorb heavy metals from polluted environments (water, air, soil) and incorporate them into their systems; likewise, animals can feed or take in heavy metals from the prevailing environmental conditions and incorporate them into the body, thereby allowing passage into the food chain or food web (Stenesh, 1998; Witkowska *et al*., 2021). Evidence illustrating the consumption of heavy metals in human diets is numerous. Parable, a study carried out by Izah *et al*. (2017) in Nigeria, mentions that iron, zinc, tin, mercury, lead, chromium, and manganese are present in beverages taken by Nigerians and often exceeding standard limits, a situation attributed to feedstocks and contaminated water applied during the preparations of the stocks. An analysis of cowpea contents of heavy metals in Ibadan Oyo state revealed contamination of the cowpea with arsenic and nickel, as contained in the report disclosed in Ailenokhuoria & Omolekan (2019). Yebpella *et al*. (2013) analyzed numerous cigarette brands in Nigeria and came up with findings that divulged cigarettes contained metals that are often exceedingly dangerous for human consumption. Henceforth, the consumption of cigarettes directly harms humans or aids in polluting the environment (soil, more especially) and resultantly affects the food chain because plants take up plants via the polluted environment. Ahmed et al.

(2017) analyzed the levels of lead and copper in consumed eggs in Egypt and disclosed that many of the samples contained lead above the standard limits. Islam et al. (2014) analyzed heavy metals in table eggs in Peshawar, Pakistan, and discovered that cadmium, zinc, and lead were three times above permissible limits; thus, they could elicit toxicity in humans.

Non-dietary Sources of Heavy Metals Hazards to Humans

Apart from food, water, and relations, other sources serve humans with a quota of heavy metals in a way that could be hazardous because the sources are numerous, excessive, and chronic. Moreover, these non-dietary sources of heavy metals easily contaminate soil, water, and air, upon which the plants or animals take the metals and dissipate them along food chains or food webs to humans unabated (Gulchin *et al*., 2022). In a Nigeria study, Adeyi *et al*. (2019) analyzed the risk of metals due to electronic waste. This work identified that the waste dissipates giant heavy metals and metalloids into the environmental components. Olubanjo *et al*. (2015) outlined how waste mismanagement elicited copper and lead pollution in electronic materials in Ibadan, Southern Nigeria. Alam *et al*. (2019) examined lead, cadmium, and arsenic levels in plastic bags and toys. They identified that tripartite metals were at excessive levels that could trigger pollution or human effects. Another examination of metals in imported China plastic toys identified that some of the materials are engulfing excessive levels of chromium, lead, and cadmium, therefore, could be ingested by humans or leach into soil, water, and air. Aliyu *et al*. (2017), in examining heavy metals in plastic bottles and sachets of different identities in Nigeria, denoted the presence of copper, zinc, nickel, cobalt, cadmium, iron, and manganese among the examined plastics. Seiyaboh *et al*. (2020) measured heavy metals contaminating local beverages and decried the likelihood of consuming heavy metals such as cadmium, arsenic, chromium, mercury, and lead due to the un-safeness of the plastics involved.

Dietary Nutrients Essential for Learning or Cognition

Dietary sources of zinc could be many, such as rice, cashews, nuts, flesh, beef, liver, chicken, seafood, and turkey. Zinc, denoted as Zn, has an atomic number of 30 and an atomic mass of 65.4 and is ranked as the most present metal in humans after iron. All parts of the body contain zinc and muscle. Zinc is available in 300 enzymes or more. Therefore, it serves in the metabolisms of lipids and carbohydrates and helps in energy provision. A healthy immune system, infection resistance, growth, cell division, DNA synthesis, insulin effects, etc require zinc. In the event of problems in zinc actions, effects could be seen as impaired cognitive function, memory impairment, issues of behavior, stunted development, stunted growth, etc; this is pronounced in young people (WHO/BASICS/UNICEF, 1999; AL-Fartuise & Mohssan, 2017).

Copper is denoted with a symbol as Cu, has an atomic number of 29, an atomic mass of 63.5, and essentially serves animals and plants. Sources of copper in diets could be milk, sunflower seeds, walnuts, beans, chicken, mushrooms, cashews, almonds, fish, etc. Catalase, lactase, tyrosinase, superoxide dismutase, ascorbic acid oxidase, and peroxidase are exemplary enzymes requiring copper. Hematology, bine making, myelination, and iron absorption are some essential features geared by copper in the biological system. People malnourished in copper could be affected by inconveniences such as reduced cognition (AL-Fartuise & Mohssan, 2017; Sousa *et al.*, 2019).

An iron chemical element is designated with the symbol Fe, an atomic number value of 26, and a mass weight of 55.8, and it is the predominantly abundant elemental metal in humans. Rich sources of iron could be poultry, red meat, fish, cereals, beans, liver, seafood, etc. Predominantly, iron in the body dwells in the hemoglobin for feeding tissues with essential oxygen. The role played by iron in development, expected growth, metabolism, and hormone-making could not be overstated. However, hair loss, pagophagia, irritability, dizziness, poor immunity, grooved nails, and poor cognition (AL-Fartuise & Mohssan, 2017; Suleiman *et al.*, 2023).

Selenium or Se has an atomic number value of 34, a mass weight of 78.97, and it acts essentially in animals and plants. It is present in selenocysteine, selenoproteins, glutathione peroxidases, thioredoxin reductase, immune system (particularly the T- lymphocyte responses), and the metal protects against colon cancer, prostate cancer, and breast cancer (Soetan *et al*., 2010; Bost *et al*., 2016; AL-Fartuise & Mohssan,2017; Anka *et al*., 2022).

Heavy Metals Implications for Brain or Nervous System Functioning

There is a bunch of evidence demonstrating that heavy metals, individuals, and mixtures are toxic or poisonous to the nervous system. Most heavy metals are risky to cognitive development and growth, as revealed by many literatures (Dahlawi *et al*., 2021; Koch *et al*., 2022). Cadmium increases the risk of mental derangement, and lead exposure during early life years is harmful to cognitive growth and neurodevelopment as well. Arsenic causes hippocampal-related behavioral problems in experimental animals; Hg is well documented for its role in neuro derangement by several worldwide studies. The role of heavy metals in neuro derangement could majorly be attached to their ability to competitively displace the micronutrients needed by the body for proper functioning in a process known as molecular mimicry. In a mixture, some metals add up their effects, for example, as in the case of As, Cd, and Pb that cause neuroproblems in rats synergistically (Reilly, 2003; Martin & Griswold, 2009; Desai & Kaler, 2008; Oruma *et al*., 2021).

Indeed, most heavy metals used mimicry by attaching molecules upon their fold before evading the blood-brain bilayer (BBB) or relations. Sometimes, they use the ideal transporters of micronutrients to be shuttled to evade BBB (Styrer, 1988; Mehrandish *et al*., 2019; Koch *et al*., 2022). Heavy metals such as Cd, Pb, As, Me, Hg can find their way into the brain when the blood circulation distributes its folds, and in turn the metals device ways to pass through the blood-brain bilayer and screenings to reach specific parts of the brain after reaching cerebrospinal fluid (Karri *et al*., 2016; Narwal *et al*., 2017; Mondal & Chandra, 2019; Balali-Mood *et al*., 2021). Mainly, Pb exerts its toxicity on neuroderangement by affecting or damaging the hippocampus through several pathways, such as affecting the signaling role of Ca^{2+}

and instigating oxidative stress. Cd affects neuroderangement through its ability to mimic Ca^{2+} and inhibit it, producing oxidative stress. Even at a low level, Ar elicits cognitive problems by involving the hippocampal area, affecting neurotransmitters, and eliciting oxidative stress. MeHg or other forms of Hg can induce neurotoxicity due to elicitation of effects on neurotransmitters, distortion or replacement of Ca^{2+}, effects upon the microtubules, as well as causing oxidative stress (Gorini *et al*., 2014; Karri *et al*., 2016; Pamplett & Bishop, 2023).

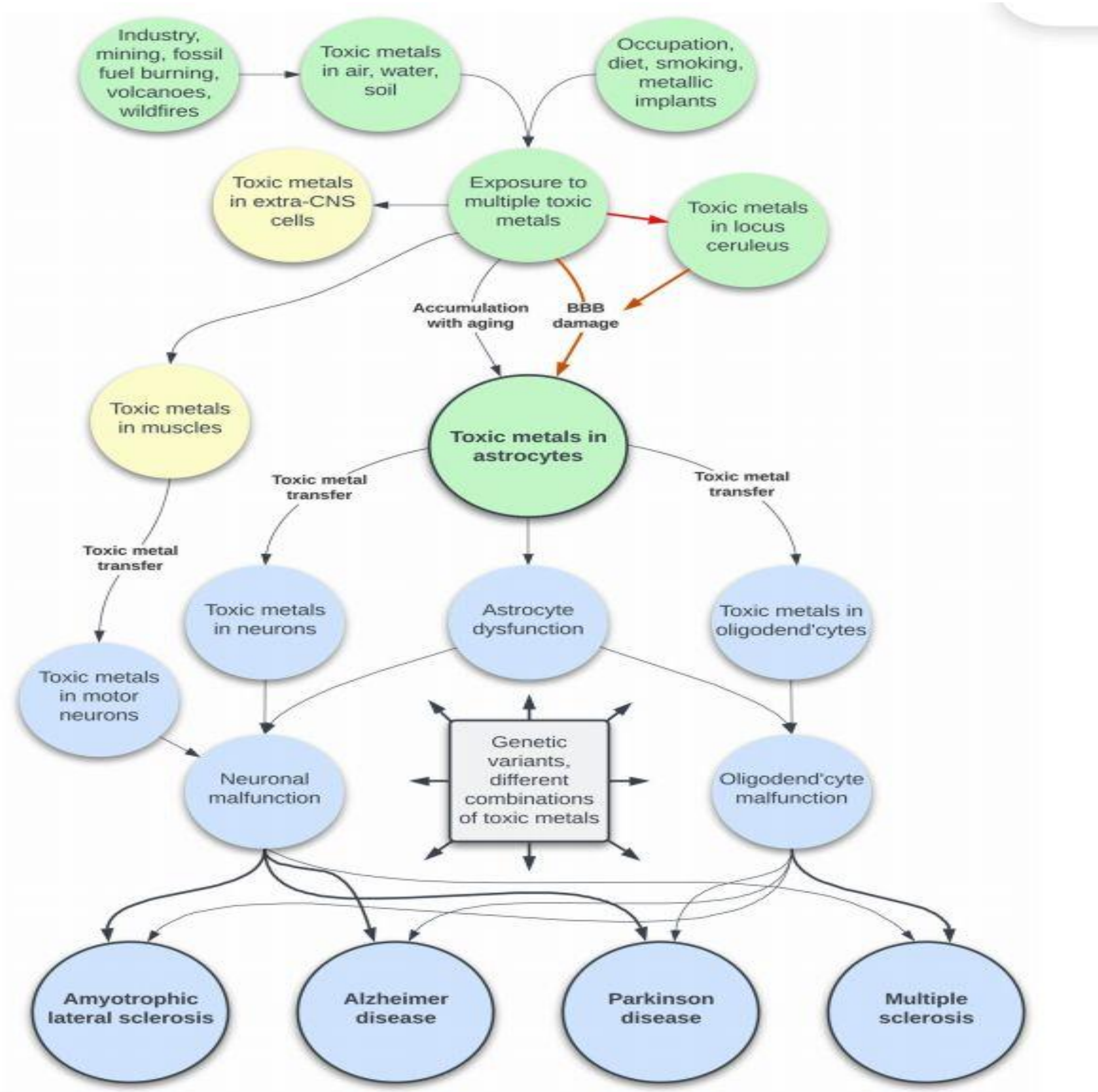


Figure 1. Various effects on brain and relations due to heavy metals; Source: Pamphlet & Bishop, (2023)

Heavy Metals Implications for Body's Health

Heavy metals love sulfhydryl groups, so they bind them and generate reactive oxygen species as well; as a consequence of heavy metals' actions, many disorders and abnormalities occur. As stated, heavy metals cling to functional cell components such as proteins, lipids, DNA, and enzymes. This binding is allowed by molecular mimicry or chelation (coordination) properties of compounds and elements. The binding of heavy metals results in aberration of the bonded biological components, generation of reactive species (that could induce cancer), and alteration of DNA works (such as making new proteins beneficial to the body) (as illustrated in Figure 2) (Duruibe *et al.*, 2007; Raji *et al.*, 2010; Balali-Mood *et al.*, 2021; Anka *et al.*, 2022; Umar *et al.*, 2022).

Specifically, and ideally, heavy metals affect the body numerously and in many ways. Chromium causes risks of intense diarrhea, vomiting, seizures, effects on the liver, problems with the kidney, cancer, malignancies, etc. (Samtiya et al., 2020; Scutaras et al., 2023). Cadmium elicits effects such as kidney destruction, liver damage, risk of cancer, high blood pressure, etc. Risks of brain cell damage, behavior defects, learning derangements, high blood pressure, kidney damage, neurodamage, and liver damage have characterized Pb toxicity. Hg badly and dangerously affects the nervous system, kidney, brain, and immune system. Arsenic effects include skin cancers, diabetes, nervous system malfunctions, genotoxicity, etc. (Mahurpawar, 2015; Jadaa & Mohammed, 2023; Magaji *et al.*, 2023).

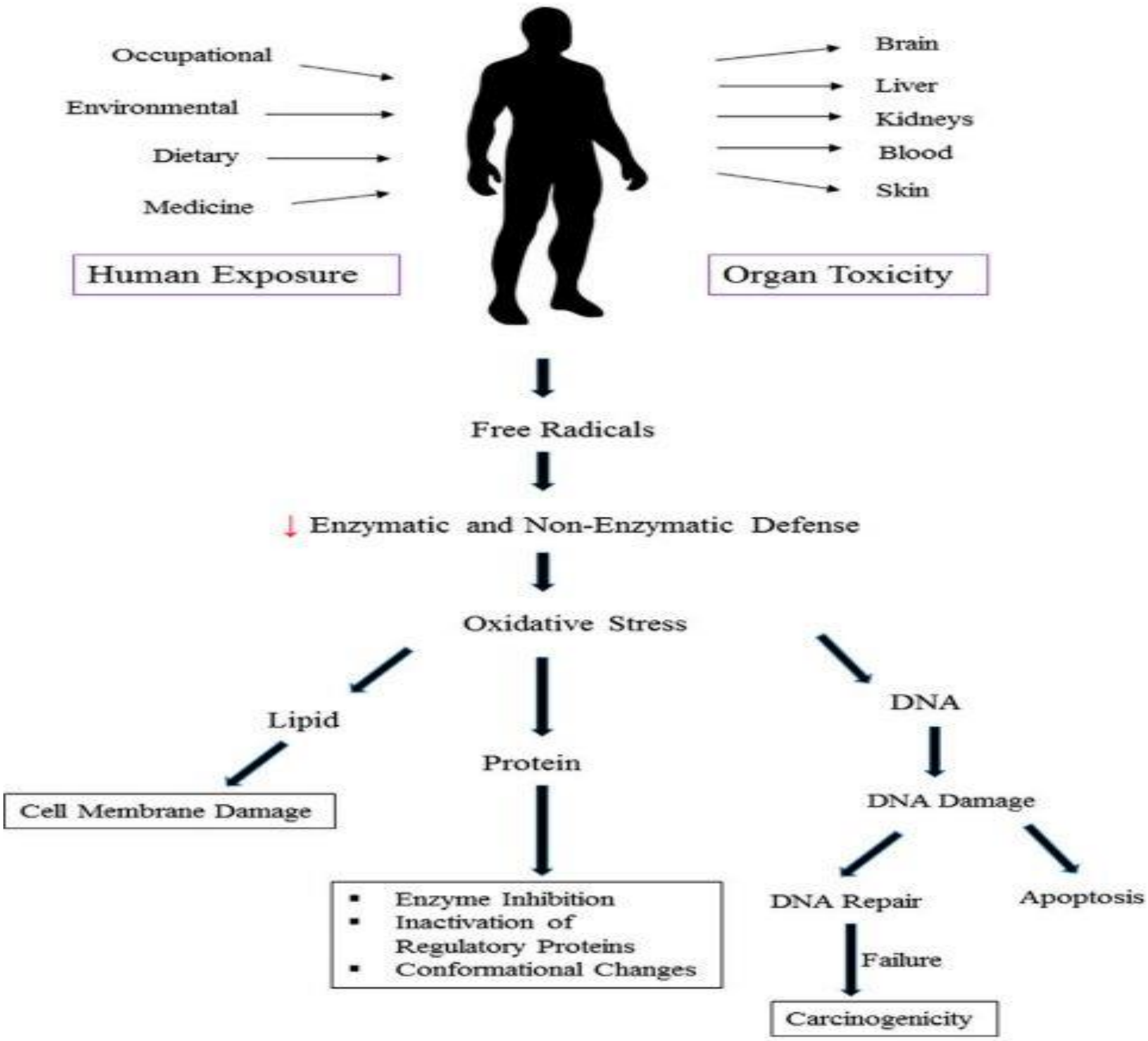


Figure 2. Effects of Heavy metals on health; Source: Balali-mood et al., (2021)

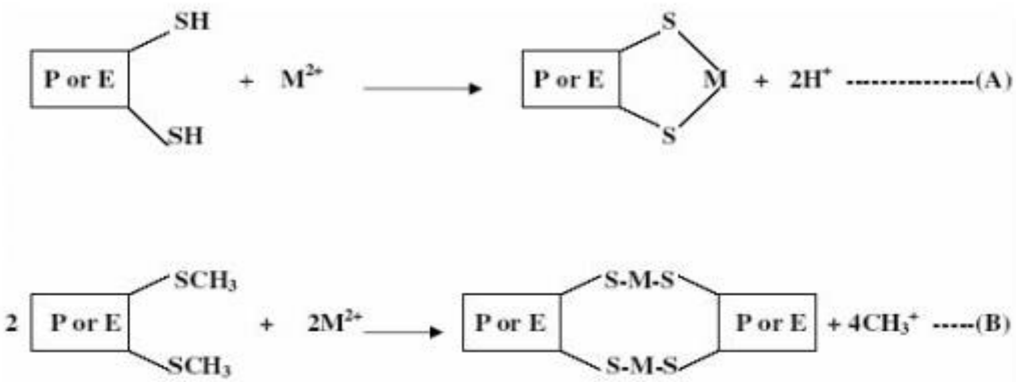
Effects or Implications of Heavy Metals on Micronutrient Nutrition

All elemental entities on Earth could be described as metals or non-metals. Metals are groups that are opaque, capable of forming alloys, capable of conducting electricity and heat, and capable of being malleable. They partner in metal-ligand compounds, enzyme activities, muscle contraction, and nerve impulse transmission. Metals could be categorized into nutritionally essential ones and non-nutritionally essential ones. In the case of Cu, Fe, Se, and Zn, they are nutritionally necessary metals. Often, through antagonistic effects and molecular mimicry, heavy metals exert their effects. In molecular or ionic mimicry, a (heavy) metal or ion, for example, falsely behaves like a standard compound (EPA, 2007; Saeed *et al*., 2011; Rahman *et al*., 2019). Parable, Pb mimics zinc and inhibits heme synthesis, and Pb mimics calcium, thereby affecting many processes, including nerve transmission (brain processes) (Awuchi *et al*., 2020). Other examples of mimicry or chelation (coordination) are:

- Cd^{2+} reaches Zn^{2+} and elicits Zn and Cu disorders in metabolism
- AS^{3+} bind -SH groups
- MeHg binds to some molecules to traverse the BBB
- Pb incites central nervous system (CNS) injury
- Hg incite CNS injury
- Ar incite CNS injury
- Pb binds to bones (EPA, 2007; Soetan *et al*., 2010; Witkowska *et al*., 2021).

Effects of Heavy Metals on Enzymes System

Heavy compounds are converted upon ingestion to stable oxidation forms such as Cd^{2+}, Ar^{3+}, Hg^{2+}, and Pb2+ that combine with biomolecules such as proteins or enzymes, thereby inactivating or inhibiting the affected biomolecules. Specifically, an enzyme has to mix with the appropriate substrate in a complex called enzyme-substrate-complex to make the correct conformation for catalysis. However, upon an enzyme encounter with a mimicking heavy metal (for example, Pb^{2+} mimicking Zn^{2+}), the enzyme involved loses the ability to accommodate or process the actual substrate needed for right body metabolic dealing. In an enzyme with a complex enzyme array, binding the wrong heavy metal to the first (rate-limiting step) enzyme entity translates/transmits the inhibition to other steps of the enzyme complex (Duruibe *et al*., 2007; Mehrandish *et al*., 2019).



Where: (A) = Intramolecular bonding; (B) = Inter-molecular bonding; P = Protein; E = Enzyme; M = Metal

Figure 3. Binding of heavy metals to biomolecules; Source: Duruibe *et al*., (2007)

Recommendations

Several methods are needed to minimize heavy metal controversies. The public should be made aware of this through public education and mass awareness strategies. Public education might compel people to behave rationally and compel policymakers to make rightful decisions. Other preventive measures for minimizing heavy metals' contact with biological systems include remediation, chelation, etc. Table 1 shows some minimization tips.

Table 1: Some minimization tips against heavy metals

Removal approach	Approach advantages	Approach disadvantages
Adsorption using conventional adsorbents	Minimal initial costs. Simple operation and working under a broad range of pH. Great metallic bonds capabilities. A successful technique effectively removes the majority of metallic elements. Excellent effectiveness with a maximum of 99% efficacy.	Method outcomes are governed by the adsorbent material. Increased costs becaus absorbents are so expensive. No potential chance of adsorbent recovery. Limited ion selectivity according to the absorbent substance kind.
Biosorption utilizing different bio-adsorbents	Inexpensive bio-adsorbents. Superior efficacy with regenerative potential. Production of little residue quantities. Metallic ions recovered without extra nutritional requirements.	Bio-adsorbents might become saturated earlier. Little possibility of progress for biological techniques uses. No possibility of biologically altering the oxidation state of eliminated metallic ions.
Chemical precipitation	An easy process with simple operational parameters. Cost-effective method. Efficient removal of a broad range of metallic ions.	Production of large residue amounts. Sludge removal results in increased running costs. The method has inadequate settling. Ineffective method for removing metallic ions at minimum levels. Reduced pH levels and high ion concentration impact the procedure' efficacy.
Electrodialysis	Highly selective process in metals separation. The process doesn't consume chemicals. Pure metals are very likely to be attained.	Significant initial and operating expenses. Substantial power amounts are required. The problem of membrane clogging. Regular maintenance is required. Operational parameters, including current, intensity of current, and pH, influence process efficacy.
Flocculation and coagulation	Sludge generated with an excellent settlement rate. The sludge produced had good dewatering properties. The process can remove metallic ions and water turbidity.	Residue production. High-priced approach. Large chemical amounts are consumed. Sludge removal requires additional running costs.
Flotation treatment	Increased generation of intensified sludge. Good selectivity of targeted metal removal. High effectiveness of elimination. The method has short retention times with large overflow quantities.	Substantial setting-up expenses. Big running and maintaining expenses.
Ion-exchange	High effectiveness of elimination. Possibility of achieving ppb levels to metallic ions. Highly selective metallic ions elimination. A quite efficient recovery rate. The capability for treating large volumes. The process is described by fast removal kinetics.	Substantial initial cost, including resin cost. Fewer number of metallic ions are eliminated The resin recovery process causes additiona contamination. The capacity to remove meta varies based on various resin types.
Membrane filtration and ultrafiltration method	It is a highly selective process. Minimal pressure is needed. Little room is required for this approach. Lower dependency on chemicals. Excellent efficacy that could pass 95%. Minimal quantities of solid residue produced.	It is a complicated process. Considerable setup, running, and maintenance expenses. Clogging of membrane. Little treated rate. Excessive amounts of energy use. Process efficiency is lowered as additional metallic ions are present.
Photocatalysis	Metallic ions, along with organic matter, are eliminated simultaneously. Fewer number dangerous side products.	Lengthy reaction periods are needed. The process has a finite number of uses.
Reverse osmosis	It is primarily utilized in seawater desalination. It could be applied to remove different organic, mineral, and bacterial pollutants.	Producing solid residue. Elevated pressure is needed for this approach. The process requires big operating expenses. Consumption of large power amounts. Ineffective method to eliminate the micro-

Source: Jadaa & Mohammed (2023).

CONCLUSION

Heavy metals are nowadays a threat. They are divulged to the contacts of man by man's effort and, therefore, cause harm. They have strategies to enter the brain and cause injury that affects functioning. Similarly, they affect the brain and cognition (learning) by down-regulating the availability of sufficient essential elements such as Zn^{2+}, Ca^{2+}, and Cu^{2+}, which are necessary for the nervous system and other purposes. Improving the public's awareness about the pollution of diets by heavy metals is essential. The stakeholders should put all their hands on deck to minimize the effects of heavy metals on men.

References

Adeyi, A.A., Olayanyu, B., & Fatade, Y., 2019. Distribution and potential risk of metals and metalloids in the soil of informal E-waste recycling sites in Lagos, Nigeria. *Ife Journal of Science,* 21, 3, 214-231.

Ahmed AA, Mohammed E.E., Yahia D., Faried A.M. 2017. Lead and cadmium levels in table eggs. *Journal of Advanced Veterinary Research*, 7, 3, 66-70.

Ailenokhuoria, B.V. & Omolekan, T.O., 2019. Heavy Metal, proximate and antioxidant composition of five cowpea cultivars (*Vigna unguiculata*) in Ibadan, Oyo state, Nigeria. *Journal of Food Science and Nutrition Research*, 2, 4,327-332.

Alam, O., Yang, L., & Yanchun, X., 2019. Determination of the selected heavy metal and metalloid contents in various plastic toys. *Journal of Environmental Health Science and Engineering*, 17,161-170.

Aliyu A. Ochigbo, S.S. & Akoyi J.N., 2017. Comparative assessment of the levels of some heavy metals in virgin and used water plastic bottles and sachets in Nigeria. *African Journal of Chemical Education*, 7, 2, 93-104, 2017.

Anka, A.U., Usman, A.B., Azizi, G. et al., 2022. Potential mechanisms of some heavy metals in the induction of inflammation and autoimmunity. *European Journal of Inflammation*, 20, 1-15.

Awuchi, C.G., Igwe, V.S., Amagwula, I.O., & Echeta, C.K., 2020. Health benefits of micronutrients vitamins and minerals and their associated deficiency diseases: A systematic review. *International Journal of Food Sciences*, 1, 1, 1-32.

Balali-mood, M., Naseri, K., Tahergorabi, Z., Khazdair, M.R., & Sadeghi, M., 2021. Toxic mechanisms of five heavy metals: Mercury, lead, chromium, cadmium, and arsenic. *Frontiers of Pharmacology*, 12-19.

Bhattacharjee, T. & Goswami, M., 2018. Heavy metals (As, Cd, and Pb) toxicity and detection of these metals in ground water sample: A review on different techniques. *Intentional Journal of Engineering Science Invention*, 7, 1,12-21.

Bost, M., Houdart, S., Oberli M.,Kalouji E., Huneau, J. & Margaritis I., 2016. Dietary copper and human health: current evidence and unresolved issues. *Journal of Trace Elements in Medicine and Biology,* 35, 107-115.

Dahlawi, S., Al Mulla, A.A., Saifullah, Salama, K., Labib, O.A., Aljassim, M.T., Akhtar, A., Asghar, W., Faraj, T.K., & Khalid, N., 2021. Assessment of different heavy metals in cigarette filler and ash from multiple brands retailed in Saudi Arabia. *Journal of King Saud University- Science*, 33, 2021, 1-10.

Dauda, J.A. Ameh, E.M., Usman, O.S., Jacob, A.D., Abdullahi, A.S., et al., 2021. Determination of heavy metals in different brands of chocolates, marketed in Anyigba, Kogi state. *Journal of Science and Technology*,3, 3, 22-27.

Desai, V & Kaler SG., 2008. Role of copper in human neurological disorders. *American Journal of Clinical Nutrition*, 88, 8655-85.

Duruibe, J.O., Ogwuegbu, M.O.C., & Egwurugwu, J.N., 2007. Heavy metal pollution and Hunan biotoxic effects. *International Journal of Physical Sciences*, *2*, 5, 112-118.

EPA, 2007. Framework for metal risk assessment EPA 120/R.07/501.wwwparge. org/OSA.

Faizal F.I., Ahmad, N.H., Yacob, J.S., Abdul Halim- Lim, S. & Abd Rahim, M.H., 2021. Food processing to reduce antinutrients in plant-based foods. *International Food Research Journal*, 30, 1, 25-45.

Gorini, F., Muratori, F. & Morales, M.A., 2014. The role of heavy metal pollution in neurobehavioural disorders: a focus on autism. *Review Journal of Autism and Development Disorders*,1, 354-372.

Gulchin, I. & Alwasel, S.H., 2022. Metal Ions, Metal Chelators, and Metal Chelating Assay as Antioxidant Method. *Processes*, 10, 132. https://doi.org/10.3390/pr10010132

Islam, MS., Zafar, M. & Ahmed M., 2014. Determination of heavy metals from table poultry eggs in Peshawar-Pakistan. *Journal of Pharmacognosy and Phytochemistry*, 3, 3, 64-67.

Izah, S.C., Inyang, I.R., Angaye, T.C.N., & Okowa I.P., 2017. A review of heavy metal concentration and potential health implications of beverages consumed in Nigeria. *Toxics*, 5,1-15.

Jadaa, W. & Mohammed, H., 2023. Heavy metals-definition, natural and anthropogenic sources methods- An overview. *Journal of Ecological Engineering*,24, 6, 249-271.

Karri, V., Schumacher, M. & Kumar, V., 2016. Heavy metals (Pb, Cd, As, MeHg) as risk factors for cognitive dysfunction: A general review of the metal mixture in the brain.

Koch, W.; Czop, M.; Iłowiecka, K.; Nawrocka, A.; Wi ˛acek, D., 2022. Dietary Intake of Toxic Heavy Metals with Major Groups of Food Products—Results of Analytical Determinations. *Nutrients*, 14, 1626. https://doi.org/10.3390/nu14081626.

Lawal, K.K. Ekeleme, I.K., Onuigbo, C.M., Ikpeazu, V.O. & Obiekezie, S.O., 2021. A review of the public health implications of heavy metals. *World Journal of Advanced Research and Reviews*, 10, 3, 255-265.

Magaji B. Ibrahim IB, Usman A, & Zubairu MS., 2023. Heavy metal analysis in some common foods and drugs available in Nigeria. *Food Science and Nutrition Technology*, 8(4),1-5.

Mahanty A, 2021. A review on heavy metal pollution, toxicity in agricultural soil and remedial measures. *IJARIIE*, 7(1), 1-7.

Mahurpawar, M., 2015. Effects of heavy metals on hand health. *Social Issues and Environmental Problems, International Journal of Research*,1-7.

Martin, S. & Griswold, W., 2009. Human effects of heavy metals. Environmental Science and Technology Briefs for Citizens. Center for Hazardous Substances Research, Kansas State University. www.engg.ksu.edu/CHSR/

Mehrandish R., Rahiman A., Shahriary A., 2019. Heavy metals detoxification: A review of herbal compounds for chelation therapy in heavy metals toxicity. *Journal of Herbmed Pharmacology*,8, 2,69-77.

Mondal, C. & Chandra, A.K., 2019. Goitrogenic/antithyroidal potential of Moringa leaves and spinach leaves of Indian Origin on thyroid status in male albino rats. *Brazilian Journal of Pharmaceutical Sciences*, 55, e18005, 1-11.

Narwal, R P., Malik, R.S., Malhotra, S.K., & Singh, B.R., 2017. Micronutrients and human health. *Encyclopedia of Soil Science*, 1443-1448.

Olubanjo, K., Osibanjo, Om, & Nmorom, I.C, 2015. Evaluation of Pb and Cu contacts of selected component parts of waste personal computers. *Journal of Applied Science and Environmental Management*, 19, 3, 470-477.

Opoku, R.B., Dankyi, E., Christian, A. & Aryeetey, R., 2024. Environmental exposure and potential health impact of heavy metals in previous mining communities in Ghana. *HSI Journal* 5, 1, 702709 https//doi.org/10.46829/hsijournal.2024.6.5.2.702-709

Oruma, Y.Y., Abraham, O.J., Odibe, P.A., Egwemi, I.O., Okwuta hi, A.M., Aye, G.A. & Yahaya, A., 2021. The effect of cooking on goitrogenic (cyanogenic glycosides and glucosinates) content of pumpkin leaves and spinach leaves. *Dutse Journal of Pure and Applied Sciences*, 7, 3b, 134-142.

Palmatier, R.W., Houston, M.B. & Hullard, J., 2018. Review articles: purposes, process, and structure. *Journal of the Academic Marketing Science*, 46,1-5.

Radu-Rusu, C.G., Pop, I.M., Albu, A., Bologa, M., & Radu-Rusu, R.M., 2013. Transferability of certain heavy metals from hens feed to table eggs laid within different rearing systems. *Lucrari Stiintifice-Seria Zootehnie*, 59, 219-222.

Rahman, M.S., Islam, M.A., & Hossein, M. S., 2019. Heavy metals accumulation in soil and uptake by plans species: focusing phytoremediation. *International Research Journal of Environmental Science*, 9, 1, 1-7.

Raji, M.I.O., Ibrahim Y.K.E., & Ehinmidu J.O., 2010. Physicochemical characteristics and heavy metals in drinking water sources in sokoto Metropolis," *Journal of Applied Science and Environmental Management,* 14, 3, 81-85.

Reilly, C., 2003. Metal contamination of food: It's significance for food quality and human health. 3rd Edition. Blackwell Science, UK.

Saeed, M., Muhammad, N., Khan, H., & Zakiullah, 2011. Assessment of heavy metal content of branded Pakistani herbal products. *Tropical Journal of Pharmaceutical Research*, 10, 4, 499-506.

Samtiya M., Aluko R. & Dhewa, T., 2020. Plant food antinutrinational factors and their reduction strategies: An overview. *Processing and Nutrition*, 2, 6,1-14.

Seiyaboh, E.I. Angaye T.C.N. Seiyaboh, & Emeka, Z., 2020. Assessment of heavy metal contaminants associated with locally processed beverages in reused plastic container. *Direct Research Journal of Biology and Biotechnology*, 6, 4, 34-36,2020.

Snyder, H., 2019. Literature review as a research methodology: An overview and guidelines. *Journal of Business Research*,104, 333-339.

Soetan, K.O., Olaiya, C.O, & Oyowele, OE., 2010. The importance of mineral elements for humans, domestics animals and plants: A review. *African Journal of Food Science*, 4, 5, 200 – 222.

Sousa, C., Moutinho, C., Vinha, A.F., & Matos, C., 2019. Trace minerals in human health; Iron, zinc, copper, manganese and fluorine. *International Journal of Science and Research Methodology*, 13, 3, 57-80.

Stenesh, J., 1998. Biochemistry. New York: Springer Science Business Media. DOI:10.1007/978-1-4757-9427-4.

Styrer, L., 1988. Biochemistry (3rd edition). New York, NY: W. H. Freeman and Company. Page 187-191.

Suleiman, F.B., Hallori, A., & Adamu, I.T., 2023. Proximate and heavy metal analysis of grasshopper species consumed in Katsina state. *World Journal of Advanced Engineering Technology and Sciences*,8, 2,359-366.

Tahir, I. & Alkheraije, K.A., 2023. A review of important heavy metals toxicity with special emphasis on nephrotoxicity and its management in cattle. *Frontiers of Veterinary Sci*ence, 10,1149720.

Thomas, R.C., 2019. Beyond potency: The importance of measuring elemental contaminants in cannabis and hemp. Cannabis Science and Technology, 2, 5, 1-5.

Umar, A.I., Sarkingobir, Y., & Dikko, M., 2022. Spectro-analytical research of selected heavy metals (Cu, Cd, Cr, and Pb) in four different single-use plastics commonly in contact with food from Sokoto, Nigeria. *Jurnal Teknokes*,15, 1,76-80.https://doi.org/10.35882/tekenokes. v15i2.199.

Vyas, M., Purohit R., Chouhan P. Katara N., Vyas A., Singh SK., 2017. A review on effects of some heavy metals on plants and human health. *Journal of Emerging Technologies and Innovative Research*, 4, 12, 132-136.

WHO/BASICS/UNICEF (1999). Nutrition essentials. A guide for health managers.

Witkowska, D., Slowik, J., & Chilicka, K., 2021. Heavy metals and human health: Possible exposure pathways and competition for protein binding sites. *Molecules*, 26, 1–16 http://doi.org/10.3390/molecules 26196060.

Yebpella, G.G., Oladipo, M.O.A., Magomya, A.M., Abechi, S.E., Udiba, U.U., & Lamba, E.A., 2013. Multi-element analysis of selected brands of cigarettes in Nigerian market. *Archives of Applied Science Research,* 5, 6, 61-67.