

Levels and Human Health Risk Assessment of Heavy Metals in Some Vegetables in Farmer's Field, Jos North, Plateau State Nigeria

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ABSTRACT: The objective of this paper was to evaluate levels and human health risk assessment of heavy metals in some vegetables in farmers' field, Jos North, Plateau State Nigeria; using X-ray fluorescence (XRF) spectrometry. The evaluation of the average daily intake for adults revealed that Ni in lettuce and cabbage exceeded the permissible levels (0.0094 mg/kg/day), Cr(0.0035mg/kg/day) and Cd(0.0012mg/kg/day) also exceeded safety limits in lettuce. For children, the average daily intake revealed that Pb exceeded permissible limits in celery, cauliflower, and onions, while Cd and Cr levels surpassed the permissible limits in all vegetables, whereas Fe and Zn remained below the DOR permissible limits. The hazard quotient analysis indicated that Cd in lettuce (2.4514) and Cr in lettuce (1.1629) posed significant non-carcinogenic risks for adults. Pb in onions, cauliflower, and celery, Cd and Cr in all vegetables—particularly lettuce—and Ni in lettuce, onions, spinach, cabbage, and celery all had hazard quotients exceeding 1, indicating significant health risks for children. The cancer risk analysis showed that both Pb and Cd posed potential risks for both adults and children, with the highest cancer risk observed for Cd in children consuming lettuce (0.0006683). The findings reveal that the daily intake of Pb, Cd, Cr, and Ni—especially in children—poses substantial health risks. Addressing these risks requires urgent implementation of regular monitoring, contamination control measures, and education on safe farming practices to protect vulnerable populations from potential long-term exposure.

DOI: https://dx.doi.org/10.4314/jasem.v28i11.7

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Cite this Article as: OIGANJI, E; ICHOR, J; UNIMKE, J. U; LENKA, R. Z. (2024). Levels and Human Health Risk Assessment of Heavy Metals in Some Vegetables in Farmer's Field, Jos North, Plateau State Nigeria. *J. Appl. Sci. Environ. Manage.* 28 (11) 3551-3557

Dates: Received: 18 September 2024; Revised: 20 October 2024; Accepted: 05 November 2024; Published: 15 November 2024

Keywords: heavy metals; permissible limit; hazard index; hazard quotient; vegetables

Heavy metals are naturally occurring elements with high atomic weight and density, often introduced into the environment through geological and anthropogenic activities. While some heavy metals are essential for biochemical cycles, others accumulate in the environment due to pollution from industrial, agricultural, and urban activities, these metals can be absorbed by plants, thus leading to contamination of the food chain (Ahmad *et al.*, 2019; Alsafran *et al.*, 2021; Prasadf *et al.*, 2021). Vegetables are an important part of the human diet as they are rich in fiber, minerals, vitamins, and antioxidants. Vegetables constitute important functional food components by contributing protein, vitamins, iron, calcium and other nutrients that have major health benefits (Arai, 2020). However, their cultivation in contaminated soils, especially in urban and industrial areas, poses significant health risks. Hence, research on accretion of heavy metal in vegetables is especially important to ensure food quality (Gupta *et al.*, 2019; Prasad *et al.*, 2021). Consuming food tainted with heavy metals can disrupt essential nutrients in the human body, leading to health issues (Arora et al., 2008). Lead, cadmium, nickel, and zinc are among the most found heavy metals in contaminated areas, such as commercial, mining, and highway regions (Gupta et al., 2021; Haque et al., 2021). Long-term exposure to these metals through food consumption can result in serious health issues like kidney, heart disease, developmental problems, and cancer (Anwar et al., 2016; Taylor et al., 2015). The persistence of these metals in the environment and their non-biodegradable nature makes them a growing concern for public health. Sources of heavy metal contamination in soils include fertilizers, pesticides, biosolids, wastewater, and industrial activities. Fertilizers, especially those containing phosphates, may inadvertently introduce heavy metals like cadmium (Cd) and lead (Pb) due to impurities (Jones and Jarvis, 2020). Pesticides, such as copper-based fungicides, have historically contributed metals like copper (Cu) and mercury (Hg) to the soil (McLaughlin et al., 2000). Biosolids, including livestock manures and sewage sludge, can introduce arsenic (As), zinc (Zn), and other metals through repeated applications (Basta et al., 2017). Long-term wastewater irrigation has also been linked to metal accumulation, while industrial activities, including mining and smelting, contribute to soil contamination with lead (Pb) and zinc (Zn), often posing ecological and health risks (Basta and Gradwohl, 2018). These sources contribute to the long-term buildup of toxic metals in agricultural land, further exacerbating food safety concerns (Jones and Jarvis, 2020; McLaughlin et al., 2000). Heavy metals like arsenic (As) and cadmium are particularly harmful, as exposure through food consumption has been linked to cancer and other health risks, including kidney and brain cancers (Liu et al., 2019; Wang et al., 2019). Noncarcinogenic risks, such as those measured by hazard quotients (HQ) and hazard indices (HI), emphasize the potential for heavy metals to impact health, with several studies confirming elevated HQ and HI values in contaminated vegetables (Kumar et al., 2019; Garcia et al., 2019).

In Jos North, Nigeria, where vegetable farming coexists with mining activities, understanding the extent of heavy metal contamination is critical for safeguarding human health. Consequently, the objective of this paper is to Levels and human health risk assessment of heavy metals in some vegetables in farmer's field, Jos North, Plateau State Nigeria.

MATERIALS AND METHOD

Study Area and sample collection: The field experiment was conducted during the 2022/2023

academic season at a site located behind the Faculty of Agriculture, University of Jos, Plateau State, Nigeria, within the Jos North Local Government Area. The region is situated between latitude 9°41' N and longitude 8°35' E, at an elevation of approximately 1,200 meters above sea level. It lies within the southern Guinea Savannah of Nigeria, characterized by a mean annual rainfall of 1,460 mm and a temperature range of 10°C to 32°C. The area covers about 291 square kilometers and has a population of approximately 492,300 people (Geography and Land Survey, 2013).

On January 25, 2024, mature vegetable samples, including onions, lettuce, cabbage, celery, broccoli, beetroot spinach, and cauliflower, were collected from farmers' fields. Samples were placed in sealed Ziplock bags to avoid contamination and transported to the Directorate of Central Laboratory, Federal University Wukari, Taraba State, for heavy metal analysis.

Sample Preparation: The vegetable samples were pretreated by washing thoroughly with tap water followed by deionized water to remove surface contaminants. The samples were then oven-dried at 105°C for 48 hours to remove moisture, weighed, and pulverized using an agate pestle and mortar. The powdered samples were sieved through a 0.5 mm mesh to ensure uniform particle size.

Sample Analysis: X-ray Fluorescence (XRF) analysis was used to quantify the concentrations of selected heavy metals (Pb, Cd, Cr, Fe, Zn, Cu and Ni) in the vegetable samples, following the protocols documented by Byers *et al.* (2018). The dried, powdered samples were placed in XRF cups and analysed using X-ray Fluorescence (XRF) spectrometer to determine the concentrations of selected heavy metals.

Health Risk Assessment: To evaluate potential health risks from the intake of heavy metals in vegetables, the following assessments were conducted: Average Daily Dose (ADD), Hazard Quotient (HQ), Hazard Index (HI), and Cancer Risk (CR).

Average Daily Dose (ADD) of Heavy Metals: The ADD represents the estimated daily intake of heavy metals based on average consumption rates, calculated as:

$$ADD = \frac{C \times IR \times EF \times ED}{BW \times AT}.$$
 (1)

Where: C: Heavy metal concentration in the vegetable (mg/kg); IR: Ingestion rate (kg/day); EF: Exposure frequency (days/year); ED: Exposure duration (years);

BW: Average body weight (kg); AT: Averaging time (days); for non-carcinogenic effects.

Hazard Quotient (HQ): The HQ assesses the noncarcinogenic risk of each metal in vegetable consumption, calculated as:

$$HQ = \frac{ADD}{RfD}.$$
 (2)

Where: RfD: Reference dose (mg/kg/day) for each metal, based on safety limits established by health guidelines.

An HQ value greater than 1 suggests potential for noncarcinogenic health effects.

Hazard Index (HI): The HI evaluates the cumulative non-carcinogenic risk from multiple metals by summing all individual HQs:

$$HI = \sum HQ. \quad . \tag{3}$$

An HI greater than 1 indicates a combined health risk from exposure to multiple metals.

Cancer Risk (CR) Evaluation: The CR estimates the lifetime cancer risk associated with heavy metal exposure and is calculated as:

$$CR = ADD \times CSF.$$
 (4)

Where: CSF: Cancer Slope Factor (mg/kg/day) for each carcinogenic metal.

Statistical Data Analysis: Data was analyzed using the Statistical Package for Social Sciences (SPSS) version 20, and the mean concentrations of heavy metals were compared against WHO (2019) international standards to assess whether the levels in the vegetables were within permissible limits and hazard index was used to check if it is detrimental to adults and children.

RESULTS AND DISCUSSION

The results from this study reveal varying levels of heavy metals in the sampled vegetables, with comparisons made against the permissible limits set by the World Health Organization (WHO, 2019). Lead (Pb) concentrations were highest in cauliflower, reaching 0.091 ± 0.001 mg/kg, which remains within the permissible limit of 0.1-0.3 mg/kg. Cadmium (Cd) levels peaked in lettuce, with 0.039 ± 0.002 mg/kg, nearing the upper limit of 0.05-0.2 mg/kg. Chromium (Cr) was most abundant in spinach, with a concentration of 0.088 ± 0.003 mg/kg, which is well

below the permissible limit of 1.3 mg/kg. The study also found that the highest iron (Fe) concentrations were recorded in spinach and celery, with values of 4.400±0.035 mg/kg and 4.300±0.015 mg/kg, respectively, both well below the allowable limit of 40 mg/kg. Zinc (Zn) was most concentrated in broccoli (0.400±0.006 mg/kg), while copper (Cu) levels were uniformly low across all vegetables and did not exceed the permissible range of 10-40 mg/kg. Lastly, nickel (Ni) concentrations were highest in lettuce and cabbage (both at 0.300±0.002 mg/kg), but still within safe limits, as the permissible level is 10 mg/kg. The adult evaluation of average daily doses of these heavy metals in various vegetables shown in Table 2 indicates that lead in cauliflower had the highest Daily Oral Reference (DOR) dose (0.0029 mg/kg), which remained within the permissible range of 0.0005-0.0035 mg/kg. Cadmium in lettuce had a DOR of 0.0012 mg/kg, which was close to the permissible limit of 0.0001-0.0005 mg/kg. Chromium in lettuce and celery exhibited high DOR values of 0.0035 mg/kg and 0.0030 mg/kg, respectively, but both were within the acceptable limit of 0.0035 mg/kg. Iron in celery had the highest DOR at 0.7000 mg/kg, but this is still far below the permissible threshold of 40 mg/kg. Zinc's DOR was highest in spinach (0.0126 mg/kg) and celery (0.3000 mg/kg), but these values did not approach the limit of 50 mg/kg. Copper levels across all vegetables remained uniformly low, with a DOR of 0.0031 mg/kg, well within safe consumption levels. Nickel had the highest DOR in lettuce and cabbage (0.0094 mg/kg), but this also fell within the permissible limit of 10 mg/kg. For children, the evaluation of average daily doses revealed that lead levels in cauliflower presented the highest risk, with a DOR of 0.0133 mg/kg, exceeding the permissible range of 0.0023-0.0038 mg/kg.

Cadmium levels in lettuce were also high, with a DOR of 0.0057 mg/kg, nearing the upper limit of 0.0005-0.0013 mg/kg. Chromium in lettuce had the highest DOR of 0.0163 mg/kg, which is at the permissible limit. The highest DOR of iron in celery (0.7000 mg/kg) and zinc in spinach (0.0587 mg/kg) were within the safe limit, as were copper values across all vegetables. Nickel concentrations in lettuce and cabbage had the highest DOR for children (0.0440 mg/kg), though this was still within permissible levels. The non-carcinogenic risk analysis, as reflected in the hazard quotient (HO) for adults, revealed that most vegetables did not pose immediate health risks from heavy metal consumption. Lead presented the highest HO in cauliflower (0.8171), but this remained below the critical threshold of 1. Cadmium in lettuce, however, had an HQ of 2.4514, surpassing the safety threshold and indicating potential health risks.

Metals	Lettuce	Onions	Broccoli	Cauli Flower	Beetroot	Spinach	Cabbage	Celery	Permissible limit (WHO, 2019)	
Pb	0.016±0.001a	0.026±0.001b	0.015±0.002a	0.091±0.001d	0.010±0.003a	0.015±0.001a	0.013±0.001a	0.039±0.002c	0.1-0.3	
Cd	0.039±0.002c	0.004±0.001a	0.006±0.002a	0.007±0.002a	0.006±0.002a	0.007±0.002a	0.007±0.001a	$0.009 \pm 0.002 b$	0.05-0.2	
Cr	0.111±0.002c	0.025±0.002a	$0.064 \pm 0.000 b$	0.094±0.001bc	0.033±0.001a	0.081±0.001bc	0.088±0.003bc	0.040±0.001a	1.3	
Fe	2.400±0.002c	1.200±0.001a	1.900±0.002ab	1.400±0.002a	$2.000 \pm 0.000 b$	4.400±0.035d	1.300±0.005a	4.300±0.015d	40	
Zn	0.200±0.003b	0.100±0.005a	0.300±0.001c	0.200±0.005b	0.100±0.050a	0.400±0.006d	0.200±0.002b	0.300±0.000c	50	
Cu	$0.100 \pm 0.000 b$	0.100±0.001b	$0.100 \pm 0.005 b$	0.100±0.002b	0.100±0.003b	0.100±0.001b	0.000±0.000a	$0.100 \pm 0.005 b$	10-40	
Ni	0.300±0.002c	$0.200 \pm 0.005 b$	0.100±0.000a	0.100±0.001a	0.100±0.002a	0.200±0.003b	0.300±0.006c	$0.200 \pm 0.001 b$	10	

 Table 1: Heavy metals/micro-minerals in vegetables (mg/kg)

Table 2: Adult and Children evaluation of average daily dose of heavy metals in vegetables

Metal	Study	Vegetable; (mg/kg/day)							Daily oral	
	Group	Lettuce	Onions	Broccoli	Cauli Flower	Beetroot	Spinach	Cabbage	Celery	reference dose
РЬ	Adult	0.0005	0.0008	0.0005	0.0029	0.0003	0.0005	0.0004	0.0012	0.0035
	Children	0.0023	0.0038	0.0022	0.00133	0.0015	0.0022	0.0019	0.0057	0.0035
Cd	Adult	0.0012	0.0001	0.0002	0.0002	0.0002	0.0002	0.0002	0.0003	0.0005
	Children	0.0057	0.0005	0.0008	0.0011	0.0008	0.0011	0.0011	0.0013	0.0005
Cr	Adult	0.0035	0.0008	0.0020	0.0030	0.0010	0.0025	0.0028	0.0013	0.0030
	Children	0.0163	0.0037	0.0094	0.0138	0.0048	0.0119	0.0129	0.0059	0.0030
Fe	Adult	0.0754	0.0377	0.0597	0.0440	0.0629	0.1383	0.0409	0.1351	0.7000
	Children	0.3520	0.1760	0.2787	0.2053	0.2933	0.6453	0.1907	0.6307	0.7000
Zn	Adult	0.0063	0.0031	0.0094	0.0063	0.0031	0.0126	0.0063	0.0094	0.3000
	Children	0.0293	0.0147	0.0440	0.0293	0.0147	0.0587	0.0293	0.0440	0.3000
Cu	Adult	0.0031	0.0031	0.0031	0.0031	0.0031	0.0031	0.0000	0.0031	0.0420
	Children	0.0147	0.0147	0.0147	0.0147	0.0147	0.0147	0.0000	0.0147	0.0420
Ni	Adult	0.0094	0.0063	0.0031	0.0031	0.0031	0.0063	0.0094	0.0063	0.0040
	Children	0.0440	0.0293	0.0147	0.0147	0.0147	0.0293	0.0440	0.0293	0.0040

Table 3: Non-carcinogenic risk analysis (Hazard quotient) consuming vegetables associated with heavy metals in adults and children

				Vegetables	5			
Vegetable	Study Group	Pb	Cd	Cr	Fe	Zn	Cu	Ni
Lettuce	Adult	0.1437	2.4514	1.1629	0.1078	0.0210	0.0748	0.4714
	Children	0.6705	11.4400	5.4267	0.5029	0.0978	0.3492	2.2000
Onions	Adult	0.2335	0.2326	0.2619	0.0539	0.0105	0.0748	0.3143
	Children	1.0895	1.0895	1.2222	0.2514	0.0489	0.3492	1.4667
Broccoli	Adult	0.1347	0.3457	0.6705	0.0853	0.0314	0.0748	0.1571
	Children	0.6286	1.6133	3.1289	0.3981	0.1467	0.3492	0.7333
Cauli Flower	Adult	0.8171	0.4589	0.9848	0.0629	0.0210	0.0748	0.1571
	Children	3.8133	2.1413	4.5956	0.2933	0.0978	0.3492	0.7333
Beetroot	Adult	0.0898	0.3457	0.3457	0.0898	0.0105	0.0748	0.1571
	Children	0.4190	1.6133	1.6133	0.4190	0.0489	0.3492	0.7333
Spinach	Adult	0.1347	0.4589	0.8486	0.1976	0.0419	0.0748	0.3143
	Children	0.6286	2.1413	3.9600	0.9219	0.1956	0.3492	1.4667
Cabbage	Adult	0.1167	0.4589	0.9219	0.0584	0.0210	0.0000	0.4714
	Children	0.5448	2.1413	4.3022	0.2724	0.0978	0.0000	2.2000
Celery	Adult	0.3502	0.5783	0.4190	0.1931	0.0314	0.0748	0.3143
	Children	1.6343	2.6987	1.9556	0.9010	0.1467	0.3492	1.4667

Chromium concentrations in spinach and cabbage posed some risk, with HQ values of 0.8486 and 0.9219, respectively, though these were still below 1. The HQ for iron, zinc, and copper in all vegetables remained low, indicating no significant risk. Nickel levels were also within safe limits, though lettuce and cabbage exhibited higher HQ values of 0.4714, which may warrant attention over extended periods of consumption. In children, the non-carcinogenic risk analysis indicated greater potential health risks due to the higher hazard quotients. Lead in cauliflower (HQ of 3.8133), cadmium in lettuce (HQ of 11.4400), and chromium in spinach (HQ of 3.9600) and cabbage (HO of 4.3022) all exceeded the threshold of 1, signaling potential health concerns. Nickel levels in lettuce and cabbage also presented some risk, with HQ values of 2.2000.

 Table 4: Hazard Index for adults and children consuming vegetables contaminated with heavy metals

Vegetable	Hazard	Hazard Index	
	Index Adult	Children	
Lettuce	4.742	22.130	
Onions	1.421	6.632	
Broccoli	1.570	7.325	
Cauli Flower	2.822	13.169	
Beetroot	1.222	5.703	
Spinach	2.436	11.367	
Cabbage	2.229	10.404	
Celery	2.333	10.890	

Table 4 presents the Hazard Index (HI) for adults and children consuming vegetables contaminated with various heavy metals. HI > 1 indicates potential health risks (US EPA, 2019). In adults, the Highest HI in Lettuce is 4.742, indicating potential health risks. Other vegetables have HI < 4.742, indicating relatively

lower risks while in children the Highest HI in Lettuce is 22.130, indicating significant potential health risks. Other vegetables have HI < 22.130, indicating relatively lower risks, but still notable. The Hazard Index for children is higher than for adults, indicating greater sensitivity and potential health risks for children.

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Evaluation of Cancer Risk in Adults: Table 5 below provides an evaluation of cancer risk associated with the consumption of vegetables contaminated with specific heavy metals (Pb, Cd, and Cr) for adults. According to US EPA (2019), the values represent the estimated cancer risk (ECR) per million people. Lead (Pb) has the Highest ECR in Cauli Flower (0.00002465) and Celery (0.0000102). Other vegetables have lower ECRs, indicating relatively lower cancer risks. Also, Cadmium (Cd) has Highest ECR in Lettuce (0.00000732), and other vegetables have lower ECRs, indicating relatively lower cancer risks. The result also showed that Chromium (Cr)in Lettuce (0.0001435), and other vegetables have lower ECRs. The result for children revealed that Lead had with highest ECR in Cauli Flower (0.0001131), indicating a potential high cancer risk. The other vegetables have lower ECRs but are still notable. Cadmium (Cd) has Highest ECR in Lettuce (0.0000348), indicating a potential high cancer risk. The other vegetables have lower ECRs, indicating relatively lower cancer risks. Chromium (Cr) also has the Highest ECR in Lettuce (0.0006683), indicating a potential high cancer risk. Other vegetables have lower ECRs, but still notable (IARC, 2019).

Vegetable	Study Group	Pb	Cd	Cr
Lettuce	Adult	0.00000425	0.00000732	0.0001435
	Children	0.0000196	0.0000348	0.0006683
Onions	Adult	0.0000068	0.00000061	0.0000328
	Children	0.0000323	0.0000031	0.0001517
Broccoli	Adult	0.00000425	0.00000122	0.000082
	Children	0.0000187	0.0000049	0.0003854
Cauli Flower	Adult	0.00002465	0.00000122	0.000123
	Children	0.0001131	0.0000067	0.0005658
Beetroot	Adult	0.00000255	0.00000122	0.000041
	Children	0.0000128	0.0000049	0.0001968
Spinach	Adult	0.00000425	0.00000122	0.0001025
	Children	0.0000187	0.0000067	0.0004879
Cabbage	Adult	0.0000034	0.00000122	0.0001148
	Children	0.0000162	0.0000067	0.0005289
Celery	Adult	0.0000102	0.00000183	0.0000533
-	Children	0.0000485	0.0000079	0.0002419

Table 5: Evaluation of cancer risk in adults and children

The findings from this study offer significant insights into the heavy metal contamination of commonly consumed vegetables in the study area, and its potential health risks to local populations. Although most of the vegetables studied in this research contained heavy metals within permissible limits established by the World Health Organization (WHO), several vegetables, notably lettuce, cauliflower, and spinach, exhibited elevated levels of toxic metals such as cadmium (Cd), lead (Pb), and chromium (Cr). The data gathered from this study generally support the notion that vegetables cultivated in the study area are safer compared to other locations in Nigeria. For instance, a study conducted in Port Harcourt by Tsor and Jombo (2021) found higher concentrations of Cr. Fe, Ni, Zn, Cu, Cd, and Pb in vegetables, surpassing WHO permissible limits. By contrast, the concentrations recorded in the current study were significantly lower, with cauliflower containing the highest Pb concentration of 0.091±0.001 mg/kg, far below the levels reported in Port Harcourt. This discrepancy can be attributed to variations in local environmental factors, industrial activities, and soil conditions. Moreover, the concentrations of Cd were found to be highest in lettuce (0.039±0.002 mg/l), consistent with findings by Moro et al. (2023) in Lagos and Badamasi et al. (2023) in Kano, where lettuce also contained the highest levels of Cd. The relatively lower levels of heavy metals in the current study, compared to other regions like Yobe (Abdulkadir et al., 2023), suggest that the environmental contamination in Jos North might be less severe, although it still raises concerns due to elevated levels of toxic metals in some vegetables.

The health risks associated with heavy metal exposure through vegetable consumption are particularly concerning for children, who are more vulnerable due to their lower body mass and developmental stage. The non-carcinogenic risk assessment conducted in this study revealed that many vegetables exceeded the safe reference doses for children, especially for metals like Pb and Cd. The Hazard Quotient (HQ) and Hazard Index (HI) further highlighted significant risks to children. Children's higher susceptibility to heavy metals, particularly Cd and Pb, has been well documented in literature. Studies by Enyoh and Isiuku (2020) and Manzoor et al. (2018) have emphasized the nephrotoxic nature of these metals, linking chronic exposure to renal impairment and developmental delays. Additionally, Pb exposure has been associated with cognitive impairments, behavioral issues, and cardiovascular diseases, particularly in children (UNICEF, 2020). The findings from this study, which show elevated levels of these metals in key vegetables, reinforce the need for immediate interventions to limit exposure. The carcinogenic risk analysis indicated generally low incremental lifetime cancer risks (ILCR) for both adults and children, although cauliflower showed consistently higher risks for multiple metals. While these risks are within acceptable limits, long-term exposure, even at low concentrations, should not be overlooked. Studies have shown a correlation between elevated heavy metal concentrations in cancer patients, indicating a potential link between chronic exposure and cancer risk (Feng et al., 2020; Coradduzza et al., 2024). In this study, copper (Cu) showed the lowest

concentration in cabbage (0.000±0.000 mg/l), aligning with the results from studies conducted in Jos South LGA by Kolawole *et al.* (2022), where copper levels in vegetables were also found to be below the WHO/FAO permissible limits. This balance between essential and toxic metals highlights the complex nature of heavy metal contamination and its diverse impact on human health.

Conclusion: This study highlights that although heavy metal concentrations in vegetables from Jos North, Nigeria, are generally within permissible limits, daily intake levels of Pb, Cd, and Cr pose potential health risks, particularly for children. These findings underscore the importance of regular monitoring and implementation of contamination control measures. It is recommended that local authorities and farmers adopt safer agricultural practices to minimize heavy metal accumulation in crops. Educational initiatives on safe farming practices could further help protect vulnerable populations, especially children, from long-term health risks associated with heavy metal exposure in the food supply.

Declaration of Conflict of Interest: The authors declare no conflict of interest.

Data Availability Statement: Data are available upon request from the first author or corresponding author or any of the other authors

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