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Biological Aspects of Cadmium Toxicity: A Review Susmita Srivastav

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ABSTRACT

Cadmium (Cd) is a toxic non-essential transition metal that poses a health risk for both human and animals. Cadmium is a naturally occurring heavy metal found in the Earth's crust. It naturally occurs in the environment as a pollutant derived from agricultural and industrial sources. Exposure to cadmium primarily occurs through the ingestion of contaminated food and water and, to a significant extent, through inhalation and cigarette smoking. Cadmium poisoning has been reported in many parts of the world. The biochemical basis for its toxicity has been the objective of research for over 50 years. Cadmium accumulates in plants and animals with a long half-life of about 16–30 years. It is one of the global health problems that affects many organs and, in some cases, can cause deaths annually. Cadmium levels can be measured in the blood, urine, hair, nail, and saliva samples. Long-term exposure to cadmium through air, water, soil, and food leads to cancer and organ system toxicity, such as skeletal, urinary, reproductive, cardiovascular, respiratory, central, and peripheral nervous system. Cadmium exposure is most often occupational-related and can occur in all industry sectors. Due to its non-corrosive properties, it is utilized in batteries, pigments, metal coatings, and plastics. This review provides an update on the effects of Cd exposure on human health, focusing on the cellular level. It has also been recommended to determine the level of food contamination and identify suspicious areas, as well as consider public education and awareness programs for exposed individuals to prevent cadmium poisoning.

Figure: 01 References: 37 Table: 01

KEY WORDS: Cadmium(Cd), Effects, Heavy metals, Poisoning, Toxic element.

Introduction

Cadmium is a heavy metal occurring as a natural constituent in the Earth's crust along with Zinc, Nickel, Copper, and Lead. It is a silvery white, soft, ductile metal belonging to period 5, group 12, and block d in the periodic table. Cadmium was discovered in 1817 by German chemist Friedrich Stromeyer as a constituent of smithsonite (ZnCO₃) from zinc ore. Its name comes from the Latin term Cadmeia and the Greek word kadmia, which was an earlier name for calamine, a common zinc ore where the impurity was found. Cadmium in the Earth's crust is estimated to be between 0.15 parts per million (ppm), and greenockite (CdS) is the most common Cadmium mineral²⁸. Natural processes, such as volcanic eruptions and the spontaneous combustion of biomass, can produce atmospheric Cadmium. As the social industry advances, human activities, including mineral extraction, metal smelting, industrial emissions, fossil fuel usage, and waste incineration, have led to the introduction of cadmium into soil and water *via* agricultural irrigation, atmospheric deposition, and urban composting. This article examines the most recent findings on the origins of cadmium, its biological effects, diagnostic techniques, and potential preventative strategies in light of the increasingly obvious risks of cadmium. It offers useful information for researchers, public health specialists, and decision-makers

Cadmium element

Cadmium (Cd) is a soft, malleable, ductile, silvery-white, highly toxic, non-essential, and non-biodegradable heavy metal³². Cadmium is widely distributed in the Earth's crust at an average concentration of 0.1 mg/kg. The maximum concentration of cadmium compounds in the environment exists in sedimentary rocks, while marine phosphate has approximately 15 mg of cadmium/

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kg³⁰.It readily combines with other compounds often used in cells and batteries, such as alloys, pigments, plastic stabilizers, paints, dyes, and nickel-cadmium rechargeable batteries, as well as in the glass and galvanic industries. Every year, after consuming contaminated food, approximately 600 million individuals, or nearly one in ten people, are affected worldwide³⁴. Heavy metal contamination of food is more prevalent in agricultural areas that are contaminated, which is a major issue globally. It is estimated that approximately 40% of lakes and rivers, over 13% of total cultivated land, and around 0.24 billion hectares of the world's arable land are contaminated with heavy metals¹³.One cigarette contains about 2µg cadmium, with 2-10% being transferred through primary cigarette smoke. Both ingestion and inhalation are the two main ways that individuals can intake cadmium, with the main source of exposure in non-smokers being ingestion and

TABLE-1 : Physicochemical properties of the Cadmium element

Symbol	Cd
Atomic number	48
Atomic weight	112.41g mol-1,
Density at 20 ^o C	8.65 g/cm ³
Boiling point	766.8°C
Melting point	321.07°C
Heat of fusion	6.21 kJ/mol
Heat of vaporization	99.6 kJ/mol
First ionization energy	867.8 kJ/mol
Second ionization energy	1631.4 kJ/mol
Electronegativity (Pauling scale)	1.69
Reduction potential Cd ²⁺ + 2e ⁻ →Cd(s)	-0.40 E°
Atomic radius	155 pm
Colour	silver-colored

in smokers being inhalation. Cadmium damages pulmonary cells, disrupting several functions such as DNA repair, enzyme activity, and membrane integrity¹⁶.Cadmium is efficiently stored in the human body and accumulates throughout life, with a biological half-life of 16 to 30 years. High blood pressure and several chronic lung diseases, including bronchitis, asthma, and emphysema, are related to slow poisoning of cadmium in small doses; however,long-term exposure to cadmium can cause various diseases, including breast, lung, prostate, nasopharyngeal, pancreatic, and renal cancersand genotoxicity9. Cadmium, when ingested excessively in food and drinking water, accumulates in the selected organs and passes through the placental barrier to the foetus, demonstrating the teratogenic effects¹⁹. Numerous epidemiological studies have shown that long-term exposure to Cadmium during pregnancy and the early years of life can result in neurological issues such as cognitive impairments, behavioral deficits, attention deficit hyperactivity disorder (ADHD), antisocial behavior, and delinguency in young children¹⁴. Numerous epidemiological studies link cadmium exposure to cardiovascular illness. cerebrovascular disease, and peripheral vascular disease4.

Among Cd salts, CdS, CdCl₂, and CdSO₄ are the best known. Despite being extremely resistant to corrosion, cadmium always generates colorless divalent cations and oxidizes readily. Cadmium is absorbed by biological systems in the form of Cd⁺² by plants and marine organisms and possesses the characteristic of bioaccumulation³¹. The chemical characteristics of cadmium (Cd) resemble those of zinc (Zn) for plant absorption and metabolic processes. Conversely, unlike Zn, an element exhibits a harmful effect on flora, fauna, and humans⁷.

Sources and exposure pathway of Cadmium

Cadmium, often utilized for the advancement of civilization, regrettably serves as a significant contaminant for both the environment and human health.

Cadmium entrance in the food chain

The main source of cadmium exposure for the population is food consumption. Cadmium enters the atmosphere through erosion and volcanic activity, mostly from human activities such as processing fossil fuels, burning municipal trash, using sewage sludge-containing fertilisers, and applying phosphate. Contaminated soil contributes to cadmium exposure through food sources. Contaminated soil significantly contributes to cadmium exposure through dietary sources, as cadmium accumulates in crops cultivated in such soil. Soil and

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leached cadmium from contaminated groundwater and soil surface disrupt aquatic species through trophic transmission²⁵. Plants subjected to toxic cadmium (Cd) exhibit reduced leaf surface area, chlorosis, necrotic spot development, inhibited leaf growth, and leaf curling. Cadmium decreases efficiency as well as quality in plant production by inhibiting photosynthesis, enzymatic activity, and ion absorption. One of the major routes for cadmiumexposure in humans is through rice consumption. Flooding rice fields during harvest is recommended as a water management strategy to reduce cadmium accumulation in rice, particularly in Japan, where soil contamination with cadmium is present^{3,10}.

The Biological Effects of Cadmium and its Toxicological properties in Humans and plants

Cadmium is found in high concentrations in crustaceans, bivalve molluscs, oysters, cephalopods, and crabs. It is also present in animal products, including liver and kidney, as well as in oil seeds, cocoa beans, and specific wild mushrooms²⁷. Cadmium compounds predominantly exist in powder and aerosol forms, and they are typically ingested through inhalation. The International Cancer Research Authority categorized substances into five classes based on their carcinogenic properties. Cadmium is included in "Group 1" of "Carcinogenic Effective Substances in Humans" due to its association with lung cancer.Living beings are frequently exposed to Cd directly through the respiratory tract (approximately 13-19%), but it can also enter through the digestive system (approximately 10-44%) orthe food chain, and subsequently, it is disseminated throughout the body⁵. About 30% of cadmium is absorbed in the kidneys, and 30% absorbed in the liver²⁶. Cd can harm the lung, liver, pancreas, muscles, adipose tissue, and skin, kidney, bone, testicular, and placenta, depending on the method, concentration, route, quality, and rate of exposure²³. Cadmium causes tissue damage via oxidative stress, epigenetic alterations in DNA expression, inhibition of homeostasis, and potential impairment of mitochondrial function, inducing programmed cell death. The effects are amplified by the presence of other metals, including lead (Pb) and arsenic (As). Individuals with diabetes exhibit increased vulnerability to renal impairment due to cadmium exposure. Acute exposure to cadmium results in inflammation characterised by symptoms including cough, nasal dryness, irritation, headache, and dizziness. Cadmium is slowly removed from the body by urine, faeces, saliva, or perspiration, posing health risks. Only 0.01-0.02 percent per day of cadmium body burden is excreted in urine and faeces¹⁸.

Sources of Cadmium

I- SOIL

- Wastewater irrigation,
- Coal combustion residues
- Disposal of heavy metal wastes
- Utilisation of high-phosphate fertilisers
- Applications of animal manure
- Sewage, Sludge Incineration, Industrial regions, Mining and smelting, Petrochemical spills, Pesticides
- Lead paints and gasoline of atmospheric deposits, treatment of industrial and municipal waste by chemical and biological methods

II- AIR

- Alloys containing Cd impurity,
- Optical window,
- Nuclear fission,
- Welding,
- Detergents,
- Petroleum,
- Chimneys,
- Paints,
- Glasses.
- Nickel Cadmium Batteries,
- Polyvinyl chloride products,
- Stabilizing plastics,
- Cadmium-coated Ferrous and non-ferrous products,
- Marine aerosol,
- Solar Panels,
- Forest fires.
- Volcanic eruptions and
- Weathering of rocks

Health Problems Caused by Cadmium

The deleterious properties of heavy metals, which persist in the environment, have resulted in significant health issues for humans. The elimination of heavy metals is essential for ensuring clean water resources for the people. Common methods used for removing heavy metals from aqueous solutions include reverse osmosis, membrane separation, ion exchange, and chemical precipitation.Cd metal or its compounds have been shown to cause sarcoma disease when they are

injected intramuscularly or subcutaneously³⁶. Excessive cadmium consumption can disrupt calcium metabolism. contribute to the formation of kidney stones, and adversely affect bone health. Studies show that when the level of cadmium (Cd) in urine reaches 1.0 nmol/mmol of creatinine, the risk of renal tubular proteinuria increases by 10%11. One of the initial indicators of cadmium damage in the liver involves impaired mitochondrial activity. The detrimental impact of cadmium on mitochondria is associated with elevated glutathione levels and decreased glutathione peroxidase activity in liver cells, rather than enhanced permeability of the mitochondrial inner membrane. Cadmium binds to the mitochondria and can inhibit both cellular respiration and oxidative phosphorylation at low concentrations²⁰. Osteomalacia and osteoporosis may manifest in individuals residing or employed in cadmium-polluted regions. For instance, in a Japanese locality where soil was contaminated with cadmium from zinc and lead mining, itai-itai disease, characterized by osteomalacia, osteoporosis, painful bone fractures, and renal impairment, were historically prevalent. Complications such as coughing, anaemia, and kidney failure may result in death. Cd exposure can occur in the air while smelting and refining metals, as well as in the production of Cd goods, including batteries, coatings, and plastics, such as workers who soldering or welding cadmiumcontaining metals. Cosmetics utilised by women, including eyeliner, blush, lipstick, mascara, eye shadow,foundation,kajal, hairstyling products,perfumes, and sindoor, contain traces of heavy metals, mainly arsenic, cadmium, lead, chromium, strontium, and may contribute to the risk of skin cancer^{16,22}. Cadmium rapidly oxidises to cadmium oxide in the air. Acute respiratory effects occur when the concentration in the air reaches 1 mg/m³. Inorganic salts, including Cd(NO₃)₂, CdSO₄, and CdCl₂, exhibit solubility in water¹. Cadmium exposure in cell lines can lead to chromosomal anomalies, increased sister chromatid exchanges, DNA strand breaks, and DNA-protein crosslinking. It has the potential to induce mutations and chromosomal deletions^{24,12}. Cadmium also induces alterations in epigenetic and signal-transduction processes, which may contribute to the deregulation of cell growth. Some chronic lung diseases, such as asthma and bronchitis, as well as hypertension, are believed to be associated with lowdose, slow cadmium poisoning. Long-term exposure to cadmium (Cd) particles through inhalation is linked to abnormalities in lung function and chest X-rays that show signs consistent with emphysema³⁰. Prolonged exposure to cadmium results in structural and functional disorders, particularly within the male and female reproductive systems³⁷. Cadmium exposure can reduce

sperm density, volume, and count, and increase the proportion of immature sperm forms^{2.,21}. Testicular necrosis caused by Cd can cause permanent infertility. Recent research investigations on female rats indicate that the application of cadmium inhibits ovulation⁸. Cadmium has been shown to inhibit the accumulation of follicle-stimulating hormone (FSH) and cAMP-induced progesterone in ovarian granulosa cells^{17,15}. Cadmium can cross the placenta and barriers to reach the fetus, causing teratogenic effects. Cadmium has the potential to affect the reproduction and development of several mammalian species. The incidence of spontaneous miscarriage and the duration to achieve pregnancy have been reported to rise, while the live birth rate has declined³⁵.

Recommendations for risk mitigation

To mitigate global environmental cadmium emissions and minimise occupational and environmental exposure to cadmium and its related health impacts, the following measures are required³³:

- Washing fruits and vegetables, as well as peeling roots and tubers, can mitigate cadmium contamination to a certain extent.
- Promote the elimination of the use of cadmium in products such as toys, jewellery, and plastics.
- □ Reduce, as much as possible, cadmium emissions—particularly into surface waters—from mining and smelting, waste incineration, land application of sewage sludge, and the use of phosphate fertilisers and cadmium-contaminated manure.
- ☐ Devise strategies for the safe disposal of cadmium-contaminated waste and effluents.
- ☐ Encourage safe and efficient ways to limit nonrecyclable uses and enhance cadmium recycling.
- Protect people from secondhand smoke in enclosed spaces such as workplaces, public transportation, and other public areas by implementing the World Health Organization's Framework Convention on Tobacco Control.
- Minimise cadmium exposure by enhancing working conditions in the non-ferrous smelting sector
- Disseminating information regarding the proper utilisation of fertilisers that may include high cadmium content.
- ☐ Enhance global consciousness regarding the critical importance of reducing cadmium waste releases.

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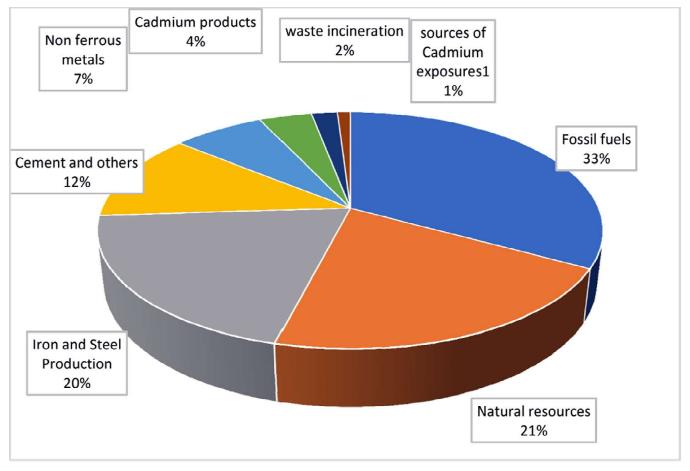


Fig. 1: Relative contribution of different sources to cadmium exposure

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