Uttar Pradesh Journal of Zoology

Volume 45, Issue 15, Page 442-450, 2024; Article no.UPJOZ.3795
ISSN: 0256-971X (P)

Cadmium Toxicity: Sources, Mechanisms and Human Health Implications: A Comprehensive Review

B. Purushottam [a++*] and R. Adhinarayana Reddy [b++]

[a] Government Degree College, Rajampet, Annamayya. DT, AP, India.
[b] Government College of Teacher Education – Kurnool. DT, AP, India.

Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

Article Information

DOI: https://doi.org/10.56557/upjoz/2024/v45i154260

Open Peer Review History:
This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: https://prh.mbimph.com/review-history/3795

Review Article

Received: 12/05/2024
Accepted: 16/07/2024
Published: 17/07/2024

ABSTRACT

Objectives: This comprehensive review thoroughly explores cadmium toxicity, covering its detection methods, sources, biological pathways, health risks, related challenges, and strategies for prevention and treatment.
Methodology: literature analysis on the toxicological effects of Cadmium on human health by utilizing databases like PubMed, Web of Science, and Google Scholar, which include reputable publications and peer-reviewed journals (2019-2024). Keywords such as "Cadmium toxicity," "Cadmium exposure," "human health effects," and others were used to gather relevant studies.
Results: Cadmium, a harmful metal, is a significant environmental pollutant that leads to oxidative stress, cell harm, hemolytic anemia, and disruption of neurotransmitters, causing severe health problems and organ damage, which can be fatal in severe cases.

[++] Principal;
**Corresponding author: Email: aristatilzoo@gmail.com;*

Cite as: *Purushottam, B., and R. Adhinarayana Reddy. 2024. "Cadmium Toxicity: Sources, Mechanisms and Human Health Implications: A Comprehensive Review". UTTAR PRADESH JOURNAL OF ZOOLOGY 45 (15):442-50. https://doi.org/10.56557/upjoz/2024/v45i154260.*

Discussion: Cadmium's adverse impacts on human health are substantial, resulting in renal dysfunction, bone demineralization, respiratory problems, and carcinogenesis. Children and pregnant women are among the most vulnerable demographics. Strategies include stringent legislation, public education, and effective treatment regimens.
Conclusion: Cadmium poisoning offers a health risk, necessitating interdisciplinary collaboration among scientists, healthcare professionals, politicians, and public health advocates to detect, prevent, and treat contamination efficiently.

Keywords: Cadmium; human health effects; toxicological effects; prevention of toxicity.

1. INTRODUCTION

Exposure to heavy metals, which has been on the rise due to industrial activities and modern industrialization, poses significant risks to human health. This increase in exposure, primarily through contaminated water and air, is a growing environmental concern affecting millions worldwide. Furthermore, the contamination of food with heavy metals further exacerbates the threat to human and animal health [1]. Heavy metal concentrations in water sources, air, and food are closely monitored due to the severe health risks they pose, including respiratory issues, kidney diseases, neurological disorders, and cancer development [2].

Cadmium, a metal prevalent in the 20th century, also saw significant emissions from non-ferrous smelters in the 19th century. Today, this element is primarily utilized in rechargeable batteries and special alloy production. While emissions have decreased in developed nations, cadmium continues to pose risks to industrial workers and residents in polluted regions, particularly those in less developed countries [3]. In industrial settings, cadmium is hazardous through inhalation and ingestion, posing acute risks that can persist in soils and sediments for extended periods. Through plant uptake, cadmium moves up the food chain, ultimately accumulating in the bodies of individuals consuming contaminated food. Additionally, cadmium is found in tobacco smoke, further increasing human exposure to this harmful substance.

Cadmium can be released into the atmosphere through natural processes or human activities, leading to exposure in both animals and humans in various ways. Pollution of the aquatic environment with cadmium can occur through industrial waste, surface runoff, and absorption into soil and sediments. Ingesting food, breathing contaminated air, or consuming water with high levels of cadmium can result in poisoning for individuals. Cadmium does not provide any benefits for plant growth or metabolic processes. The biological half-life of cadmium in the human body can span from 16 to 30 years [4]. Long-term exposure to low doses of cadmium is thought to be linked to certain chronic lung conditions like emphysema, asthma, and bronchitis, as well as hypertension [5]. Long-term exposure to cadmium (Cd) can lead to a range of diseases, including cancer, leukemia, and genetic toxicity [6]. Studies have shown that even low levels of exposure to heavy metals can cause significant harm to human organs. Symptoms of acute ingestion may include abdominal pain, nausea, vomiting, muscle cramps, dizziness, shock, and even convulsions within a short period [6]. Recent research suggests that Cd exposure could be linked to various cancers such as prostate, bladder, pancreatic, kidney, and breast cancer. It may also contribute to con ditions affecting the central nervous system like Alzheimer's disease, Parkinsonism, Huntington's disease, ALS, and MS, as well as cognitive and behavioral impairments [7]. Chronic diseases such as osteoporosis and osteomalacia in different bones can also result from Cd exposure. Cadmium can pass through the placenta to the fetus, potentially causing teratogenic effects and is associated with conditions like Itai-Itai disease, cardiovascular issues, lung dysfunction, kidney damage, and more [8,9]. The kidneys are particularly vulnerable to Cd contamination, with a reduced glomerular reabsorption rate being a common effect.

2. SOURCES, CONTAMINATION AND MECHANISM OF CADMIUM TOXICITY

Cadmium is a common environmental pollutant with well-documented harmful effects on human health, animals, and plants. To address its widespread distribution and dangerous characteristics, it is essential to comprehend the origins, pathways of contamination, and mechanisms of cadmium toxicity. This review seeks to offer a thorough analysis of these

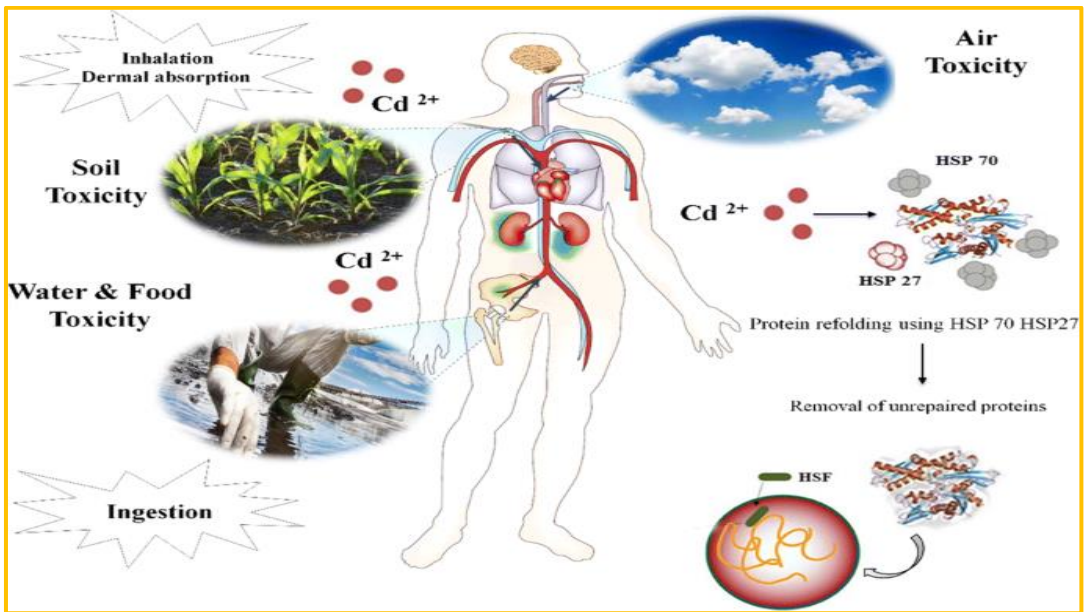

Fig 1. Contamination and mechanism of cadmium toxicity
(Mohammad Ehsan Taghavizadeh Yazdi.et.al.,2021)

factors, enhancing the credibility and breadth of existing knowledge on cadmium's adverse effects.

Sources of Cadmium: Cadmium pollution comes from both natural and manmade causes. Cadmium naturally occurs in the Earth's crust and can be released into the environment as a result of volcanic activity, rock weathering, and forest fires [10]. Anthropogenic sources are more widespread and include:

Cadmium is a byproduct of mining and smelting processes for zinc, lead, and copper, as well as being utilized in the production of batteries, pigments, coatings, and plastics [11]. The use of phosphate fertilizers in agriculture, which often contain cadmium, can contaminate soil, leading to its uptake by crops and entry into the food chain [10,11]. Consumer products like tobacco, jewelry and certain traditional remedies can also contribute to cadmium exposure [11]. Environmental pollution from industrial emissions, improper waste disposal, and the incineration of cadmium-containing items can contaminate air, water, and soil [12]. Cadmium can enter the human body through inhalation, ingestion, and dermal contact [10]. Industrial workers and those living near industrial areas are at risk of inhaling cadmium, with tobacco smoking being a significant source of inhalation

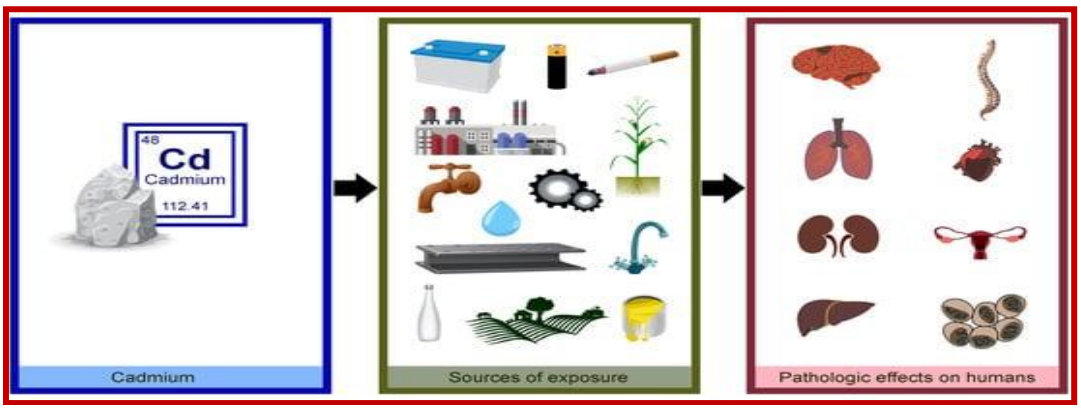

Fig. 2. Cadmium Toxicity and Health Effects
Source: Angelika Edyta Charkiewicz et. Al., 2023

for smokers [12]. The general population can be exposed to cadmium through consuming contaminated food and water, with leafy vegetables, cereals, and seafood commonly serving as dietary sources. Dermal exposure, while less common, can occur through contact with contaminated soil or water [13].

3. MECHANISMS OF CADMIUM TOXICITY

Cadmium exerts its toxic effects through several biochemical and molecular mechanisms: Cadmium induces oxidative stress by producing reactive oxygen species (ROS) and depleting antioxidant defenses like glutathione, leading to lipid peroxidation, protein oxidation, and DNA damage. It disrupts metal homeostasis by displacing essential metals such as zinc and calcium, affecting numerous enzymes and proteins. Cadmium also hinders DNA repair mechanisms, increasing the risk of mutations and cancer development. Additionally, it triggers cellular apoptosis and necrosis through mitochondrial dysfunction, disruption of calcium signaling and activation of pro-apoptotic pathways [10]. Cadmium can disrupt the endocrine system by mimicking or interfering with hormones, causing associated health problems. Understanding the sources, contamination pathways, and toxicity mechanisms of cadmium is crucial for various reasons [11]. This knowledge can guide public health interventions, regulatory policies, and risk assessments to reduce cadmium exposure, especially for vulnerable populations. It also helps in developing therapeutic strategies [13] to counteract the harmful effects of cadmium toxicity and contributes to scientific advancements in environmental health and toxicology [11].

4. PATHOLOGICAL EFFECTS ON THE RESPIRATORY SYSTEM

Cadmium (Cd) exposure in the respiratory system can lead to irritation of the nose's mucous membranes, resulting in impaired smell and throat discomfort. Those in occupations like metallurgy, where cadmium-containing materials are welded, melted, or soldered, are at risk of poisoning from inhaling fumes [5]. Symptoms of cadmium poisoning, such as metallic fever and pulmonary edema, may appear within 24 hours of exposure. Acute poisoning can occur at concentrations as low as 0.5 mg/m3 from fumes and 3 mg/m3 from dust. Chronic exposure often leads to conditions like chronic bronchitis, loss of smell, nasal dryness, and coughing. Long-term inhalation can result in lung function abnormalities [14], emphysema, and reduced olfactory function. Detection of respiratory changes can be done through laryngological exams, spirometry, and chest X-rays [15].

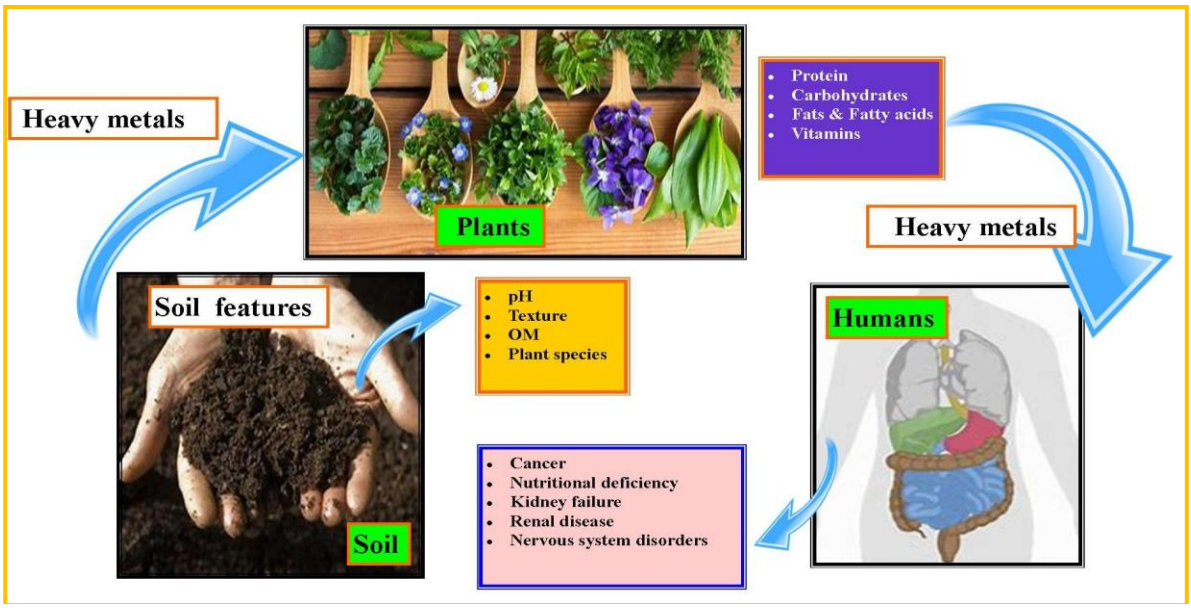

Fig. 3. The diagrammatic presentation shows the heavy metal sources, plant uptake, and health effects (Ref: self made)s

Nephrotoxicity: In cases of chronic cadmium (Cd) poisoning, scientists now agree that the kidney, where Cd is primarily stored, is the key target organ and the first to show signs of toxicity [16]. Cd nephropathy has been observed in industrial workers exposed mainly through inhalation and in the general population exposed to contaminated foods. Both studies on human populations and experiments with animals have shown that Cd causes renal toxicity in a dose-dependent manner, with harmful effects appearing only when the Cd concentration in the kidney cortex reaches a crucial threshold. It is estimated that renal damage is likely to occur when the total Cd concentration in the renal cortex reaches 150-200 ppm (µg/g of wet weight of the renal cortex), in both humans and animals [17]. The initial sign of Cd-induced renal damage, considered critical, is an increase in the urinary excretion of microproteins.

Neurotoxicity: The precise impact of cadmium's neurotoxic effects remains uncertain. However, it is known that elevated concentrations of cadmium exceeding >0.8 µg/L in urine and 0.6 µg/L in blood can harm the human nervous system. Such heightened levels are currently prevalent in industrialized nations, indicating that environmental exposure to this metal could jeopardize nervous system health. Cadmium is also suspected to be linked to the development of neurodegenerative conditions. It is thought to potentially contribute to diseases affecting the central nervous system, such as Alzheimer's, Parkinsonism, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, multiple sclerosis, and the decline of cognitive and behavioral functions [18]. Previous research has demonstrated increased cadmium content in the hair of children with neurological disorders, learning difficulties, behavioral issues, as well as memory and attention impairments. Even at lower concentrations (>0.38 µg/L in blood and

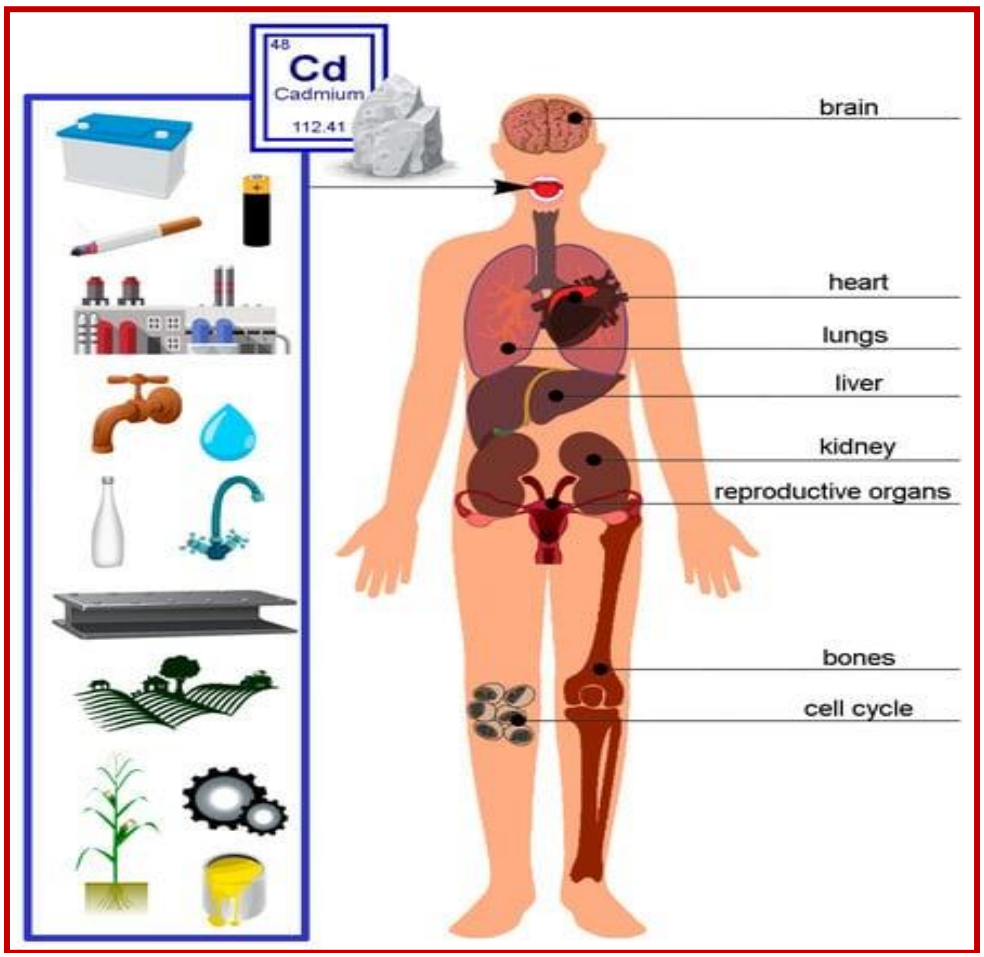

Fig. 4. Sources of cadmium and its effects on various regions of the human body
Angelika Edyta Charkiewicz et. Al., 2023

>0.1802 µg/L in urine), cadmium could disrupt nervous system function in children, potentially playing a role in the onset of these conditions in this population [18].

Carcinogenicity: Various regulatory bodies have determined that there is enough evidence to classify Cadmium (Cd) as a human carcinogen. The strongest evidence supporting this classification comes from studies showing increased risks of lung cancer in individuals exposed to Cd through inhalation, as well as from animal research demonstrating that Cd exposure through various routes can lead to cancer in multiple areas of the body, particularly the lungs [19]. While data from animal studies is clear, investigations on occupationally exposed populations must be approached cautiously due to potential confounding factors like simultaneous exposure to arsenic. Recent studies that have adjusted for co-exposure to arsenic and nickel have reported lower relative risks of lung cancer compared to previous findings [16]. Cd exposure in industrial settings has also been associated with prostate and renal cancer, although these links are not as strong as those with lung cancer. Despite previous research indicating no increased cancer mortality in environmentally exposed populations, the potential for Cd to contribute to environmental carcinogenesis cannot be ruled out. In a Cd-contaminated area in China, a correlation has been observed between urinary Cd levels and elevated levels of prostate-specific antigen, suggesting a possible role of Cd in prostate cancer development [20]. The exact mechanism by which Cd induces cancer remains largely unknown. This metal is not highly genotoxic and does not cause direct genetic damage, so potential mechanisms could involve epigenetic changes and/or indirect genotoxic processes such as interference with apoptosis, disruptions in cell signaling, or inhibition of DNA repair mechanisms [21].

4.4 Hepatotoxicity

Cadmium targets two main human tissues: the renal cortex and the liver. In cases of acute exposure, it tends to accumulate in the liver, leading to various hepatic dysfunctions [22]. By disrupting the cellular redox balance, Cadmium triggers oxidative stress and harm to hepatocytes. This hepatotoxicity from Cadmium, whether acute or chronic, can eventually lead to liver failure and heighten the chances of cancer development [23].

5. CARDIOVASCULAR TOXICITY

Cadmium is a dangerous metal known for its toxicity and carcinogenic effects. Exposure to cadmium can lead to various health issues, including kidney disease, bone disease, and cardiovascular problems. Even low to moderate levels of cadmium exposure have been linked to hypertension, diabetes, atherosclerosis, peripheral arterial disease, chronic kidney disease, heart attacks, strokes, and heart failure [24,25,26].

6. CADMIUM IN THE FOOD CHAIN

The main source of cadmium exposure for the population is through food consumption. Cadmium can enter the atmosphere naturally through erosion and volcanic activity, but it is primarily introduced by human activities such as ore processing, burning fossil fuels, and using municipal waste and sewage sludge-containing fertilizers and phosphate applications. Contaminated soil plays a significant role in cadmium exposure through crops grown in it, with the metal leaching into groundwater and surface soil, affecting aquatic organisms through trophic transmission. Certain plants, like tobacco, are hyperaccumulators of cadmium, which is why smoking tobacco can lead to cadmium exposure. The level of nutritional exposure is closely linked to consumption rates. Since wheat, rice, and other grains are consumed more extensively than vegetables, the exposure to cadmium through these foods is high. Cadmium typically exists as Cd^{2+} and forms stable complexes with proteins like metallothionein in kidney and liver tissues. The destruction of proximal tubular cells in the kidney is the most critical mechanism of toxicity, but other harmful effects include hypertension, skeletal damage, and carcinogenic effects. European and United States regulations permit total cadmium levels of 0.005 mg per kg in natural diets, such as water. For nutritional supplements, the cadmium content can range from 1.0 mg per kg for those without seaweed to 3.0 mg per kg for those with seaweed included [27,28].

7. RISK MITIGATION RECOMMENDATIONS

People with conditions such as kidney diseases, chronic bronchitis, emphysema, rhinitis, osteoporosis, osteomalacia, anemia, liver damage, and hypertension, as well as regular

smokers, should avoid working in environments exposed to cadmium due to its harmful effects. It is crucial to take preventative measures to promote healthy habits, such as avoiding smoking and excessive drinking, practicing good personal hygiene, and educating employees about cadmium exposure.

To reduce global environmental cadmium pollution and mitigate health risks associated with cadmium exposure, the following actions are necessary: -

Enforce the WHO Framework Convention on Tobacco Control to protect individuals from secondhand smoke in various settings. –

Minimize cadmium emissions, particularly into water bodies, from sources like mining, smelting, waste incineration, sewage sludge application, phosphate fertilizers, and cadmium-containing manure. Develop safe disposal methods for cadmium-containing waste. Adopt practices like washing fruits and vegetables, and peeling roots and tubers, to lower cadmium contamination levels. Encourage recycling efforts for cadmium and restrict its use in non-recyclable products like toys, jewelry and plastics. Improve working conditions in industries that handle cadmium and educate on the proper use of cadmium-rich fertilizers. Raise awareness globally on the importance of reducing cadmium waste discharge to safeguard public health and the environment.

8. CONCLUSION

Cadmium is a toxic metal that can cause cancer in humans at low environmental levels. Human actions such as toy and plastic garbage disposal, as well as technology disposal, enhance the population's exposure. Living things can migrate and accumulate over long distances. Cadmium exposure comes mostly through the ingestion of food, inhalation of tobacco smoke, and occupational exposure. According to all aspects, humans do not expose themselves to the cadmium metal.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

This content is collected from different sources like pubmed, Google scholar. Author used AI only reference base. AI efforts have been made to ensure accuracy and reliability, the information provided may not be complete or up-to-date. Always cross-check facts and consult authoritative sources. This AI does not provide professional, legal, or medical advice. Use this information at your own risk. ChatGPT is an AI tool that delivers generic information, but it should not be relied on for expert guidance. It is not a licenced professional and does not provide legal, medical, or financial advice.

The AI cannot guarantee the correctness or completeness of the data, and its developers and operators accept no responsibility for any errors or inaccuracies. External links supplied by the AI are for convenience and informational reasons only, and do not constitute endorsements. Users are responsible for verifying facts and making their own choices. The AI is supplied "as is" and without warranty.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Ghorani-Azam A, Riahi-Zanjani B, Balali-Mood M. Effects of air pollution on human health and practical measures for prevention in Iran. J. Res. Med. Sci. 2016; 21:65.
   DOI: 10.4103/1735-1995.189646
2. Luo L, Wang B, Jiang J, Huang Q, Yu Z, Li H, et al. Heavy metal contaminations in herbal medicines: Determination. comprehensive risk assessments. Front. Pharmacol. 2020;11:595335.
3. Hyder O, Chung M, Cosgrove D, Herman JM, Li Z, Firoozmand A, et al. Cadmium exposure and liver disease among US adults. J. Gastrointest. Surg. 2013;17(7): 1265–1273
4. Genchi G, Sinicropi MS, Lauria G, Carocci A, Catalano A. The Effects of Cadmium Toxicity. Int. J. Environ. Res. Public Health. 2020;17:3782.
5. Charkiewicz AE, Jamiołkowski J, Pędzinski B, Krzyzak M, Maslach D, Szpak A, Omeljaniuk WJ. Changes in dietary patterns and the nutritional status in men in the metallurgical industry in Poland over a 21-year period. Ann. Nutr. Metab. 2018; 72:161–171.

6. Nejabat M, Kahe H, Shirani K, Ghorbannejad P, Hadizadeh F, Karimi G Health risk assessment of heavy metals via dietary intake of wheat in Golestan Province, Iran. Hum. Ecol. Risk Assess. 2017;23:1193–1201
7. Qing Y, Yang J, Zhu Y, Li Y, Zheng W, Wu M, He G. Dose-response evaluation of urinary cadmium and kidney injury biomarkers in Chinese residents and dietary limit standards. Environ. Health. 2021;20:75.
8. Syeda T, Cannon JR. Environmental exposures and the etiopathogenesis of Alzheimer's disease: The potential role of BACE1 as a critical neurotoxic target. J. Biochem. Mol. Toxicol. 2021; 35.
9. Zając-Nędza M, Langauer-Lewowicka H, Kadm Mark Kazimierz (Pod Red.): Choroby Zawodowe, Wydawnictwo Lekarskie PZWL: Warszawa, Poland. 2001;195–199.
10. Eissa MA, Negim OE. Heavy metals uptake and translocation by lettuce and spinach grown on a metal-contaminated soil. J. Soil Sci. Plant Nutr. 2018;18:1097-1107.
11. Mao C, Song Y, Chen L, Ji J, Li J, Yuan X, et al. Human health risks of heavy metals in paddy rice based on transfer characteristics of heavy metals from soil to rice. Catena. 2019;175:339-348.
12. Munir N, Jahangeer M, Bouyahya A, El Omari N, Ghchime R, Balahbib A, et al. Heavy metal contamination of natural foods is a serious health issue: A review. Sustainability. 2021;14(1): 161.
13. Ohiagu F, Chikezie P, Ahaneku C. Human exposure to heavy metals: Toxicity mechanisms and health implications. Mater. Sci. Eng. 2022;6(2):78–87.
14. Nordberg G, Nogawa K, Nordberg M, Friberg L. Cadmium. In: Handbook on toxicology of metals. Nordberg G, Fowler B, Nordberg M, Friberg, L editors New York: Academic Press. 2007; 65-78.
15. Li H, Fagerberg B, Sallsten G, Borné Y, Hedblad B, Engström G, Barregard L, Andersson EM. Smoking-induced risk of future cardiovascular disease is partly mediated by cadmium in tobacco: Malmö Diet and Cancer Cohort Study. Environ. Health. 2019;18:56.
16. Bernard A, Roels H, Buchet JP, Cardenas A, Lauwerys R. Cadmium and health: the Belgian experience. IARC Sci Publ. 1992;118:15-33.
17. Ruczaj A, Brzóska MM. Environmental exposure of the general population to cadmium as a risk factor of the damage to the nervous system: A critical review of current data. J. Appl. Toxicol. 2023;43:66–88.
18. Wang B, Du Y. Cadmium and its neurotoxic effects. Oxid. Med. Cell. Longev. 2013;898034.
19. Zeng X, Jin T, Jiang X, Kong Q, Ye T, Nordberg GF. Effects on the prostate of environmental cadmium exposure-a cross-sectional population study in China. Biometals. 2004;17:559-65.
20. Waalkes MP. Cadmium carcinogenesis. Mutat Res. 2003;533:107-20.
21. Bernard A. Renal dysfunction induced by cadmium: biomarkers of critical effects. Biometals. 2004;17(5):519–523.
22. Hyder O, Chung M, Cosgrove D, Herman JM, Li Z, Firoozmand A, Gurakar A, Koteish A, Pawlik TM. Cadmium exposure and liver disease among US adults. J. Gastrointest. Surg. 2013;17(7):1265–1273.
23. Toxicological Profile for Cadmium, ATSDR's Toxicol. Profiles; 2002.
24. Tellez-Plaza M, Navas-Acien A, Menke A, Crainiceanu CM, Pastor-Barriuso R, Guallar E. Cadmium exposure and all-cause and cardiovascular mortality in the U.S. general population. Environ. Health Perspect. 2012;120(7):1017–1022.
25. Everett CJ, Frithsen IL. Association of urinary cadmium and myocardial infarction. Environ. Res. 2008;106(2):284–286.
26. Dudka S, Miller W. Accumulation of potentially toxic elements in plants and their transfer to human food chain. J Environ Sci Health. 1999;34:681-708.
27. Abdel-Rahman GN-E. Heavy metals, definition, sources of food contamination, incidence, impacts and remediation: A literature review with recent updates. Egypt. J. Chem. 2021;65(1):419-437.

28. Peters JL, Perlstein TS, Perry MJ, McNeely E, Weuve J. Cadmium exposure in association with history of stroke and heart failure. Environ. Res. 2010;110(2): 199–206.

Peer-review history:
The peer review history for this paper can be accessed here:
https://prh.mbimph.com/review-history/3795