

CADMIUM TOXICITY IN NATURE GENERATES THE CANCEROUS PROBLEMS

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ABSTRACT

A naturally occurring metal, cadmium is noticed in tiny amounts in a variety of sources such as food, water, soil, and the atmosphere. Cadmium may be edified in all soils and rocks, including coal and mineral fertilizers. In general, non-smoker people are getting affected by food contamination. The main theme of this paper is cancer activity by cadmium pollution of our environment. Foods are getting contaminated by industrial wastes. Wastes have Cd²⁺ ions which can bind with plant materials and also bind with animal muscles. On the other hand, the smoker people take the cadmium by smoking tobacco. The cadmium can easily bind up with the organs like the lung, prostate, breast, bone, etc. When industrial wastes are thrown into rivers, ponds, or open spaces, particularly in South Asian nations, the water becomes poisoned and the soil becomes deteriorated; as a result, the environment becomes more hazardous. In consequence, people can be oppressed by significant sicknesses that occurred by Cd²⁺, such as osteoporosis, renal dysfunction, anemia, alveolar malignancy, and also other conditions.

KEY WORDS : Cadmium, Carcinogenesis, Alveolar malignancy, Smoking Tobacco, Osteoporosis, etc.

INTRODUCTION

Cadmium (Cd²⁺) is a trace and heavy molecular pollutant that is often found in industrial production and so is detrimental to human health, producing ailments such as pneumonia, lung disease, and emphysema (Xiangyu Cao, *et al.*, 2021). It is a heavy metal contaminant that is commonly found in air, water, and soil. Agronomic and industrial factors contribute to the formation of this pollutant in

nature. Although Cd²⁺ is most often absorbed by the repast of defiled food and also water, it is also absorbed to a significant extent via respiration and severe cigarette smoking (Hogervorst *et al.*, 2007; Pan *et al.*, 2010). Nature's spontaneous sources of Cd²⁺ involve volcanic eruptions, feeling of Cd²⁺ enriched rocks, coastal floods, and the deposition of cadmium in soil, sediment, and waste dump. Excessive smoking, mining sites and processing of zinc ores flaring of petrification fuels, open burning,

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and discharges from municipal landfills are among the anthropogenic sources of cadmium that lead to the bulk of the Cd^{2+} present in the atmosphere (Pan *et al.*, 2010). Humans are exposed to cadmium mostly as a result of inhalation and food consumption. Except for smokers, respiration provides much less to overall Cd^{2+} body burden; nevertheless, food intake plays a major role more to body accumulation of inhaled Cd^{2+} . According to current thinking, humans have a biological half-life of ten to thirty-five years (WHO, 2008). Cd^{2+} accumulates mostly in the kidneys and has a biological half-life of ten to thirty-five years in the kidneys. Cd^{2+} is largely absorbed via the RT and, to a lesser amount, through the GIT, with skin consumption being rare in contrast to this. When Cd^{2+} is consumed, it proscribes into the circulation through R.B.C and also albumin, where it greatly accumulates in the renal tract, liver, and even the GIT (Tinkov *et al.*, 2018; Satarug, 2018). Gradual excretion of cadmium from the body occurs via the renal tract, saliva, and milk when a woman is lactating. In humans, exposure to it may result in renal functional problems and hepatic dysfunction, as well as osteomalacia, pulmonary edema, testicular problems, and damage to the adrenal gland and hemopoieticsystem (Tinkov *et al.*, 2018).

No biological function for cadmium has been established yet. Among humans, the renal system and liver are the most significant sites of cadmium accumulation. A human carcinogen, as well as being damaging to the renal, endocrine, and reproductive systems, is present in this substance. It has been suggested that cadmium may interfere with DNA replication at the cell membrane, leading to genotoxicity (Rani, *et al.*, 2014). It has been shown that cadmium toxicity is most severe in fish embryonic and also early larval stages, with prolonged manifestation resulting in larval death

and growth suppression (AMAP, 1998). Thyroid function is compromised in adult fish, as is the case with spinal deformities and behavioral issues (AMAP, 2002). Several studies have shown that salmonids are both susceptible to and susceptible to cadmium poisoning (NCM, 2003).

Objective

We reviewed 37 scientific papers on how cadmium of the atmosphere affects our health and induces malignancy in our bodies. The main theme of this paper is cancer activity by cadmium pollution of our environment.

Environmental issues with cadmium pollution

Global human cadmium emissions were estimated to be roughly 25000 tons per year in the most current research of global human cadmium emissions. Identifying and estimating natural sources may be challenging, and estimates might vary vastly. Natural excretions, on the opposite side, are known to be far greater than human emissions. The metal is not mined since there is more than sufficient cadmium created as a sub-breed thing of the melting of Zn^{2+} from its ore, zincblende (ZnS), in which greenockite (CdS) is a substantial defiled, accounting for up to 3 percent of the total. As a result, the most important mining regions are those involved with zinc production. The world's annual output is around 14.000 tonnes, with Canada being the primary producer and the United States, Australia, Mexico, Japan, China (Chao Yu, *et al.*, 2010), and Peru serving as key suppliers.

Human intake of cadmium takes done mostly via diet. Food things that are high in Cd^{2+} may considerably enhance the Cd^{2+} levels in our body. Examples include cod-liver, mushrooms, crayfish, oysters, cocoa ruffian and so slimy red algae (Järup, 1998).

Other toxins may arise with those who reside near polluted sites or enterprises that liberate Cd^{2+} into the aerial space and those who act in the thematic refining sector. While people respire in Cd^{2+} , it may significantly injure the RT system of our body. This will even lead to fatality. It is originally transmitted to the liver via the bloodstream. There, it is coupled to protein molecules to generate complex agents which are transported to the renal tract. Cd^{2+} concentrates in the renal system, where it impairs the filtration process. This promotes the elimination of vital proteins and carbs from the body and extrarenal depreciation. This takes many years

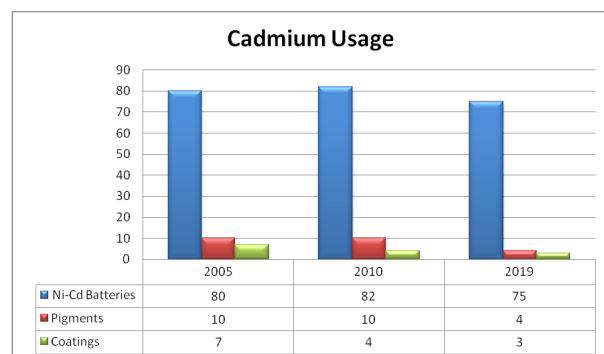


Fig. 1. Cadmium Consumption Patterns [8]

before cadmium that has gathered in the renal tract is removed from a body (Järup, 1998).

There is a high concentration of cadmium pollution in soils from industrial waste streams. Waste streams such as bio-industrial manure and zinc production are the result of these processes. Household garbage combustion and the burning of fossil fuels may potentially contribute to the emission of Cd²⁺ into the ambiance. Only a small amount of cadmium is currently entering the waterways due to restrictions governing wastewater disposal from homes and businesses (Lenntech, 2017).

It is well known that in soils, cadmium is highly adsorbable. Cadmium contamination in soils may be particularly harmful since food consumption increases cadmium intake. Acidification of soils increases plant absorption of cadmium. The creatures that rely on plants for their existence might be at risk. Cadmium may make up in our body if we take a lot of different plants. As a result, cows' kidneys may take huge quantities of cadmium (Adedapo and Adeoye, 2016).

The genesis of synthetic PO₄³⁻ fertilizers is another principal source of Cd²⁺ excretion. Only when manure is delivered to fields, some of the Cd²⁺ gets embedded in the soil, while the remainder of the Cd²⁺ is released into surface rivers and streams by manure-giving farms. When absorbed by sludge, cadmium is capable of being carried across long distances. Sludge with high concentrations of cadmium may harm surface waterways and soils (World Bank Group, 1998)..

Earthworms and other important soil creatures are particularly vulnerable to cadmium toxicity, which may be fatal. They are capable of dying in very low quantities, which has implications for the soil structure. Because of the high amounts of cadmium in soils, soil processes involving

microorganisms may be influenced, putting the whole soil ecosystem at risk. Animals which consume or drink cadmium may develop high blood pressure, liver illness, nerve or brain damage, among other symptoms (Lenntech, 2017).

Carcinogenic Development

Cadmium, identified in 1817, was not economically employed until the late nineteenth century (Hiatt and Huff, 1975). It is a smell-less, silver-whitish, grayish-white powder or blue-tinged metal that occurs in nature in eight stable and two radioisotopes (NTP, 2004). Cadmium oxidizes slowly in wet air but produces cadmium oxide vapors when overheated (Beryllium, 1993). It is present in the market in powders, ingots, slabs, foils, sticks, and also crystals. CdCl₂, CdSO₄, and Cd(NO₃)₂ are commercially valuable cadmium salts, as are CdO and CdS to a lesser level (Hammons *et al.*, 1978).

Considering the aforementioned complicated considerations, the IARC deemed the totality of current material until early 1993 to be enough to include Cd²⁺ in its Group-1 category of evidence: "Cd²⁺ and cadmium metals are cancer-inducing agents to humans (Huff *et al.*, 2007). Their choice was founded on - there is strong evidence in human bodies for the malignancy of Cd²⁺ and components of Cd²⁺, adequate information in empiric animals for the carcinogenic effects of cadmium substances, and also little information in animal studies for the carcinogenic possibilities of cadmium metal (Huff *et al.*, 2007).

Pulmonary Cancer

It is estimated that lung carcinoma is one of the keyreasons for cancer-related annulment in the U.S.A, with one of the highest occurrences of any malignancy in both men and women (Bell *et al.*, 2000). Cadmium-induced lung damage has just recently been identified, indicating that it induces lung injury and inflammatory responses via the generation of cytokines (Kataranovski *et al.*, 1998

Cadmium is a toxic heavy metal that thus ranks sixth on the PLHS. It is a prevalent natural contaminant as a byproduct of smelters. It is also a major ingredient of tobacco smoking, also e-smoking, and breathing has been connected to reducing pulmonary function, lung carcinoma, and COPD (Jessica Rennolds, *et al.*, 2010). Cohort research was administrated on 926 male employees from 1947 to 2000, showed that pharyngeal cancer

Table 1. A summary of the harmful consequences of acute cadmium inhalation exposure

Symptoms	Dose Amount (mg/m ³)
The throat Irritation, Abdominal pain	0.01-0.15
Facial oedema, Pulmonary oedema, Tracheobronchitis	1-5
Lethal activities after 28,800 seconds	5
Lethal activities after 1,200 seconds	39
Lethal activities after 600 seconds	250
Lethal activities after 60 seconds	2500

(Obs) 4, (Exp) 0.7, (SMR) 559, $p < 0.05$) (Sorahan, 2003).

Prostate Cancer

Historically, prostate cancer was first cancer linked to cadmium exposure (Lemen *et al.*, 1976). With some, but not all, epidemiologic studies, it has been linked to human prostatic cancer. According to several researches, tissue concentrations of cadmium in the mammalian prostate are associated with malignant illness (Waalkes and Rehm, 1994).

Diet is the most common cause of cadmium consumption. It is entrusted that a nonsmoker adult male intakes 0.35g of Cd per kg in a day (Farooq, *et al.*, 2019). The usage of phosphate fertilizers, origins of contamination, soil pH, and growing techniques all have an impact on the quantity of cadmium available in crops (Kirkham, 2006). Cadmium levels in the ambient air extent from 0.1 to 5.0 ngm^{-3} , and in urban regions, concentration range from 2 ngm^{-3} to 15 ngm^{-3} , but in industrial regions, concentrations can reach 150 ngm^{-3} (ATSDR, 2012).

Gastro-intestinal Cancer

Cadmium ingestion has been related to a variety of ailments in humans, most notably stomach cancer, according to recent research. Its effects on the transcription of uPAR or CD87 in human peptic cancer biomarkers, and also the signaling pathways that underlie them, have been investigated. In addition, the actions of the uPAR promoter have risen in prominence. It activates the extracellular signal-regulated p38 MAPK, ERK-1/2, ATK, JNK-1, which are all extracellular signal-regulated proteins. Cd^{2+} toxicity treatment is resulted in a huge increase in aggressive behaviors and also metastasis, which was somewhat lowered by transcriptional antibodies and also inhibitors of activator protein-1, nuclear factor kappa-B cells, and extracellular signal-regulated kinases function. A study was done

in Korea among the 1245 people to find the association between gastric cancer and Cd^{2+} . Cd^{2+} disrupts the mucosal layer of the GIT, that ultimately leading to DNA damages, and inducing the carcinogenesis of the gastro-intestinal.

Concluding Remarks

Cadmium, the most useful metal at present, is formed as a consequence of mining, processing, and purgatory of non-ferrous metals such as Zn^{2+} , Pb^{2+} , and Cu^{2+} . Instead of throwing it into the environment, innovators have been able to exploit its specific properties for specialized industrial purposes. Cd^{2+} is also manufactured through the recycling of discarded nickel-cadmium batteries, which is its major purpose, and secondary or recycled cadmium today accounts for roughly 23 percent of the total cadmium supply (ICdA, 1975).

Cadmium and cadmium derivatives, like many other carcinogens, have long been informed to be cancer-inducing agents in empirical animals and just recently in people (IARC, 2006). Long-term biological assays in animals were responsible for the findings of around 25–30% of known possibly malignant to humans (Huff, 1993). This situation is often the consequence of a growing controversy

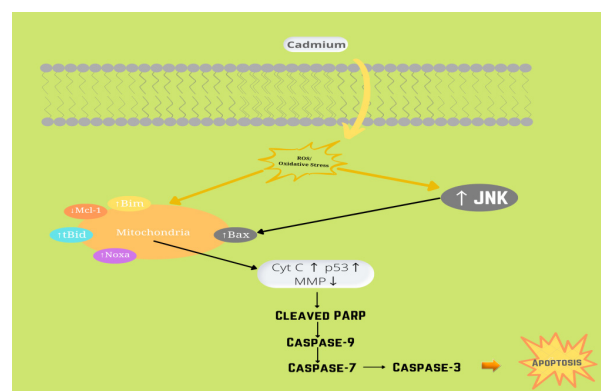


Fig. 2. Cadmium induces carcinogenesis

Table 2. Epidemiological studies of prostate cancer by cadmium

Study Type	Exposure Type	Result	Reference
Case-control	Occupational	Slightly Positive	(Armstrong and Kazantzis, 1985)
Case-control	N/A	Positive	(Vinceti <i>et al.</i> , 2007)
Case-control	Environmental	Positive	(Zeng <i>et al.</i> , 2007)
Cohort	Environmental	Negative	(Arisawa <i>et al.</i> , 2007)
Cohort	Environmental	Increased prevalence of prostate	(Nyqvist <i>et al.</i> , 2017)
Cross-sectional	Occupational	Positive	(Hengstler <i>et al.</i> , 2003)
Retrospective	Occupational	Positive	(Lemen <i>et al.</i> , 1976)

beyond whereas chemical carcinogenesis bioassay data are incidental and verified for predicting human cancer presumption (Knight *et al.*, 2006). Cadmium toxicity is linked with weak and brittle bones, a condition known as osteomalacia (Yoshida, *et al.*, 1999). This causes joint and back discomfort, and also an increase in the likelihood of fractures. Cough, anemia, and renal failure are further side effects of cadmium overdose.

Conflict of interest

There is no conflict of interest.

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REFERENCES

- Armstrong, B.G. and Kazantzis, G. 1985. Prostatic cancer and chronic respiratory and renal disease in British cadmium workers: a case control study. *Br J Ind Med.* 42: 540-545.
- Arisawa, K., Uemura, H. and Hiyoshi, M. 2007. Cause specific mortality and cancer incidence rates in relation to urinary beta2-microglobulin: 23-year follow-up study in a cadmium-polluted area. *Toxicol Lett.* 173 : 168-174.
- ATSDR, 2012. (Agency for Toxic Substances and Disease Registry). Public Health Statement Cadmium. Division of Toxicology and Human Health Sciences.
- AMAP, 1998. Assessment report: Arctic pollution issues. Arctic Monitoring and Assessment Programme, Oslo.
- AMAP, 2002. Arctic Pollution 2002. Arctic Monitoring and Assessment Programme, Oslo.
- Adedapo, A.A. and Adeoye, B.O. 2016. Cadmium, an Environmental Pollutant: A Review. *West African Journal of Pharmacology and Drug Research.*
- Bell, R.R., Nonavinakere, V.K. and Soliman, M.R. 2000. Intratracheal exposure of the guinea pig lung to cadmium and/or selenium: a histological evaluation. *Toxicol Lett.* 114: 101-109.
- Beryllium, 1993. Cadmium, mercury, and exposures in the glass manufacturing industry. Working Group views and expert opinions, Lyon, 9-16 February 1993. *IARC Monogr Eval Carcinog Risks Hum.* 58:1-415.
- Chao, Yu, Qicong Ling, Sha Yan, Jing Li, Zhongda Chen and Zhenyu Peng, 2010. Cadmium contamination in various environmental materials in an industrial area, Hangzhou, China. *Chemical Speciation & Bioavailability.* 22(1) : 35-42
- Farooq, O., Ashizawa, A., Wright, S., Tucker, P., Jenkins, K., Ingerman, L. and Rudisill, C. 2019. Toxicological Profile for Cadmium; Agency for Toxic Substances and Disease Registry (US): Atlanta, GA, USA.
- Jessica Rennolds, Susie Butler, Kevin Maloney, Prosper N. Boyaka, Ian, C. Davis, Daren, L. Knoell, Narasimham, L. Parinandi and Estelle Cormet-Boyaka, 2010. Cadmium Regulates the Expression of the CFTR Chloride Channel in Human Airway Epithelial Cells. *Toxicological Sciences.* 116 (1): 349-358.
- Järup, L. Berglund, M., Elinder, C.G., Nordberg, G. and Vahter, M. 1998. Health effects of cadmium exposure – a review of the literature and a risk estimate. *Journal of Work, Environment & Health.* 1-51.
- Hogervorst, J., Plusquin, M., Vangronsveld J., Nawrot, T., Cuypers, A., Van Hecke, E., Roels, H.A., Carleer, R. and Staessen, J.A. 2007. House dust as possible route of environmental exposure to cadmium and lead in the adult general population. *Environ Res.* 103(1) : 30-37.
- Hiatt, V. and Huff, J. 1975. The environmental impact of cadmium: an overview. *Int J Environ Studies.* 7: 277-285.
- Hammons, A.S., Huff, J. and Braunstein, H.M. 1978. ORNL/EIS-106 and EPA-600/ 1-78-026. Oak Ridge, TN: Oak Ridge National Laboratory. *Review of the environmental Effects of Pollutants: IV. Cadmium;* p. 274
- Huff, J., Lunn, R.M., Waalkes, M.P., Tomatis, L. and Infante, P.F. 2007. Cadmium-induced cancers in animals and in humans. *Int J Occup Environ Health.* 13(2) : 202-212.
- Hengstler, J.G., Bolm-Audorff, U. and Faldum, A. 2003. Occupational exposure to heavy metals: DNA damage induction and DNA repair inhibition prove co-exposures to cadmium, cobalt and lead as more dangerous than hitherto expected. *Carcinogenesis.* 24: 63-73.
- Huff, J. 1993. Chemicals and cancer in humans: first evidence in experimental animals. *Environ Health Perspect.* 100 : 201-210.
- ICdA, 2019. Evolution of Cadmium use and Consumption. *Int Cad Ass.*
- IARC, 2006. Working Group on the Evaluation of Carcinogenic Risks to Humans. Cobalt in hard metals and cobalt sulfate, gallium arsenide, indium phosphide and vanadium pentoxide. *IARC Monogr Eval Carcinog Risks Hum.* 86(1) : 294.
- Kataranovski, M., Kataranovski, D., Savic, D., Jovicic, G., Bogdanovic, Z. and Jovanovic, T. 1998. Granulocyte and plasma cytokine activity in acute cadmium intoxication in rats. *Physiol Res.* 47 : 453-461.
- Kirkham, M.B. 2006. Cadmium in plants on polluted soils: Effects of soil factors, hyperaccumulation, and amendments. *Geoderma.* 137: 19-32.
- Knight, A., Bailey, J. and Balcombe, J. 2006. Animal carcinogenicity studies: 1. Poor human predictivity. *Altern Lab Anim.* 34(1):19-27.

- Kim, H., Lee, J. and Woo, H.D. 2019. Association between dietary cadmium intake and early gastric cancer risk in a Korean population: a case-control study. *European Journal of Nutrition*. 58: 3255-3266.
- Lemen, R.A., Lee, J.S., Wagoner, J.K. and Blejer, H.P. 1976. Cancer mortality among cadmium production workers. *Ann N Y Acad Sci*. 271: 273-279.
- Lenntech, 2017. Chemical properties of cadmium - Health effects of cadmium - Environmental effects of cadmium.
- NTP, 2004. Report on Carcinogens. 11th. U.S. Department of Health and Human Services, Public Health Service, National Toxicology Program. Cadmium and cadmium compounds; pp. III-42-44.
- Nyqvist, F., Helmfrid, I., Augustsson, A. and Wingren, G. 2017. Increased Cancer Incidence in the Local Population Around Metal-Contaminated Glassworks Sites. *J Occup Environ Med*. 59(5) : 84-90.
- NCM, 2003. Cadmium Review. Report No. 1, Issue No. 4. Nordic Council of Ministers, Copenhagen. 26 pp.
- Pan, J., Plant, J.A. and Voulvoulis, N. 2010. Cadmium levels in Europe: implications for human health. *Environ Geochem Health*. 32: 1- 12.
- Tinkov, A.A., Gritsenko, V.A., Skalnaya, M.G., Cherkasov, S.V., Aaseth, J. and Skalny, A.V. 2018. Gut as a target for cadmium toxicity. *Environ Pollut*. 235 : 429-434.
- Rani, A., Kumar, A., Lal, A. and Pant, M. 2014. Cellular mechanisms of cadmium-induced toxicity: a review. *International Journal of Environmental Health Research*. 24: 378-399.
- Satarug S. 2018. Dietary Cadmium Intake and Its Effects on Kidneys. *Toxics*. 6(1).
- Tinkov, A.A., Filippini, T., Ajsuvakova, O.P., Skalnaya, M.G., Aaseth, J., Bjørklund, G., Gatiatulina, E.R., Popova, E.V., Nemereshina, O.N., Huang, P.T., Vinceti, M. and Skalny, A.V. 2018. Cadmium and atherosclerosis: A review of toxicological mechanisms and a meta-analysis of epidemiologic studies. *Environ Res*. 162240-16260.
- Sorahan, T. and Esmen, N.A. 2003. Lung cancer mortality in UK nickel-cadmium battery workers, 1947-2000. *Occupational and Environmental Medicine*. 61 : 2.
- Vinceti, M. Venturelli, M. and Sighinolfi, C. 2007. Case control study of toenail cadmium and prostate cancer risk in Italy. *Sci Total Environ*. 373 : 77-81.
- WHO, 2008. *Cadmium. Guidelines for Drinking-Water Quality*, 3rd edition incorporating 1st and 2nd addenda. Vol. 1. *Recommendations*. Geneva: *World Health Organization*. 317- 319.
- Waalkes, M.P. and Rehm, S. 1994. Cadmium and prostate cancer. *Journal of Toxicology and Environmental Health*. 3(3): 251-269.
- World Bank Group. 1998. *Pollution Prevention and Abatement Handbook*. 212-215 pp.
- Xiangyu Cao, Mingyang Fu, Ruochen Bi, Xiaomei Zheng, Baorong Fu, Siqi Tian, Chengying Liu, Qijiu Li and Jianli Liu, 2021. Cadmium induced BEAS-2B cells apoptosis and mitochondria damage via MAPK signaling pathway. *Chemosphere*.
- Yoshida, F. and Hata, A. 1999. Tonegawa H. Itai-Itai disease and the countermeasures against cadmium pollution by the Kamioka mine. *Environmental Economics and Policy Studies*. 2 (3) : 215-229.
- Zeng, X., Jin, T., Jiang, X., Kong, Q., Ye, T. and Nordberg, G.F. 2007. Effects on the prostate of environmental cadmium exposure- a cross-sectional population study in China. *Biometals*. 17: 559-565.
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