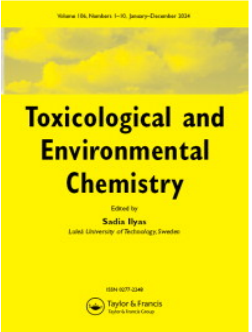

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Determination of metals in *Diplorhynchus condylocarpon* (Müll.Arg.) Pichon (Apocynaceae) using ICP OES and health risk assessment

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ABSTRACT
Diplorhynchus condylocarpon (Müll.Arg.) Pichon (Apocynaceae) is a popular medicinal plant in Zambian traditional health-care system. However, the health risks associated with its consumption have not been assessed. Therefore, the study analyzed the concentration of multiple metals in the plant samples using inductively coupled plasma optical emission spectroscopy (ICP-OES). Arsenic, lead, and selenium were not detected. Still, Cadmium levels in root (2.8 mg/kg), bark (2.6 mg/kg), and leaf (2.4 mg/kg), as well as chromium in root (42.6 mg/kg), bark (26.4 mg/kg), and leaf (25.6 mg/kg) were found to exceed the recommended limit of 0.3 mg/kg for Cd and 25.0 mg/kg for Cr set by WHO/FAO for medicinal plants. The estimated daily intake (EDI) of toxic metals in the plant was lower than the acceptable daily intake values, except for aluminum. The calculated health risk shows that the consumption of D. condylocarpon grown in the Copperbelt region of Zambia involves exposure to metals such as Al, Cd, Cr and Ni with a potential risk to human health if the plant is consumed in excess. This report provides a comprehensive analysis of the metals found in D. condylocarpon, commonly consumed in the traditional healthcare system in the mining region of Zambia.

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Introduction

Throughout history, medicinal plants and herbs have played a vital role in traditional medicine, providing immense benefits to many communities and their overall health (Qadir and Raja 2021; Chibuye et al. 2023a).

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The ability of medicinal plants to heal is linked to their content of biologically active metabolites with diverse structures and therapeutic properties such as alkaloids, tannins, oils, and vitamins (Sun and Shahrajabian 2023). Moreover, there is a growing interest in the chemical composition of pharmacologically active compounds, due to ongoing progress in the areas of nutrition, biochemical analysis, and mineral investigation (Sheikha 2022). Raw plant materials are obtained from sources that are impacted by the natural biogeochemical environment. Plants are at high risk of contamination by pesticides, harmful microorganisms, toxic chemicals, and heavy metals during their cultivation and processing. Medicinal plants and herbs have a significant impact on transferring small amounts of metals from the soil to people (Sarma et al. 2011). The quantity of metals in plants varies and is affected by the chemical characteristics of the soil, as well as the plant's ability to accumulate specific metals selectively. The way metals are bound to soil components affects their availability. Plants can effortlessly absorb metals through their root system from various sources such as rainwater, air pollutants, plant protection chemicals, and leaf-absorbed fertilizers (Eichert and Fernández 2023). Therefore, it is essential to utilize comprehensive methods when conducting studies on medicinal plants. Due to the importance of metals present in medicinal plants, several research studies have been carried out to determine the concentrations of metals in plants using graphite furnace atomic absorption spectrometry (GF-AAS) and flame atomic absorption spectrometry (F-AAS) (Ite, Udousoro, and Ibok 2014; Ite et al. 2016; Coufalík et al. 2020). In addition, inductively coupled plasma optical emission spectrometry (ICP-OES), inductively coupled plasma mass spectrometry (ICP-MS), or X-ray fluorescence spectrometry (XRF) have been employed to determine the concentration of metals in plant samples (Ali, Ola, and Mazahar 2019; Victório et al. 2020; Brahimi et al. 2021; Česynaitė, Praspaliauskas, and Sujetovienė 2023). These techniques offer exceptional sensitivity, versatility, the ability to analyze multiple metals, ruggedness, and fast analytical speed.

While X-ray fluorescence (XRF) is indeed a convenient method for elemental analysis, this study opted for inductively coupled plasma optical emission spectrometry (ICP-OES) due to its higher sensitivity and precision, particularly for detecting trace elements, accurately measure multiple metals, has a wide range of linear measurements, minimal interference from spectra and chemicals, very low detection limits, and quick and simple data management and reporting (Gao et al. 2017; Česynaitė, Praspaliauskas, and Sujetovienė 2023; Bitwell et al. 2024).

In the current study, metal concentrations found in the dried plant samples of *D. condylocarpon* were analyzed for the first time, and compared with the FAO and WHO-established permissible limits for metal concentrations in medicinal plants. Additionally, the levels of metals found in these dried plant samples were compared to the daily recommended maximum intake as set by the World Health Organization (WHO), Food and Agriculture Organization (FAO), and the United States Pharmacopoeia Convention (USP). The careful literature search shows that there are no published scientific studies evaluating the risk that certain metals in *D. condylocarpon* pose to human health. The health risks associated with aluminum (Al), arsenic (As), cadmium (Cd), chromium (Cr), lead (Pb), and tin (Sn) were evaluated by analyzing the estimated daily intake (EDI) the hazard quotient (HQ), and the carcinogenic risk (Cr).

It may suffice to add that plants that grow in mining regions, such as the Copperbelt province of Zambia, may possess specific bioactive metabolites and metals that help them withstand the pollution caused by mining activities and other factors commonly found in such areas. Therefore, it is possible to consider that mining activities can affect the chemical composition of the plant being studied. In addition, plants that thrive in contaminated surroundings might contain elevated levels of specific metals, such as copper. Certain metals may contribute to the distinctive therapeutic characteristics observed in medicinal plants used by traditional healers in mining towns to treat different illnesses (Brahimi et al. 2021; Farzaneh and Carvalho 2015). Furthermore, by determining macro and microelements, the nutritional significance and toxicity of medicinal plants can be assessed. Essential microelement levels, such as Cu, Fe, Mn, Se, and Zn, are required for a living organism to function properly. However, high metal concentrations can harm the body (Ghouma et al. 2022; Fu and Xi 2020). It is necessary to identify and measure the levels of toxic metals such as arsenic (As), cadmium (Cd), and lead (Pb) due to their harmful properties and importance to metabolism.

The objective of this study was to determine the concentration of selected metals; and to assess the health risk associated with the consumption of the popularly used medicinal plant known as *D. condylocarpon*, which is used in Zambian traditional healing practices to treat diseases caused by oxidative stress (Chibuye et al. 2023b). In addition, *D. condylocarpon* is used to treat conditions such as lack of appetite, abdominal pain, termination of pregnancies, increase sexual arousal, elimination of intestinal parasites, and mitigating the effects of snakebites (Moshi and Mbwambo 2002; Lautenschläger et al. 2018; Chibuye et al. 2023b). Further, the plant is used to treat a number of other medical conditions, including bilharzia, blackwater fever, common fever, malaria, diabetes, gonorrhea, syphilis, venereal diseases, nausea, uterine sterilization, and respiratory issues such as pneumonia, cough, tuberculosis, hydrocele, and inflammation of the testicles (Bruschi et al. 2011; Amuri et al. 2018; Chibuye et al. 2023b).

While ICP-OES is a well-established technique for metal analysis, the novelty of this study lies in its application to *D. condylocarpon* within a copper mining region, where the study conducted a comprehensive assessment of metal accumulation and its implications for medicinal use. This research not only establishes baseline metal concentrations in this plant species but also evaluates the plant's potential as a safe resource despite its proximity to contamination sources.

Materials and methods

Reagents

The reagents used for the experiments included high-quality 65% HNO_3 (Merck, RSA), 50% hydrogen peroxide (H_2O_2), and ultra-pure water from a purification system, Milli-Q, Millipore (Merck Chemicals (PTY) Ltd. in Johannesburg, South Africa). A standard solution containing all the metals that were analyzed was utilized for the calibration of ICP-OES (Spectro Genesis, Germany) ranging from 0.1 mg/L to 10 mg/L. The stock solution with a concentration of 1000 mg/L was dissolved in 5% HNO_3 to prepare a range of calibration standards. ICP-OES utilizes ultrahigh purity argon gas.

Collection, drying, and authentication of *D. condylocarpon*

The plant materials were collected from the forest in Kalulushi, a mining town in Zambia's Copperbelt Province. Fresh leaf, bark, and root samples were collected and then allowed to air dry in the shade. At the Kitwe District Herbarium of the Forest Department of the Ministry of Green Economy and Environment of the Republic of Zambia, the plant was recognized and confirmed as *D. condylocarpon* as reported by Chibuye et al (2023b). For analysis, three samples of each part of the plant were prepared.

Metal extraction by microwave digestion

The extraction and analysis of metals took place at the Environmental Analytical Chemistry Laboratory in the School of Chemistry at the University of Witwatersrand, in South Africa. Microwave digestion was used for metal extraction using a multiwave Go digester (Anton Paar, Switzerland) according to the method of Thabit, Elgeddawy, and Shokr Abdelsalam (2020) with modifications (Thabit, Elgeddawy, and Shokr Abdelsalam 2020). In brief, the ground powdered medicinal plant sample was placed through a 25 micron sieve. Then 0.25 g of plant samples were weighed directly in poly reaction vessels (PTFE – TFM) (20 mL in capacity). Then, 9 mL of concentrated HNO_3 and 3 mL of H_2O_2 were added to each reaction vessel. The extraction vessels were kept for 5 min before being placed on the rotor. The digestion temperature was increased from 40 °C to 180 °C in 10 min and maintained for 30 min. After cooling, the resulting clear digests were filtered using 0.22 µm simple pure syringe filters and diluted with distilled deionized water up to 50 mL in 50 mL Falcon tubes. Blanks and spikes were prepared in the same manner as the samples. For spiked samples, three replicate acid digests were also performed.

Quality control and assurance, limits of detection (LOD) and limits of quantification (LOQ)

To guarantee the reliability and quality of the results, appropriate precautions were taken in the cleaning and handling of glass equipment. Analytical grade reagents together with distilled, high-purity deionized water was utilized for diluting and rinsing purposes throughout the research. Blank analyses were utilized to adjust the instrument's readings. Calibration standards were made from the stock solution of each metal to prepare the instrument for accurate measurements. The analysis was carried out repeatedly to ensure its precision and accuracy.

The method was validated by performance parameters, that is, limits of detection (LOD), quantification (LOQ), and recoveries (%). Essential macro-, microelements, and toxic metals were determined in the medicinal plant. Limits of detection (LOD) and limit of quantification (LOQ) were calculated using Equations (1) and (2) as follows:

$$\mathrm{LOD} = \frac{3.3\,X\,\sigma}{S} \tag{1}$$

and

$$\mathrm{LOQ} = \frac{10\,X\,\sigma}{S}; \tag{2}$$

where σ = standard error of the results obtained and S = slope of the standard calibration curve.

Furthermore, the percent recovery was calculated using Equation (3):

$$\mathrm{Recovery}\,(\%) = \left(\frac{S_{spiked\,X\,R_{Real}}}{S_{spiked}}\right)\mathrm{X}100 \tag{3}$$

where S_{spiked}= calculated metal concentration in the spiked sample (mg/kg) and R_{Real}= metal concentration in the real sample solution (mg/kg).

To ensure quality control, a continuous calibration verification (CCV) analysis was performed for every run. The correlation coefficient values (R^2) for CCV were determined by testing different concentrations (0, 0.1, 0.5, 1, 2, 5, and 10 mg/L) of a standard mixture containing all the measured metals after each set of samples.

The descriptive analysis of the data was performed using the Origin (2018) software. LOD, LOQ, and percentage (%) recoveries were also calculated.

Inductively coupled plasma optical emission spectroscopy (ICP-OES) analysis

The ICP-OES instrument (Spectro, Kleve, Germany) was used to detect and quantify a total of 21 metals, namely Al, As, Ca, Cd, Co, Cr, Cu, Fe, K, Mg, Mn, Mo, Na, Ni, P, Pb, S, Se, Si, Sn, and Zn. The identification and quantification method was based on the method developed by Nuapia, Chimuka, and Cukrowska (2018), with specific modifications tailored for this study (Nuapia, Chimuka, and Cukrowska 2018). Before calibration, the twenty-one (21) individual metals were measured using external standard solutions with a minimum concentration of 1000 mg/L. Instrumental parameters and operating conditions were meticulously adjusted for precision and sensitivity. Metals were analyzed using specific conditions, which included a plasma power of 1400 W, a nebulizer pressure of 2.81 bar, a nebulizer flow of 1.0 mL/min, a pump speed of 2 rpm, a coolant flow of 14 mL/min, a rinse time of 10 s, an auxiliary flow of 1.5 mL/min, a replicate read time of 10 s, an instrument stabilization time of 20 seconds, and a sample uptake delay of 30 s. The experiments were carried out in triplicates and the results were presented as mean ± standard deviation (SD), maximum, and minimum concentrations.

Assessment of human health risk

Estimated daily intake: The average estimated daily intake (EDI) of metals depends on both the concentration of metals in plants and the amount of plant consumption. The EDI for Human subjects for macro-, micro-elements, and toxic metals was calculated using Equation (4) recommended by the US EPA (US Environmental Protection Agency 2011; Bitwell et al. 2024).

$$EDI = \frac{IR}{BW} x\left[X\right] \tag{4}$$

EDI refers to the estimated average daily intake or dose that is consumed through oral ingestion. X represents the concentration of a macro, microelement, or toxic metal in the leaf, bark, or root of the plant. IR is the daily rate at which adults in Zambia consume vegetables, which is 0.06 kg/day, and the average body weight of an adult in Zambia is generally around 70 kg (Bitwell et al. 2024).

The target hazard quotient (THQ): The THQ is a measure of the relationship between the amount of exposure to a potentially hazardous metal and the reference dose, and it estimates the risk of non-cancerous health effects caused by exposure (Tiwari et al. 2020). It was calculated using Equation (5):

$$THQ = \frac{EDI}{RfD} \tag{5}$$

Here, RfD represents the oral reference dose in mg/kg per day, determined based on the safe maximum level for oral ingestion of each metal by an adult. The specific RfDs for various metals are as follows: copper (0.04), aluminum (1.0), manganese (0.14), iron (0.7), zinc (0.3), cadmium (0.001), lead (0.0035), chromium (1.5), arsenic (0.014), nickel (0.91), tungsten (0.0008), tin (0.6), cobalt (0.0003), molybdenum (0.005), and selenium (0.005 mg/kg/day) (Mohammadi et al. 2019; USEPA 2015; Tiwari et al. 2020). For each metal, a Target Hazard Quotient (THQ) less than 1 indicates a low risk of adverse effects resulting from exposure. At the same time, a THQ greater than 1 suggests potential health risks associated with exposure to that specific metal.

The hazard index (HI): The hazard index can be calculated as the total of the target hazard quotients, which is explained in Equation (6):

$$\mathrm{HI} = \sum \mathrm{THQ} = \mathrm{THQ\ Cd} + \mathrm{THQ\ Cr} + \mathrm{THQ\ Sn} + \mathrm{THQ\ Al} \tag{6}$$

Where ΣTHQ is the sum of the target hazards of metals. THQ Cd, THQ Cr, THQ Sn, and THQ Al are the target hazard quotients for cadmium, chromium, tin, and aluminum, respectively. The assumption suggests that the severity of negative effects is directly influenced by the total amount of exposure to various metals. If the total hazard quotients add up to less than 1, it indicates that the population is exposed to some level of risk. If the sum of THQ is equal to or greater than 1, it means that the population is facing health problems (Mohammadi et al. 2019).

Carcinogenic risk (CR)

Cancer risk (CR) is a calculation of the likelihood that a person may develop cancer as a result of being exposed to a potential carcinogen throughout their lifetime. The calculation of CR was done using Equation (7) of the USEPA Region III Risk-Based Concentration Table (USEPA 2015; USEPA 2021).

$$CR = EDI \, x \, CPSo \quad (7)$$

The value of CPSo, which represents the oral slope factor for a specific carcinogen in milligrams per kilogram per day, is 6.1, 0.84, 8.5, 1.5, 0.2, and 41 specifically for cadmium, nickel, lead, arsenic, aluminum, and chromium, respectively (USEPA 2021; USEPA 2015; Mohammadi et al. 2019; Lučić et al. 2023). Values greater than 10^{-4} suggest an increased likelihood of CR. If there are several metals that can cause cancer, the combined risk of cancer can be calculated by adding up the individual risks (assuming that their effects are cumulative). Acceptable risks fall within the range of $1.0x10^{-6}$ to $1.0x10^{-4}$ (Taghizadeh et al. 2020; Lučić et al. 2023; Bitwell et al. 2024).

Results and discussion

Quality assurance results

All R^2 values obtained were above 0.999. A test sample was spiked with a combination of standard solutions containing metals to be analyzed at different concentrations (0.1, 0.5, and 5 mg/L), and the percentage of recovered metals was determined. The choice of metals was determined by their importance in the maintenance of human health or by considering their toxicity and associated health hazards. In simple terms, a good number of metals were quantified to obtain a comprehensive understanding of the composition and accumulation of metals in the medicinal plant chosen found in the copper mining region of Zambia. A stock solution containing multiple metals obtained from Merck, RSA, was utilized to prepare standard solutions. Three samples were analyzed in triplicate. LOD, LOQ, and recovery values were determined to analyze 21 metals (Table 1).

The calculations for the LOD, LOQ, and the recovery show that the method was valid (Table 1). For example, the minimum amount of each particular metal that can be accurately measured (LOQ) is higher than the minimum amount needed to simply detect its presence (LOD) (Paramasivam, Karthik, and Muralitharan 2022). Moreover, recovery rates exhibit a commendable achievement in extraction of metals, while complying with the designated efficiency criteria. The percentage recovery values were measured at varying concentration levels, specifically low, medium, and high. Recovery percentages ranged from a highest value of 107.62% for arsenic to a lowest value of 6.56% for silicon. Several metals exhibited favorable results, exceeding recovery rates of 95%. The results

Table 1. Instrumental LOD, LOQ, and recovery.

#	Metal	LOD (mg/L)	LOQ (mg/L)	R^2	Spike recovery (%)
1	Al	0.18	0.53	1.000	101.94
2	As	0.30	0.92	1.000	107.62
3	Ca	0.14	0.44	1.000	99.71
4	Cd	0.06	0.19	1.000	98.79
5	Co	0.16	0.47	1.000	97.37
6	Cr	0.08	0.23	1.000	87.86
7	Cu	0.43	1.31	0.999	87.99
8	Fe	0.14	0.42	1.000	94.24
9	K	0.99	3.00	0.999	65.97
10	Mg	0.07	0.22	1.000	105.61
11	Mn	0.06	0.19	1.000	44.82
12	Mo	0.04	0.12	1.000	21.43
13	Na	1.24	3.75	1.000	18.22
14	Ni	0.21	0.63	1.000	90.74
15	P	0.36	1.10	0.999	13.10
16	Pb	0.19	0.58	1.000	101.62
17	S	0.12	0.36	1.000	0.94
18	Se	0.14	0.43	1.000	106.74
19	Si	0.20	0.62	1.000	6.56
20	Sn	0.16	0.49	1.000	10.19
21	Zn	0.12	0.35	1.000	96.79

of the recovery values, which ranged from 95% to 107%, demonstrate that there are no signs of systematic errors caused by the operational impacts of the analyte that was added. This indicates that no losses were caused during the process. The acceptable percentage of metal recoveries from plants varies depending on the type of metal and the plant species (Garbisu and Alkorta 2001). Therefore, the acceptable percentage of metal recoveries from plants varies depending on the type of metal and the plant species. However, there are no universally accepted standards for acceptable percentage recoveries of metals in plants.

The concentration of metals in the current study are presented and discussed in three classes—toxic metals, micro elements, and macroelements (Chen et al. 2022; Ferreira et al. 2023). This classification is important as it helps to contextualize the varying effects metals have on human health and aquatic ecosystems based on their concentration and biological role. Firstly, toxic metals, such as lead and arsenic, are known to have significant adverse effects on health and the environment even at low concentrations due to their persistence and bioaccumulation in biological systems (Chen et al. 2022; Lučić et al. 2023). In contrast, microelements such as zinc and copper are essential for various biological functions but can become toxic at elevated levels (Nieder et al., 2018; Ferreira et al. 2023). Macro elements, such as magnesium and calcium, are necessary for physiological processes but can also pose risks if present in excessive amounts (Fiorentini et al. 2021; Ferreira et al. 2023). This differentiation allows for a better understanding of the specific risks associated with different metals, which is crucial for effective management and remediation strategies in both public health and environmental contexts.

Toxic metals

To determine the safe use of *D. condylocarpon* as a medicine, the following toxic metals were analyzed: cadmium (Cd), arsenic (As), lead (Pb), tin (Sn), and aluminum (Al) (Table 2).

The results indicate significant variations in the concentration levels of toxic metals in the plant investigated in this study (Table 2). The acceptable concentration limits for Cd, As, and Pb in medicinal plants and herbs, as established by the World Health Organization (WHO) and the Food and Agriculture Organization (FAO), are 0.3, 10.0, and 10.0 mg/kg, respectively (Dghaim et al. 2015; Nkansah et al. 2016). As and Pb were not detected in all plant samples. Similar studies in medicinal plants did not detect the presence of these metals (Soomro et al. 2021; X. Wu, Gao, et al. 2022). A noteworthy observation from the distribution of the measurements is their proximity to one another. As an illustration, the highest and lowest amounts of Cd found in the root are 3.0 and 2.8 mg/kg, respectively, which gives an average value of 2.8 ± 0.2 mg/kg. The leaf's Sn measurements show a standard deviation of zero, indicating that the measurements taken in this study are highly accurate and can be reproduced consistently.

The concentration of cadmium (Cd) in *D. condylocarpon* varied from a low value of 2.4 ± 0.2 in the leaf, 2.6 ± 0.2 in the bark, to 2.8 ± 0.2 mg/kg in the root. There were higher and therefore unsafe levels of cadmium in all plant samples exceeding 0.3 $mg \cdot kg^{-1,}$ the permissible limit (PL) set by FAO/WHO for medicinal plants and herbs (Dghaim et al. 2015). Previous studies have also reported comparable findings of elevated cadmium levels in medicinal plants and herbs of Ghana, the United Arab Emirates, and Egypt (Dghaim et al. 2015; X. Wu, Gao, et al. 2022). The relatively high concentration of cadmium in the plant poses a threat to human health. For example, the kidney is the target organ that is most severely affected by higher levels of cadmium in the exposed community (Alengebawy et al. 2021). Excretion of cadmium is infinitesimally slow,

Table 2. Mean, maximum and minimum concentrations of toxic metals (mg/kg), *n* = 3.

Sample	[ ]	Cd	As	Pb	Sn	Al
Root	Mean	2.8 ± 0.2	Nd	Nd	53.2 ± 0.8	1623.6 ± 18.8
	Max	3.0			54.2	1732.6
	Min	2.8			52.4	1515.2
Bark	Mean	2.6 ± 0.2	Nd	Nd	110.2 ± 1.2	1323.4 ± 10.4
	Max	2.6			111.6	1334.6
	Min	2.2			109.0	1314.0
Leaf	Mean	2.4 ± 0.2	Nd	Nd	63.2 ± 0.0	1044.6 ± 3.0
	Max	2.6			63.2	1046.8
	Min	2.4			62.8	1041.2
WHO/FAO Limit		0.3	10.0	10.0		

[ ] = concentration, max = maximum, min = minimum.

and thus the metal accumulates in the human kidney over time, causing irreversible damage to the kidney tract. Additionally, the high cadmium content is carcinogenic and has lethal effects on the immune system, vascular system, and liver (Alengebawy et al. 2021).

The aluminum content in the samples of *D. condylocarpon* plants varied from 1044.6 ± 3.0 (leaf), 1323.4 ± 10.4 (bark) to 1623.6 ± 18.8 (root) mg/kg (Table 2). The values for the aluminum concentration seem to be high. However, a study conducted in Sanandaj, Kurdistan, Iran, analyzed the levels of heavy metals in eight different medicinal herbs and herbal distillates available on the market. The research discovered that the levels of Al concentration in the herbs analyzed were 3064 mg/kg in Borago officinalis and 2839 mg/kg in Viola odorata (Kohzadi et al. 2019). These findings were much higher compared to the levels of aluminum in the medicinal plant determined in the present study. Although there is no acceptable WHO/FAO guideline for the concentration of aluminum in medicinal plants, it is present in the sample. However, the metal builds up in the human brain and, to a lesser degree, in the bones. As a result, it is essential to constantly monitor the levels of aluminum in medicinal plants, as consuming these remedies over a prolonged period may cause toxicity (Balasubramanyam et al. 2009).

In general, plants are highly effective at accumulating toxic metals. Phytoremediation is a common application for this particular property (Muthusaravanan et al. 2018; Babangida et al. 2021). However, the accumulation of toxic metals in plants can pose a risk if they are used as traditional remedies in healthcare or consumed as part of a regular diet.

Macro- and microelements

In this study, metals considered essential to normal biological functions in humans were analyzed for their concentration in plant samples. These were sodium (Na), magnesium (Mg), phosphorus (P), potassium (K), sulfur (S), calcium (Ca), chromium (Cr), manganese (Mn), iron (Fe), cobalt (Co), nickel (Ni), copper (Cu), zinc (Zn), molybdenum (Mo), selenium (Se), and silicon (Si). Tables 3 and 4 present mean, maximum, and minimum concentrations of macroelements and microelements, respectively, present in *D. condylocarpon* leaf, bark, and root samples.

According to the results, macro elements (Na, Mg, P, K, S, and Ca) were observed to accumulate differently in the root, bark and leaf parts of the medicinal plant (Table 3). The sodium content varied between 1793.0 ± 25.8 in the leaf and 1562.2 ± 19.4 mg/kg in the root sample. For potassium, the content ranged from 19058.8 ± 266.4 in the leaf to 4320.4 ± 64 mg/kg in the root. There are no upper recommended

Table 3. Mean, maximum and minimum concentrations of essential macro elements (mg/kg), *n* = 3.

Sample	[ ]	Na	Mg	P	K	S	Ca
Root	Mean	1562.2 ± 19.4	1836.8 ± 2.6	1519.6 ± 21.6	4320.4 ± 64	1216.4 ± 10.2	13338.6 ± 129.6
	Max	1583.2	1839.6	1498.4	4374.6	1227.2	13479.4
	Min	1545.2	1834.6	1518.8	4249.8	1206.6	13224.6
Stem bak	Mean	1507.2 ± 13.0	2461.8 ± 51.2	1550.2 ± 19.4	17105.6 ± 122.2	1467.8 ± 3.4	9314.8 ± 75.2
	Max	1522.0	2515.4	1561.8	17246.6	1470.2	9381.2
	Min	1497.8	2413.2	1527.8	17033.8	1464.0	9233.2
Leaf	Mean	1793.0 ± 25.8	3137.6 ± 26.6	2654.8 ± 12.4	19058.8 ± 266.4	3057.0 ± 12.8	7637.2 ± 49.6
	Max	1811.0	3258.2	2666.8	19295.4	3070.8	7672.8
	Min	1763.6	3207.4	2642.0	18770.4	3045.4	7580.4

[ ] = concentration, max = maximum, min = minimum.

tolerable levels set for sodium and potassium concentrations in medicinal plants. The sodium intake should always be checked as elevated sodium intake leads to a host of health complications, especially cardiovascular disease (Chakraborty et al. 2019). However, for potassium, in healthy individuals, excess intake is promptly excreted through the kidneys. Thus, potassium concentration in medicinal plants and herbs is not likely to cause adverse effects (Werdemberg dos Santos et al. 2022).

Furthermore, Table 3 shows that the calcium levels found in the three samples ranged from 13338.6 ± 129.6 in the root to 7637.2 ± 49.6 mg/kg in the leaf. The levels of magnesium concentration range from 1836.8 ± 2.6 to 3137.6 ± 26.6 mg/kg in the root and leaf, respectively. The importance of macroelements in medicinal plants for human health cannot be understated. Calcium is necessary for the development of healthy bones and teeth and plays a role in various bodily functions, such as widening and narrowing blood vessels, transmitting nerve signals, enabling muscle movement, promoting hormone release, and facilitating communication within cells (Fikri 2023). In contrast, magnesium is found in more than 300 enzymatic systems and plays a role in regulating different metabolic processes such as blood pressure, blood sugar regulation, protein formation, and muscle and nerve function (Wu, Gao, et al. 2022). At present, there are no WHO/FAO suggested acceptable levels of calcium and magnesium in medicinal plants.

There is a wide variability of the concentration of essential microelements found in *D. condylocarpon* (Table 4). The World Health Organization (WHO) and the Food and Agriculture Organization (FAO) suggest that acceptable levels of Cr, Mn, Fe, Co, Ni, Cu and Zn in medicinal plants and herbs should be within the range of 25.0, 200.0, 425.5, 5.0, 67.9, 150.0, and 100.0 mg/kg, respectively (Bitwell et al. 2024; Kntapo, Said, and Mosunmola 2019; Zhuang et al. 2014). Some metals such as Zinc, Copper and nickel fell within tolerable limits, while others such as chromium, iron and cobalt fell out of the tolerable range as

Table 4. Mean, maximum, and minimum concentrations of essential microelements (mg/kg), $n = 3$.

Sample	[ ]	Cr	Mn	Fe	Co	Ni	Cu	Zn	Mo	Se	Si
Root	Mean	42.6 ± 0.60	174.4 ± 1.6	5099.0 ± 41.4	11.2 ± 0.0	30.2 ± 0.4	68.2 ± 1.0	55.8 ± 0.0	Nd	Nd	1844.2 ± 14.6
	Max	43.2	175.4	5138.0	11.2	30.6	68.8	55.8			1858
	Min	41.8	172.6	5055.6	11.0	29.6	67.2	55.8			1829
Bark	Mean	26.4 ± 1.4	305.4 ± 1.8	1061.4 ± 12.0	5.4 ± 0.4	22.0 ± 0.4	32.8 ± 0.6	88.8 ± 1.0	2.2 ± 0.2	Nd	898.4 ± 6.4
	Max	28.0	307.2	1070.2	6	22.2	33.2	89.4	2.4		903.6
	Min	25.4	303.4	1047.6	5	21.4	32.2	87.4	2.0		891.2
Leaf	Mean	25.6 ± 1.2	2289.4 ± 18.2	664.6 ± 1.2	6.8 ± 0.6	21.6 ± 0.6	63.6 ± 0.4	51.4 ± 0.0	3.2 ± 0.4	Nd	846.6 ± 2.4
	Max	26.6	2302.2	666.0	7.4	22.4	63.8	51.6	3.6		849.0
	Min	24.4	2268.6	663.6	6.2	21.2	63.2	51.4	3.0		844.4
WHO/FAO tolerable Limit		25.0	200.0	425.5	5.0	67.9	150.0	100.0			

[ ] = concentration, max = maximum, min = minimum.

recommended by WHO/FAO, while selenium was not detected and molybdenum was only present in leaf and bark.

The highest and lowest manganese content was quantified in *D. condylocarpon* leaf (2289.4 ± 18.2 mg/kg) and root (174.4 ± 1.6 mg/kg), respectively. Our study has found much lower magnesium content than the study by Werdemberg dos Santos et al. (2022), which found higher concentrations in the medicinal plant 'espinheira santa' (6,170.52 mg/kg) and devil's claw (4,505.29 mg/kg) (Werdemberg dos Santos et al. 2022). Manganese is important because it functions in many different enzyme systems, including pyruvate carboxylase, kinases, transferases, and hydrolases. It also acts as an antioxidant thanks to Mn superoxide dismutase. Enzymes are required for micronutrient metabolism as well as the growth of cartilage and bones. It is essential for digestion, wound healing, reproduction, and energy regulation (Wu, Gao, et al. 2022). But manganese can be hazardous when it's present in excess since it can cause brain oxidative stress, apoptosis, neurodegeneration, and notably in the basal ganglia, a key brain region in Parkinson's pathogenesis, and mitochondrial dysfunction (Werdemberg dos Santos et al. 2022). The manganese quantified in *D. condylocarpon* root is below the recommended level (200 mg/kg) in medicinal products proposed by the Brazilian Pharmacopeia (Wu, Gao, et al. 2022).

The concentration of zinc (Zn) in the samples of the medicinal plant analyzed, *D. condylocarpon,* ranged from a high of 88.8 ± 1.0 mg/kg in the stem bark to a low of 51.4 ± 0.0 mg/kg in the leaf. In general, the results reveal that the zinc content in all parts of the analyzed medicinal plants was lower and within the 100 mg/kg permissible limit set by FAO/WHO for zinc in medicinal plants (Dghaim et al. 2015; Nkansah et al. 2016). Zinc is an essential microelement required for proper human growth, thyroid function, blood clotting, and DNA and protein synthesis (Khanna et al. 2023). Even though, there is a lack of information on the toxicity of zinc, excessive zinc intake produces toxic effects on the blood lipoprotein and the immune system (Nieder et al. 2018).

The analyzed medicinal plant contained Ni concentrations ranging from 21.6 ± 0.6 to 30.2 ± 0.4 mg/kg. Among the three parts of the plant, the leaf had the lowest concentration of Ni, while the bark had the highest concentration. The most prevalent condition associated with nickel is allergic contact dermatitis (Alinaghi et al. 2019). Additionally, nickel is a potential cancer-causing agent that has an impact on the lungs and nasal cavities (Buxton et al. 2019). Nickel is essential in small amounts for the body, primarily in the pancreas, where it plays a crucial role in producing insulin (Dubey, Thakur, and Chattopadhyay 2020). The disorder of the liver occurs when there is a lack of this nutrient. The American Contact Dermatitis Society recognized nickel as the allergen of the year in 2008. They established a minimal risk level of 0.2 µg/m^3 for inhaling nickel for 15 to 364 days (Mustapha et al. 2019). However, no specific limit has been imposed on the amount of nickel present in food and herbs. A study has reported much lower Ni concentrations of 0.09, and 1.6 mg/kg (Maobe et al. 2012). Further, a study conducted in Baghdad, Iraq, found the Ni content range between 8.81 and 10.25 mg/kg, much lower than the limit set by the World Health Organization (WHO) in medicinal plants of 67.9 mg/kg (Latif Mohammed et al. 2014).

The observed copper (Cu) content in *D. condylocarpon*, ranging from 32.8 ± 0.6 mg/kg in the bark to 68.2 ± 1.0 mg/kg in the root, reflects the plant's capability to accumulate this metal. While the plant was harvested from a copper mining region, its Cu concentrations were significantly lower than the World Health Organization/Food and Agriculture Organization (WHO/FAO) regulatory limit of 150 mg/kg for medicinal plants. This finding is noteworthy for several reasons. First, the relatively low levels of copper may indicate that *D. condylocarpon* has effective mechanisms for regulating heavy metal uptake and accumulation, which can be an adaptive strategy to mitigate potential toxicity (Jan and Parray 2016; Skuza et al. 2022; Chadwick and Bury 2023). This behavior is often seen in plants that grow in contaminated environments, where they either limit metal uptake or sequester metals in ways that minimize their biological impact (Jan and Parray 2016; Skuza et al. 2022; Chadwick and Bury 2023). Second, the findings suggest that while copper mining activities may increase the availability of Cu in the environment, the bioavailability and subsequent uptake by plants can vary significantly based on several factors, including soil chemistry, plant physiology, and environmental conditions (Jan and Parray 2016; Skuza et al. 2022; Chadwick and Bury 2023). The results indicate that *D. condylocarpon* may be well-adapted to its environment, potentially reducing the risk of copper toxicity in medicinal applications.

The concentrations of copper determined in the selected medicinal plant in the current study are comparable to those determined in other medicinal plants by Stanojković-Sebić et al. (2017), which also fell within the maximum permissible concentration (Stanojković-Sebić et al. 2017). It must be mentioned that copper is a fundamental component of many enzymes and therefore plays a significant role in a variety of physiological processes such as elimination of free radicals, iron utilization, melanin production, and bone and connective tissue development. However, consuming too much copper can harm the liver and result in dermatitis, nausea, upper respiratory tract irritation, vomiting, diarrhea, and abdominal pain (Islam et al. 2023).

In the present study, the iron (Fe) content showed significant variability, ranging from 5099.0 ± 41.4 to 664.6 ± 1.2 mg/kg. The maximum amount of iron allowed in medicinal plants according to WHO/FAO is 425 mg/kg. The iron concentration values found in this study are significantly higher than those reported in a previous study on Brazilian medicinal plants, which ranged from 4.16 to 21.99 mg/kg (Aragão Tannus et al. 2021). The variation in results can be explained by the fact that the current research primarily concentrated on the medicinal plant growing in the mineral rich area of Zambia. Iron serves multiple important roles in the human body, including generating energy, providing oxygen, and supporting the immune system. However, excessive consumption of iron can result in adverse effects, such as the production of free radicals when iron transitions between the ferrous (Fe^{2+}) and ferric (Fe^{3+}) forms, which can cause cell death (Wan, Ren, and Wang 2019).

Estimated daily intake (EDI)

The findings of this study indicate that the levels of toxic metals (Cd, As, Pb, Sn, Ag, and Al) differ significantly. Table 5 shows the estimated daily intake (mg/day) of toxic metals in the leaf, bark, and root of *D. condylocarpon*.

The differences in the results may be due to the fact that metals have varying tendencies to accumulate biologically in various plant components (Santoyo-Martínez et al. 2020). It is important to note that the data on the metal concentrations determined in this study are derived from dried plant samples. Therefore, almost all of the digestion process leads to full recovery. However, when the herb is used, people often boil or soak it in water and consume only the water extract, discarding the solid plant material such as the marc. In that case, some metals remain in the discarded solid plant material, resulting in a recovery rate of less than 100%, possibly around 50%. If an individual consumes the herb as a powder mixed in water, they can consume any metal present, leading to higher metal ingestion similar to the metal concentrations obtained in this study. Hence, the levels of metals found in this study are higher than those ingest when consuming the herb as an extract, such as infusion, decoction, or tincture form. The recommended daily intake for Cd, Pb, Sn, Ag, and Al is 0.0025, 0.025, 0.025, 14.0, 0.025, and 1.0 mg/day, respectively (Zárate-Quiñones et al. 2021). Apart from aluminum (root and bark), the EDI of all toxic metals in the rest of the plant samples were

Table 5. Estimated daily intake (EDI) of toxic metals in *D. condylocarpon* in mg/day.

Sample	Cd	Pb	Sn	Ag	Al
Root	0.002	Nd	0.046	0.070	1.392
Bark	0.002	Nd	0.095	0.014	1.134
Leaf	0.002	Nd	0.054	0.004	0.895
WHO limit	0.003	0.025	14.000	0.025	1.000

below the recommended daily intake set by WHO/FAO. Other research studies have also found comparable, minimal amounts of EDI associated with toxic metals in herbal plants (Zárate-Quiñones et al. 2021).

Macro-elements such as calcium, potassium, magnesium, and sodium are essential for the health and well-being of individuals. Table 6 shows the EDI values for macro elements, together with the acceptable intake levels recommended by WHO/FAO.

EDI levels for essential macro elements were significantly lower than the acceptable limits set by the WHO/FAO. For example, the amounts of sodium, magnesium, potassium, and calcium in the root were 1.339, 1.574, 3.703, and 11.433 mg/day, respectively (Table 6). This was much lower than the recommended daily intake values by WHO/FAO for sodium, magnesium, potassium and calcium, which are 2300.0, 320.0, 2300.0, and 2000.0 mg/day, respectively (Barreca et al. 2023; Institute of Medicine 2006). This indicates that the consumption of medicinal remedies for *D. condylocarpon* does not provide sufficient amounts of essential macroelements. Microelements are essential for normal human body functions, especially when present within tolerable limits. Table 7 shows the EDIs for the microelements in *D. condylocarpon*

The WHO/FAO recommended EDI limits for Cr, Mn, Fe, Co, Ni, Cu, and Zn, are 0.025–0.035, 1.8–2.3, 8.0, 0.05, 1.0, 0.5, and 1.0 mg/day, respectively (Kntapo, Said, and Mosunmola 2019; Barreca et al. 2023; Patel 2011; Tschinkel et al. 2020). The levels of essential microelements in *D. condylocarpon* were below the recommended intake levels set by WHO/FAO, except for chromium in the root sample. Daily chromium intake in the root sample was 0.037 mg/day, slightly higher than the acceptable intake level of 0.035 mg/day. However, prior research discovered that the EDI for Cr in a medicinal plant was low and posed less risk at 0.0024 mg/day (Kong et al. 2020). Consuming the root of *D. condylocarpon* for a prolonged period can result in the risk of chromium poisoning.

Table 6. Estimated daily intake (EDI) of the essential macro-elements under study.

Sample	Na	Mg	P	K	S	Ca
Root	1.339	1.574	1.303	3.703	1.043	11.433
Stem bark	1.292	2.110	1.329	14.662	1.258	7.984
Leaf	1.537	2.689	2.276	16.336	2.620	6.546
WHO Limit	2300.000	320.000	700.000	2300.000	—	2000.000

Table 7. Estimated daily intake (EDI) of the essential microelements under study (mg/kg).

Sample	Cr	Mn	Fe	Co	Ni	Cu	Zn	Mo	Se	Si
Root	0.037	0.149	4.371	0.010	0.026	0.058	0.048	0.000	1.581	0.037
Bark	0.023	0.262	0.910	0.005	0.019	0.028	0.076	0.002	0.770	0.023
Leaf	0.022	1.962	0.570	0.006	0.019	0.055	0.044	0.003	0.726	0.022
WHO Limit	0.025–0.035	1.8–2.3	8.000	0.050	1.000	0.500	1.000	—	—	—

Health risk to humans of toxic metals

Estimation of target hazard quotients (THQ) and hazard index (HI)

THQ was calculated for toxic heavy metals including Cd, Pb, Sn, and Al. Cr was included because its essentiality or toxicity can vary depending on its oxidation state. Cr (III) is an essential microelement in the diet. The oxidation state of concern is Cr (VI), which is highly toxic and has been identified as a carcinogen for humans. However, chronic exposure to Cr (III) can cause harm, although it is essential to health in small amounts. The level of toxicity is determined by the valence state and solubility in water of chromium compounds (DesMarias and Costa 2019). However, As and Pb were not included because these metals were not detected. Furthermore, it was impossible to calculate the THQ values for essential elements such as Na, Ca, K, Cr, Mg, and Na, for which EPA does not give an oral reference dose (US Environmental Protection Agency 2011). Table 8 shows the estimated THQ values for Cd, Sn, and Al. The THQ for individual metals followed the order; Root sample: Al > Sn > Cr > Cd; bark sample; Al > Sn > Cr > Cd; and leaf sample: Al > Sn > Cr > Cd.

The root sample had the highest THQ values. The broadest range of THQ was attributed to Al in all samples. However, it is important to mention that THQ only reveals the cause of health risk and does not quantify the level of health risk involved. The leaf had the lowest values of 0.015, 0.001, 0.090, and 0.0895 for Cr, Cd, Sn, and Al, respectively. On the other hand, the bark had the lowest quotients for Cd and Cr, with values of 0.002 and 0.015, respectively. The Cd values in all samples were the smallest, with quotients of 0.001, 0.022, and 0.002 in the leaf, bark, and root, respectively. Apart from the Al quotients (root and bark), the rest of the metal hazard quotients in all samples were less than 1.

The magnitude of adverse effects of toxic metals in a sample is proportional to the sum of multiple metal exposures (Effiong et al. 2023). We have calculated the HI as the sum of the THQ of the toxic metals analyzed (Table 8). The values of the total hazard indices for all the metals are more than 1, indicating potential health risks to the Copperbelt population that consumes excessive amounts of *D. condylocarpon* for medicinal purposes (Table 8). Among the different metals, Al may be the main contributor, as it accounted for 93.11%, 86.63%, and 89.41% of the total health hazard indices in the root, bark, and leaf, respectively. When

Table 8. Target hazard quotient (THQ) and hazard index (HI) of metals in *D. condylocarpon*.

Sample	Cr	Cd	Sn	Al	Hazard index (HI)
Root	0.025	0.002	0.076	1.392	1.495
Bark	0.015	0.002	0.158	1.134	1.309
Leaf	0.015	0.001	0.090	0.895	1.001

Table 9. Exposure risk for each specific metal, as well as the overall risk.

Sample	Cd	Cr	Ni	Al	∑ CR (Cd, Cr, Ni, Al)
Root	0.015	1.497	0.022	0.278	1.811
Bark	0.013	0.927	0.016	0.227	1.244
Leaf	0.013	0.898	0.016	0.179	1.105

the total hazard indices exceed 1.0, there is concern for possible health effects as exposure to more than one toxic metal may produce an additive effect on the consumer (Tschinkel et al. 2020).

Determined carcinogenic risk (CR)

The potential to cause cancer was evaluated when regularly consuming *D. condylocarpon* root, bark, and leaf for medicinal purposes in terms of cadmium, chromium, nickel, and aluminum. As and Pb were not included because these metals were not detected in all samples. Table 9 shows the exposure risk for each specific toxic metal, as well as the overall risk.

All the carcinogenic risk values for individual carcinogenic metals; Cd, Cr, Ni, and Al exceed 0.0001 suggesting an increased probability of CR (Table 9). Additionally, none of the sum of carcinogenic risks fall within the range of $1.0x10^{-6}$ to $1.0x10^{-4}$. This suggests that consumption of *D. condylocarpon* for medicinal purposes over an extended period of time poses carcinogenic risks to consumers in the Copperbelt Province of Zambia.

Conclusions

This study concludes that the leaf, bark, and root of *D. condylocarpon* are generally safe for short-term use in Zambia's traditional medicine. Metal levels detected in this research are elevated compared to the actual amount individuals typically consume when using the herb in the form of extracts such as infusion, decoction, or tincture. The reason for this is that the levels of metals found in the study were obtained from dried plant samples. As a result, almost all the digestive process contributes to complete metal recovery. However, when people use the herb, they usually boil it or soak it in water and only drink the water extract, removing the solid plant material. In such situations, certain metals are left behind in the waste from plants, leading to metal ingestion much less than recovery. If a person consumes the herb by mixing it as a powder in water, they may end up ingesting any metal contained in the plant. This could result in their body absorbing higher levels of metal, similar to the metal concentrations determined in the study. In Zambia, where medicinal plants are commonly consumed as regular food, regulatory bodies should take steps to oversee their use. The results of this study indicate that the estimated daily intake (EDI) values for essential and toxic metals are below recommended limits except for Al and Cr, which were slightly above tolerable limits set by WHO/FAO, The presence of metals such as Al, Ni, and Cd in *D. condylocarpon* from the Copperbelt region suggests a possible risk of health. Although the study notes that the presence of a single toxic metal may not be hazardous, the simultaneous presence of multiple toxic metals could increase the risk of carcinogenic effects. Given the limited number of such studies in Zambia, the findings of the current investigation provide valuable information on Zambian perspectives, contributing to the existing literature. The study findings highlight a toxicological concern in the selected Zambian area, paving the way for more comprehensive investigations. Further studies with larger sample sizes and rigorous statistical analyses will help to better understand the health risks associated with medicinal plant contamination and the potential synergistic effects of contaminants.

Disclosure statement

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