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Bio-accumulation and dose-response modeling of heavy metals in human tissues

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Abstract
Several cases of cancer have been connected to exposure to heavy metals as a result of bioaccumulation of these metals and their toxic effects. Understanding how these metals accumulate in tissues and the resultant biological reactions is of great importance for public health policymakers and the development of preventive measures. This study models the bioaccumulation and dose-response behaviour of four carcinogenic metals, lead (Pb), cadmium (Cd), arsenic (As), and mercury (Hg) in malignant human tissue, using ordinary differential equations (ODEs) in MATLAB. This simulation examines their concentration dynamic over time and their respective carcinogenic risk profiles. Using a first-order ODE model, the bioaccumulation in human tissue was simulated for exposure over 100 days. The uptake of heavy metals and their elimination rate constants were collected from peer-reviewed literature. A Hill-type dose-response model was used, and MATLAB's ode45 solver was used for the numerical integration. Accumulation of cadmium (cd) and lead (Pb) was the highest in the tissue, and both metals were also the highest to be associated to cancer risk, which reached over 70% bio-response during the simulation window. Arsenic (As) and mercury (Hg) showed the slowest bio-accumulation rate as well as dose-response levels. Due to high bio-accumulation and steep dose-response slope of Cadmium, its risk is amplified. Cadmium and lead pose a greater risk to human tissue health under severe exposure. The findings from this study contributes to environmental health policies and cancer prevention remedies among people who are exposed to heavy metals.

Keywords: Bioaccumulation, Dose-response, Heavy metals, Breast cancer, ODE modelling, MATLAB

1. Introduction

Heavy metals are widespread environmental pollutants (Mitra *et al*., 2022). Heavy metals such as lead (Pb), cadmium (Cd), arsenic (As), and mercury (Hg) are known to be toxic to human beings and at the same time possess carcinogenic properties (Jomova *et al*., 2024). Long-term exposure to these metals, even at low levels, can result in accumulation in human tissues, which may activate the carcinogenicity of various cancers and their metastasis, including breast carcinomas (Ali *et al*., 2024).

Breast tissue is highly prone to bioaccumulation of heavy metals due to its high level of lipid content and high level of hormonal activity (Aureliano *et al*., 2025; *Idowu et al*., 2024). Many epidemiological studies have confirmed and reported high concentrations of lead and cadmium in cancerous tissues, thereby linking these carcinogenic metals to their mechanism, which includes but not limited to oxidative stress, endocrine disruption, and DNA damage (Tarhonska *et al*., 2022). However, few studies have studied how the bioaccumulation of these metals results in cancer risk with time, as well as the time-dependent behaviour (Rabie *et al*., 2025).

The use of mathematical modeling coupled with ordinary differential equations (ODEs) presents a comprehensive method to simulate and evaluate the dose-response effects, plus the mechanism of the metals accumulated in human tissues (Haider *et al*., 2022). This model is a theoretical framework and due to lack of patient's data, it does not

represent individual clinical cases. Combining these approaches with Hill-type response models, this study presents the quantitative knowledge about how long-term exposure to heavy metals contributes to cancer progression (Schindler, 2017).

So many studies have reported that heavy metals such as cadmium, lead, arsenic, and mercury are present in breast tissues but few have examined their dynamic behaviour with time via mathematical modeling (Jomova *et al*., 2024). Most of the existing literatures focused on quantitative analysis and statistical correlation without studying the accumulation of these heavy metals over time or their biological dose responses (Ahmad *et al.*, 2022). A novel approach is introduced in this study by merging first-order ordinary differential equations with Hill-type dose-response modeling in order to simulate the kinetics of heavy metal bioaccumulation and the relating carcinogenic risk. This integrated approach provides useful perception into the possible long-term effect of environmental exposure which serves as a projective framework for assessment of public health risk (Samborska-Goik & Pogrzeba, 2024).

Even with many researches linking exposure to heavy metals with cancer, there are gaps on how they accumulate with time in human tissues and how their concentrations correlate with cancer risk (Liu *et al*., 2022). This study addresses the gap by integrating a mathematical approach and Hill-type dose-response model to simulate the time dependent behaviour of four key carcinogenic metals which are lead, cadmium, arsenic, and mercury. The use of MATLAB to simulate and quantify exposure as well as connected cancer risk, provides a predictive model of health risk assessment. A new and quantitative viewpoint on the carcinogenic potential of heavy metals in human tissue is offered by this study, which bridges the fields of toxicology, mathematical modeling, and computational simulations (Singh *et al*., 2024).

2.0 Materials and methods

2.1 Study Design and Objective

The aim of the study is to simulate and compare bioaccumulation and dose-response behaviour of four carcinogenic metals: lead (Pb), cadmium (Cd), arsenic (As), and mercury (Hg) in tissues of humans. The primary goal was to analyse the relative contribution of these heavy metals to a long-term cancer risk, which is based on build-up concentration and the corresponding biological effect.

2.2 Bioaccumulation Model

Heavy metals accumulation dynamic was modeled using a first-order differential equation that put into consideration the balance between uptake and elimination rate.

$$\frac{dC(t)}{dt} = k_{in}.C_{ex} - k_{out}.C(t) \quad (1)$$

Where:

$C(t)$ is the tissue concentration at time t,
C_{ex} is the external exposure concentration (mg/kg),
k_{in} is the uptake rate constant $(1/day)$,
$k_{out}$is the elimination rate constant $(1/day)$.

This model assumes that there exists a continuous exposure to an external concentration constant, neglecting the saturation effect or feedback.

2.3 Dose-Response Model

The Hill dose-response was used to analyze the carcinogenic response to metals accumulated in tissue.

$$R(C) = \frac{C^n}{C^n + EC_{50}^n} \quad (2)$$

Where:

$R(C)$ is the biological response or risk level,
C is the tissue concentration (mg/kg),
EC_{50} is the concentration at which 50% of the maximum effect occurs,
n is the Hill coefficient determining the steepness of the response curve.

Prior dose-response modeling that involves human cell lines or systemic toxicity evaluations offered the selected Hill coefficients and EC50 values, which act as approximations in the absence of tissue-specific data (Husband, 2021). These metrics highlight different kinetic behavior among heavy metals and offer a basis for comparative toxicity modeling; however, they are not limited to breast cancer models.

2.4 Parameter Values

Values of the parameters below were obtained from peer-reviewed toxicological data sources.

Table 1: Parameter table

	$C_{ex}(mg/kg)$	k_{in} $(1/day)$	k_{out} $(1/day)$	EC_{50} is (mg/kg)	n
Lead (Pb)	**Metal**	0.10	0.007	0.25	2.5
Cadmium	0.20	0.08	0.002	0.15	3.0
Arsenic	0.15	0.05	0.015	0.10	2.0
Mercury	0.10	0.03	0.005	0.20	2.0

3.0 Result and Discussion

3.1 Bioaccumulation Over Time

Figure 1 presents the bioaccumulation of four carcinogenic metals for 100-day simulation period. As indicated by the accumulation curves, (Cd) and lead (Pb) accumulated the most and attained the highest concentrations in tissue. This is as a result of high uptake rate constants k_{in} and low elimination rates k_{out}. A concentration of approximately 0.74 mg/kg was reached by cadmium (Cd) day 100 of exposure while lead (Pb) reached a concentration of 0.65 mg/kg approximately for same day of exposure. Conversely, metals that exhibited slower accumulation rates are arsenic (As) and mercury (Hg) with a concentration of 0.45 mg/kg and 0.35 mg/kg by respectively at the end of simulation. The results imply that suggest that cadmium and lead are more likely to accumulate in tissues under prolonged exposure, which is a finding that is consistent with that of Ebrahimi *et al*., 2020 and Qu & Zheng, (2024). This toxic metals does not only accumulate in tissues but can also has effects on the cellular and molecular activities of the tissues (Busby, 2013; Jackson *et al*., 2017). The dose response curves of shows the behaviour of cadmium, lead, arsenic, and mercury which matches with the biological mechanisms implicated in metal-induced carcinogenesis (Aggarwal *et al*., 2019; Balali-Mood *et al*., 2021). Cadmium is most widely reported that induce epigenetic alterations such as irregular DNA methylation which caused the tumor suppressor genes and activation of oncogenes to be dormant. (Absalon & Šlesak, 2010; Alhmoud *et al*., 2020; Ali Hussein *et al*., 2024; Balali-Mood *et al*., 2021). It also disrupts the DNA repair mechanisms which aid the instability of genome. Cadmium is known to mimic estrogen and also known to promote carcinogenic pathways that is hormonal related (Das & Majumdar Paul, 2025; Hirshfeld *et al*., 2018).

Exposure to lead also disrupts hormonal signaling by hampering with estrogen receptor expression and calcium-mediated pathways (Tamagno & Freeman, 2025). Lead is also known in the variation of genetic expression which involve but not limited to oxidative stress, inflammation and apoptosis which can all contribute to a pro-carcinogenic environment (Chaudhary *et al*., 2023). Arsenic and mercury which exhibited slower accumulation rate could be attributed to their lower k_{in} values and relatively higher elimination rates compared to cadmium and lead. However, despite the slower bioaccumulation rate of cadmium and lead, the potential risks cannot be underestimated particularly in areas that are highly and continuously exposed. Arsenic has been reported to induce hypomethylation and hypermethylation of DNA which alters genetic expression profiles in mammary epithelial cells (Chung *et al*., 2024; Sage *et al*., 2017). It has also been reported that exposure to arsenic promotes the formation of reactive oxygen species (ROS) which can lead to the damage of oxidative DNA and chromosomal aberrations (Tam *et al*., 2020; Zhou *et al*., 2021). In our model, mercury exhibits slower accumulation kinetics. It has been reported that exposure to mercury can interfere the mitochondrial function, oxidative phosphorylation and also it can aid changes in genetic expression linked to apoptosis and cell proliferation (Wang *et al*., 2023). Some progenies of mercury also interact with thiol-containing enzymes which has been reported to hinder cellular redox status (Jomova *et al*., 2024; Rupa *et al*., 2023)

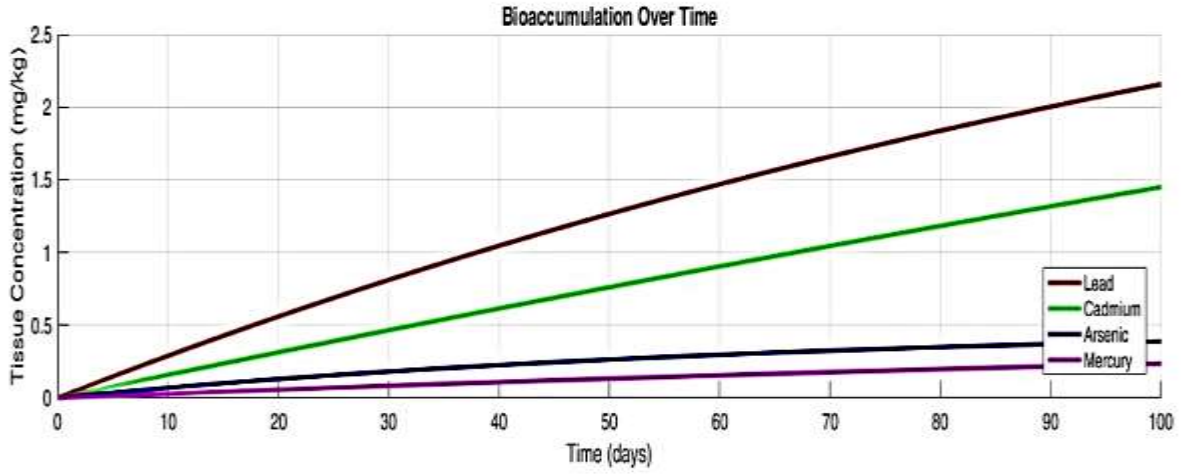


Figure 1: Bioaccumulation of heavy metals in human tissue over 100 days.

3.2 Dose-Response Analysis

Figure 2 presents the dose-response curve which describe the bio-risk that is connected to each of the carcinogenic metal. The Hill-type dose-response model used in this study reiterates that cancer risk increases non-linearly with tissue concentration. The dose-response curves revealed that Cadmium and Lead exhibited the steepest accumulation trends, indicating a rapid progression toward potentially hazardous concentration levels within the first 30 days of exposure, based on the simulated model parameters. This surge in cancer risk indicates that cadmium and lead is highly toxic and has strong biological impact which are known to cause cellular disruption leading to carcinogenesis (Parida & Patel, 2023). In contrast to Cadmium and Lead, Arsenic and Mercury exhibited a more gradual increase in predicted cancer risk, with model outputs below their maximum response levels even after 100 days of exposure. The slower dose-response of arsenic can be linked to its lower potency in carcinogenesis of tissue carcinogenesis despite its potential toxicity. This aligns with the study of Patwa *et al*., (2022) where it was reported that arsenic has a gradual increase impact on biological systems when compared with cadmium and lead.

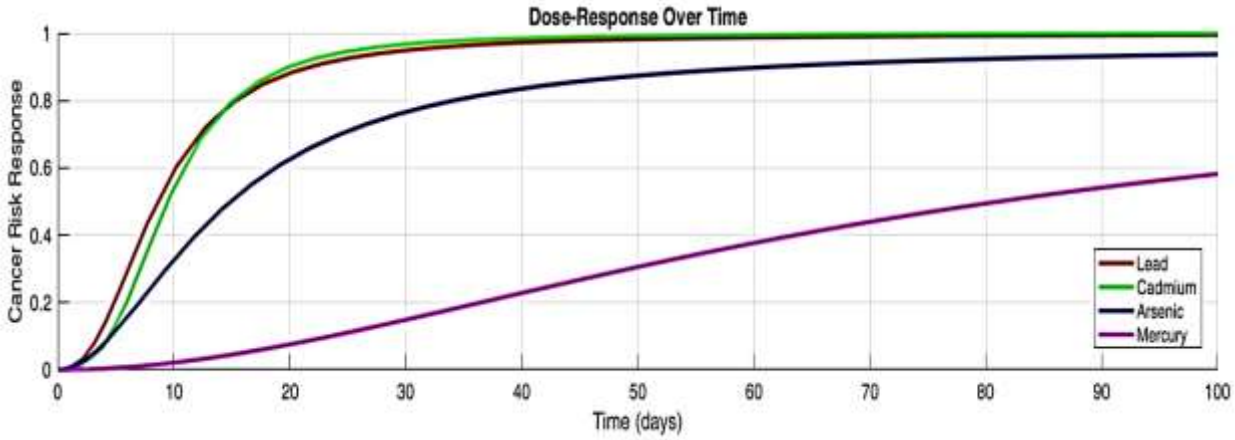


Figure 2: Dose response of heavy metals in human tissue over 100 days.

3.3 Bioaccumulation of Heavy Metals with Confidence Intervals

Figure 3 presents the bioaccumulation levels of selected heavy metals; lead (Pb), cadmium (Cd), arsenic (As), and mercury (Hg) in mg/kg with their respective 95% confidence intervals. The variability and reliability of the measured mean values for each metal was represented for visualization in the error bar. Of all the analyzed metals, cadmium (Cd) has the highest mean bioaccumulation level (~3.5 mg/kg) which align with the report of Peana *et al*., 2023. Followed closely by lead (Pb) with approximately 3.0 mg/kg. Arsenic (As) and mercury (Hg) showed

comparatively lower levels of bioaccumulation, with mean values around 2.3 mg/kg and 2.0 mg/kg respectively. This is on the same note with the report of Najem *et al*., 2024. Due to high accumulation of Cd and Pb, they may pose a greater toxicological risk in biological tissues (Charkiewicz *et al*., 2023). The inclusion of 95% confidence intervals boosts the statistical dependability of the results. The relatively short error bars means that the data are consistent and that the mean values are reliable approximates of the true bioaccumulation levels. Notably, the confidence intervals for Cd and Pb are slightly wider than those for As and Hg, which suggested a relatively higher variability in their uptake and retention. The differences in the bioaccumulation of the heavy metals may be attributed to varying chemical properties, metabolic interactions, and affinities for biological tissues among the metals.

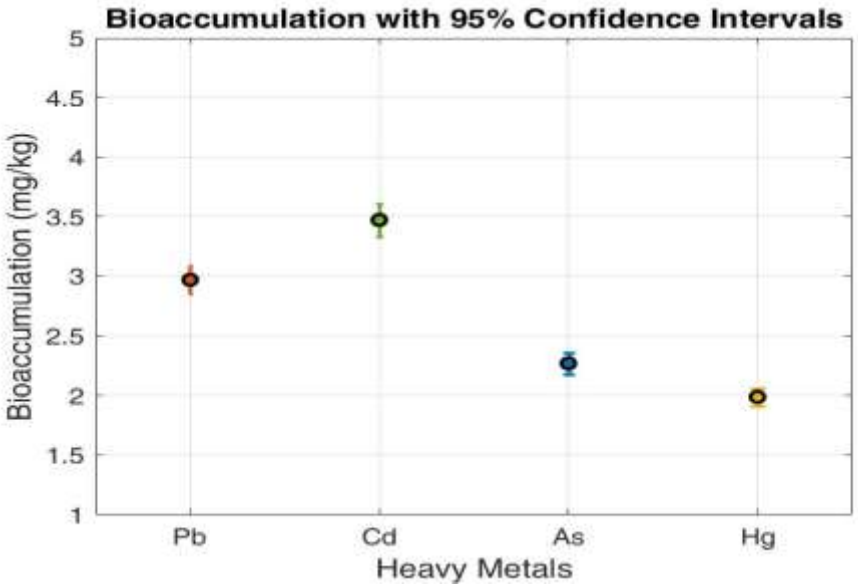


Figure 3: Bioaccumulation of Heavy Metals with 95% Confidence Intervals

4.0. Conclusion

This study utilizes a mathematical modeling framework for bioaccumulation simulation and associated health risks of carcinogenic heavy metals in cancerous tissues. By bridging first-order kinetics with Hill-type dose-response functions, the model offers a preliminary but valuable look into the possible dose-risk relationship with respect to time. While the model highlights the likelihood of long-term accumulation that may contribute to cancer progression, the lack of patient-specific clinical or histological data poses limitation on the generalization of the findings. In addition, the complex nature of human metabolic activities and environmental variability was not fully reflected due to constant exposure and simplified elimination pathways.

5.0 Recommendation

This work presents basis for future studies that aim to quantify bio-risk in biologically terms despite its limitation. Future works should incorporate stochastic variables such as exposure patterns, nonlinear kinetics, and feedback mechanisms like tissue saturation, protein-binding, and cellular excretion. To validate and contextualize this model, experimental and clinical data should be integrated with an interdisciplinary approach involving oncologists and toxicologists. In order to improve the model's translational relevance, it would be essential for the bio-risk threshold to be establish with clearer toxicological justification and comparison of simulation results with epidemiological cancer data. In all, this study adds to the evolving terrain of predictive environmental health modeling and offers an avenue for multidisciplinary approaches to assessment of environmental health to heavy metal exposure.

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