



Nutrients and toxic heavy metals in *Strychnos cocculoides* (Loranthaceae): Implications for traditional medicine

Bitwell Chibuye^{a,b,c,*}, Indra Sen Singh^{b,2}, Luke Chimuka^{c,3}, Mokgaetji Monyai^c

^a Department of Chemistry, Mukuba University, Kitwe, Zambia

^b Department of Chemistry, School of Mathematics and Natural Sciences, Copperbelt University, Kitwe, Zambia

^c Molecular Sciences Institute, School of Chemistry, University of the Witwatersrand, Johannesburg, South Africa

ARTICLE INFO

Keywords:

Carcinogenic risk
Health risk assessment
Nutrients
Strychnos cocculoides (Loranthaceae)
Heavy metals

ABSTRACT

This study investigates the medicinal and toxicological profiles of *Strychnos cocculoides*, used in traditional medicine in Zambia, focusing on its nutrient content and heavy metal accumulation. Metals were extracted from dried plant samples using microwave digestion, and metal concentrations were determined using inductively coupled plasma optical emission spectrometry (ICP-OES). The concentrations of key nutrients such as calcium (Ca), potassium (K), and magnesium (Mg) were quantified in the plant's root, stem, and leaves, revealing its medicinal potential. However, some heavy metals were detected at concentrations above recommended values, raising concerns about health risks. Elevated metal concentrations in the plant include cadmium (Cd) at 2.8 mg/kg in the root and stem and 3.0 mg/kg in the leaf, exceeding the 0.3 mg/kg WHO/FAO limit; chromium (Cr) at 60.4 mg/kg in the root and 29.8 mg/kg in the stem, surpassing the 25.0 mg/kg guideline; iron (Fe) at 15,433.0 mg/kg in the root and 1421.8 mg/kg in the leaf, far exceeding the 425.5 mg/kg limit; and manganese (Mn) at 379.6 mg/kg in the root, 963.0 mg/kg in the stem, and 2069.0 mg/kg in the leaf, which exceeds the 200 mg/kg threshold. Toxicological profiling predicted neurotoxicity and ecotoxicity for aluminum (Al), Cd, Cr, and nickel (Ni), with a particular focus on their ability to cross the blood-brain barrier and cause long-term damage. While *S. cocculoides* offers medicinal benefits, its heavy metal content poses significant health risks, necessitating further research on safe processing techniques and its role in environmental management. These findings emphasize caution in traditional medicine and the plant's potential for human health and environmental remediation.

1. Introduction

Medicinal plants have long played a crucial role in traditional healthcare systems, particularly in developing regions where access to modern pharmaceuticals is limited. Among these, the use of plant-based remedies for treating various ailments has gained significant attention due to their therapeutic potential and rich phytochemical composition. As traditional medicine continues to be integrated into modern health practices, there is a growing need to scientifically validate the efficacy and safety of these plants. This validation not only aids in the safe application of these natural remedies but also supports the potential for their use as nutritional supplements [1].

The elemental composition of medicinal plants, particularly their nutrients, plays a vital role in their health-promoting properties. Nutrients such as calcium, magnesium, potassium, and zinc are essential for various physiological functions in humans, contributing to bone health, immune response, and enzyme activation [2,3]. However, the accumulation of toxic heavy metals, including lead, cadmium, and mercury, poses a significant risk to human health, as these metals can induce toxicity at even low concentrations [4]. Therefore, a comprehensive analysis of both nutrients and toxic metals in medicinal plants is critical for assessing their medicinal value and safety [5]. However, one limitation of this study is that metal concentrations in soil can vary significantly across different geographic regions [6]. As a result, the degree of

* Corresponding author at: Department of Chemistry, Mukuba University, Kitwe, Zambia.

E-mail address: bchibuye@mukuba.edu.zm (B. Chibuye).

¹ 0000-0002-6658-6695

² 0000-0001-8062-7089

³ 0000-0002-8552-2478

bioaccumulation in plant samples may also differ based on these regional soil characteristics, potentially influencing the overall findings.

In this study, the root, stem, and leaf of *Strychnos cocculoides* (Loranthaceae) a widely used medicinal plant was analyzed to determine its nutrients and heavy metals content and assess its safety concerning heavy metal contamination. The selected plant has been traditionally used to treat a variety of diseases. For instance, the root of *S. cocculoides* is commonly chewed to alleviate stomach disorders and has been noted for its efficacy in treating skin conditions such as eczema and sores [7]. Additionally, the plant's roots, bark, and leaves can be macerated in water and the water extract used as a remedy for male organ disorders, including erectile dysfunction, highlighting its potential in addressing reproductive health issues [7].

Heavy metal pollution is a significant environmental concern, particularly in areas impacted by industrial activities such as mining. Kalulushi town, located in the Copperbelt province of Zambia, is predominantly influenced by copper mining operations, which are a known source of heavy metal contaminants [8]. The mining process can lead to the release of metals such as lead, cadmium, copper, and arsenic into the surrounding environment, affecting soil and water quality and posing risks to local flora and fauna [9]. Elevated levels of heavy metals in plants can result in bioaccumulation, which may then enter the food chain, posing serious health risks to humans who consume contaminated plants or water [10,11]. Research has highlighted the potential human health consequences associated with exposure to heavy metals [12,13]. Given the historical context of mining in Kalulushi and its environmental implications, understanding the levels and effects of heavy metals in local plant species is important for assessing both environmental health and public safety in the region. In the context of similar studies, there is a growing body of literature examining heavy metal contamination in mining regions worldwide [10]. Studies in sub-saharan countries such as the Democratic Republic of Congo, and even within the Copperbelt province itself have documented the impact of mining activities on soil and plant health [14–18]. These studies provide a framework for understanding the environmental dynamics at play in Kalulushi and the potential risks to human health and ecosystems. To address these concerns, our research sought to evaluate the concentrations of key heavy metals in *S. cocculoides* samples collected from Kalulushi town, drawing connections to the broader implications of heavy metal pollution in mining areas.

Despite the popular use of *S. cocculoides* little is known about its elemental composition or potential health risks associated with heavy metal exposure. By evaluating its metal profile, this study aims to provide essential data that supports the safe use of the plant in traditional medicine and modern healthcare practices. Moreover, the findings may offer insights into the plant's potential as a source of nutrients and as a candidate for phytoremediation, where plants are used to extract heavy metals from contaminated soils [19,20].

2. Materials and methods

2.1. Laboratory materials

The laboratory materials required for this study were acquired from the chemical supply stores in the University of Witwatersrand' School of Chemistry, in South Africa. The materials included 50 mL polytetrafluoroethylene (PTFE) centrifuge tubes, 10 mL syringes, 2.0 mL vials, and needles, along with various glassware such as test tubes and flasks. Additionally, 0.22 µm PTFE filters (Millipore, Milford, USA) were employed during the experiments.

2.2. Plant samples and selection of the study site

Fresh plant samples were collected from the forest surrounding Kalulushi Airstrip, located at the coordinates Latitude: −12.8415, Longitude: 28.0948. The root, stem, and leaf of *S. cocculoides* were

harvested, packed in UV-resistant plastic bags to maintain sample purity, and immediately transported to a controlled environment at the Copperbelt University. They were air-dried in the shade for 30 days at ambient temperature. To minimize potential exposure to aerial deposition of heavy metals, the drying area was located away from industrial sites and traffic. Additionally, the plants were covered with fine mesh netting to protect against airborne contaminants. After drying, the materials were pulverized (DFT-200, Dahai Ltd., China) into a fine powder for further analysis. The botanical identification was verified and authenticated (Voucher specimen ID: BC104) by a botanist at the Herbarium for the Forest Department of the Ministry of Green Economy and Environment of the Republic of Zambia in Kitwe District.

Kalulushi Town, located in the Copperbelt Province of Zambia, was chosen as the study site due to its rich copper mining history. This selection was strategically motivated by the rampant use of *S. cocculoides*, a plant of significant importance in traditional medicine among local healers. Traditional healers frequently utilize this plant for its medicinal properties, highlighting the need to understand the potential environmental impacts on its efficacy and safety. Given the region's industrial context, characterized by intensive mining operations, there is an increased risk of soil and water contamination with heavy metals, which can adversely affect metal bioaccumulation in plants [21]. The sampling was conducted in forests around Kalulushi, where *S. cocculoides* is commonly found alongside historically and currently impacted mining areas.

2.3. Chemicals

Chemicals used in the study were sourced from Merck (Johannesburg, South Africa) and included ACN (HPLC grade, ≥ 99.9%), high-purity 65 % HNO₃ (Merck, RSA), 50 % H₂O₂, and ultra-pure water from a Milli-Q purification system (Millipore, Merck Chemicals (PTY) Ltd., Johannesburg, RSA) were utilized. Calibration for Inductively Coupled Plasma Optical Emission Spectroscopy (ICP-OES) was conducted using a multi-element standard solution (Spectro Genesis, Germany) with concentrations ranging from 0.1 mg/L to 10 mg/L, prepared from a 1000 mg/L stock solution dissolved in 5 % HNO₃. The ICP-OES instrument was operated with ultra-high purity argon gas to ensure accurate measurements.

2.4. Metal extraction

Metals were extracted from plant samples using the microwave digestion method. In brief, dried and pulverized plant samples were sieved using a 25 micron sieve. Then 0.25 g of samples were weighed directly in 20 mL poly (PTFE – TFM) digestion vessels. Then 3 mL of H₂O₂ and 9 mL of concentrated HNO₃ were added, closed, and placed in the multiwave Go digester (Anton Paar, Switzerland). The microwave oven heating program was carried out as follows: Temperature of 40–180 °C for 10 min and maintained for 30 minutes. After cooling, digested samples were filtered using 0.22 µm PTFE filters and diluted to a final volume of 50 mL with ultrapure water. Reagent blanks were tested for possible interference in each set of samples. Reagent blanks and spiked samples were prepared in the same manner as the test samples. For each sample, three replicate digests were prepared.

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

To ensure accuracy and reliability, there was careful handling and cleaning of various glassware. High-quality deionized water was used for rinsing and diluting throughout the study, alongside analytical grade reagents. Blank analyses were used for instrument calibration. Calibration standards were prepared using the stock solution of each metal to set up the instrument for precise measurements. The analysis was subjected to repeated checks to ensure its accuracy and precision. Validity

of the method was achieved through limits of detection (LOD) and quantification (LOQ) as well as the spike recovery test. The presence of multiple metals in medicinal plants was evaluated. Calculations for the limits of detection (LODs) and limit of quantification (LOQs), and recoveries were performed as reported by Chibuye et al. [22].

2.6. Metal concentration determination

The ICP-OES (Spectro, Kleve, Germany) was used to analyze and measure the concentration of various metals, including aluminum, arsenic, calcium, cadmium, cobalt, chromium, copper, iron, potassium, magnesium, manganese, molybdenum, sodium, nickel, phosphorus, lead, sulfur, selenium, silicon, tin, and zinc. The identification and measurement technique used in this study followed the procedure described by Chibuye et al. [22]. Prior to calibration, the levels of individual metals were determined using external standard solutions containing at least 1000 mg/L of concentration. The instrumental parameters and operating conditions were carefully fine-tuned to achieve a high level of precision and responsiveness. Metals were analyzed with a nebulizer flow of 1.0 mL/min, nebulizer pressure of 2.81 bar, plasma power of 1400 W, a pump speed of 2 rpm, a coolant flow of 14 mL/min, a replicate read time of 10 s, a rinse time of 10 s, a sample uptake delay of 30 s, an auxiliary flow of 1.5 mL/min, and an instrument stabilization time of 20 s. The tests were performed three times and the findings were reported as the average $\pm$ deviation concentration (SD).

2.7. Assessment of human health risks of metals

The potential danger to human health from the consumption of plants contaminated with heavy metals was assessed using calculations of estimated daily intake (EDI) of metals, the hazard quotient (HQ), and the hazard indices (HI). The EDI (daily intake dose) was computed to determine the typical amount of metals that enter the body system of a specific consumer based on their body weight. Eq. (1) was used to determine the value of EDI [23].

$$EDI = \frac{C_{\text{metal}} \times XIR}{BW} \quad (1)$$

In this context, C_{metal} represents the concentration of metal (mg/kg) in the unprocessed plant material. The term IR denotes the daily average consumption rate of raw medicinal plant preparations, which is estimated at 0.06 kg/day [22,23]. B_w corresponds to the average body weight, assumed to be 70 kg for adults in Zambia [21,22].

The Hazard Quotient (HQ) is utilized to evaluate the potential risk (non-carcinogenic) to humans that could result from prolonged ingestion of heavy metals present in fruits, vegetables, and medicinal plants. If HQ equals to 1, it means that there may be health dangers associated with being exposed to the metal. The HQ was determined using the formula provided in Eq. 2 [22,23].

$$THQ = \frac{EDI}{RfD} \quad (2)$$

The Recommended Daily Intake (RfD) is a guideline for the maximum amount of a metal that can be safely consumed per kilogram of body weight each day, accounting for both adults and children. The RfD values for various metals are as follows: copper (0.04 mg/kg), aluminum (1.0 mg/kg), zinc (0.3 mg/kg), iron (0.7 mg/kg), cadmium (0.001 mg/kg), manganese (0.14 mg/kg), lead (0.0035 mg/kg), chromium (1.5 mg/kg), arsenic (0.014 mg/kg), nickel (0.91 mg/kg), tin (0.6 mg/kg), silver (0.005 mg/kg), cobalt (0.0003 mg/kg), and selenium (0.005 mg/kg/day). A Target Hazard Quotient (THQ) value greater than 1 suggests that exposure to a particular heavy metal could pose health risks [23,24]. The Hazard Index (HI) is utilized to evaluate the overall non-carcinogenic health risk associated with exposure to multiple heavy metals. The combined effect of these metals can amplify potential harm. If the sum of Hazard Quotients ($\sum HQ$) is less than 1, it

indicates potential adverse effects on human health.

Carcinogenic Risk (CR) quantifies the probability of an individual developing cancer due to exposure to a carcinogenic substance over their lifetime. The calculation is based on Eq. 3 [25,26]:

$$CR = EDI \times CPSO \quad (3)$$

The oral slope factors (CPSO) for specific carcinogens are as follows: cadmium (6.1), nickel (0.84), lead (8.5), arsenic (1.5), aluminum (0.2), and chromium (41). A CR value exceeding 0.0001 indicates a heightened risk of developing cancer [23]. When multiple carcinogenic metals are present, the total cancer risk is obtained by summing the individual risks, assuming cumulative effects on the body. The acceptable risk range is from 0.000001 to 0.0001 [22].

2.8. Statistical analysis

All measurements were performed in triplicate and expressed as mean $\pm$ standard deviation (SD). Numerical data analysis and the generation of calibration curves were conducted using Origin 2018 for precise processing and evaluation of the experimental results.

2.9. Toxicity Assessment Using ProTox-II

Toxicity of the heavy toxic metals was analyzed and predicted using the online web tool ProTox-II (<https://ox-new.charite.de/prottox>; accessed on 22 October 2024).

3. Results, analysis and discussion

3.1. Quality assurance results

All R^2 values exceeded 0.999. The metals chosen for analysis were selected based on their importance in maintaining human health or their potential toxicity and associated health risks. To achieve a comprehensive assessment of the metal content and accumulation within the medicinal plant, concentrations of several metals were measured. The instrument's limits of detection (LOD), limits of quantification (LOQ), and recovery rates were determined and are summarized in Table 1.

A limitation of this study is the significant variability in soil metal concentrations across different geographic regions [6]. Consequently, the extent of bioaccumulation in plant samples may vary according to these regional soil characteristics. As such, the findings of the study may be considered with such calibration.

3.2. Metal determination in raw plant samples and health risk assessment

The findings of this study indicated that metals, Ca, K, Mg, K, P, S, Ag, Al, As, Cd, Co, Cr, Cu, Fe, Hg, Mn, Ni, Pb, Se and Si, were found in different amounts within the root, stem bark and leaf samples of the three medicinal plants. Table 2 presents the concentrations of nutrients and heavy metals (Mean $\pm$ SD, $n = 3$) including the maximum and minimum values (mg/kg) dry weight. Table 3 shows the Estimated Daily Intake (EDI, mg/day). Table 4 details the Hazard Quotient (HQ) and hazard index, while Table 5 outlines the Cancer Risk (CR) associated with consumption of the various parts of *S. cocculoides*.

3.3. Analysis and discussion of metal concentrations in *S. cocculoides* and health risk assessment

The nutrients found in the root, stem, and leaf of *S. cocculoides* include calcium (Ca), potassium (K), magnesium (Mg), sodium (Na), phosphorus (P), and sulfur (S), all of which are critical for human nutrition. Calcium, which is particularly abundant in the stem (49.257 mg/kg), is vital for bone health, muscle function, and nerve transmission [27]. The high levels of calcium observed in the plant parts

Table 1
Instrumental LOD, LOQ, Linearity, and Percent recovery.

Metal	LOD (mg/L)	LOQ (mg/L)	Regression Equation	R ²	Spike Recovery (%)
Ag	0.103	0.313	y = 329694.94x + 103349.42	0.999	85.71
Al	0.176	0.532	y = 158320.49x + 254106.98	0.999	101.94
As	0.305	0.923	y = 15976.54x + 16220.26	0.999	108.61
Ca	0.144	0.436	y = 177758.49x + 60658.36	0.999	101.87
Cd	0.062	0.187	y = 167489.98x + 28263.45	0.999	98.87
Co	0.156	0.474	y = 51710.65 + 31295.24	0.999	100.98
Cr	0.075	0.229	y = 96337.30x + 84490.47	0.999	89.16
Cu	0.431	1.307	y = 314906.38x + 83944.31	0.999	97.12
Fe	0.138	0.417	y = 186681.78 + 35439.28	0.999	102.87
K	0.989	2.998	y = 102153.50 + 14537.59	0.995	78.54
Mg	0.071	0.216	y = 1925540.34x + 59698.12	0.999	107.69
Mn	0.061	0.186	y = 837462.48x + 59129.93	0.999	56.87
Mo	0.038	0.116	y = 48726.45x + 15270.98	0.999	24.87
Na	1.236	3.746	y = 965721.50x + 77147.87	0.991	22.43
Ni	0.209	0.634	y = 50478.36x + 30793.56	0.999	95.76
P	0.365	1.105	y = 14660.26 + 25031.24	0.999	15.98
Pb	0.191	0.580	y = 11282.62x + 27957.79	0.999	102.03
S	0.118	0.358	y = 5949.65x + 7646.23	0.999	51.87
Se	0.141	0.426	y = 17939.58x + 15188.90	0.999	108.76
Si	0.203	0.615	y = 140284.96x + 42368.67	0.999	8.61
Sn	0.163	0.495	y = 19190.97x + 13438.01	0.999	16.71
Zn	0.117	0.354	y = 284787.76x + 23411.41	0.999	99.93

indicate that *S. cocculoides* could be an important source of this nutrient, especially for populations with low dairy intake. The Estimated Daily Intake (EDI) values (16.82 mg/day for the root, 42.22 mg/day for the stem, and 17.73 mg/day for the leaf) further suggest the plant’s potential contribution to calcium intake (Table 3).

Table 2
Nutrients and heavy metal concentration (Mean ± SD, n = 3), maximum, minimum (mg/kg) dry weight of the root, stem, and leaf of *S. cocculoides*.

Nutrient	Concentration (mg/kg)									
	Root sample			Stem bark sample			Leaf sample			WFL
	Mean	Max	Min	Mean	Max	Min	Mean	Max	Min	
Ca	19619.6 ± 61.0	19689.8	19579.0	49257.0 ± 641.2	49921.2	48641.6	20681.8 ± 190.8	20878.0	20497.0	–
K	5485.4 ± 145.2	5616.6	5329.6	17562.6 ± 171.4	17746.2	17406.4	8244.0 ± 57.0	8306.8	8195.4	-
Mg	2322.6 ± 5.6	2327.4	2316.4	3943.0 ± 52.4	3994.8	3889.8	6412.6 ± 54.0	6468.6	6360.6	-
Na	1410.6 ± 39.4	1443.4	1367.0	1700.4 ± 17.8	1720.6	1687.4	1446.6 ± 6.4	1452.6	1440.0	-
P	1247.2 ± 6.0	1252.4	1240.6	1491.8 ± 14.0	1508.0	1483.2	1794.2 ± 7.2	1799.2	1786.0	-
S	991.8 ± 2.0	993.8	989.8	1317.4 ± 7.4	1323.6	1309.2	2250.6 ± 7.0	2258.2	2244.4	-
Heavy Metal										
Ag	207.0 ± 0.2	208.0	206.0	36.4 ± 0.4	36.8	36.0	22.0 ± 0.6	22.6	21.6	-
Al	26447.6 ± 607.0	26944.6	25771.0	3817.4 ± 52.4	3863.6	3760.4	1980.4 ± 3.8	1984.4	1977.0	-
As	Nd	Nd	Nd	Nd	Nd	Nd	Nd	Nd	Nd	5.0
Cd	2.8 ± 0.2	3.0	2.8	2.8 ± 0.2	2.8	2.4	3.0 ± 0.0	3.0	3.0	0.3
Co	9.6 ± 0.2	9.8	9.4	7.8 ± 0.2	8.0	7.6	11.4 ± 0.6	11.8	10.6	-
Cr	60.4 ± 0.6	61.0	59.6	29.8 ± 1.0	30.8	29.0	32.0 ± 1.4	33.4	31.0	25.0
Cu	151.4 ± 0.8	152.2	150.6	53.8 ± 0.4	54.2	53.4	151.02 ± 0.2	151.4	151.0	150.0
Fe	15433.0 ± 63.2	15482.8	15454.2	1771.0 ± 4.6	1775.8	1766.6	1421.8 ± 6.8	1428.6	1415.0	425.5
Mn	379.6 ± 8.0	384.8	370.2	963.0 ± 3.0	965.6	959.6	2069.0 ± 11.2	2079.4	2057.2	200.0
Ni	27.8 ± 0.0	27.8	27.8	21.4 ± 0.4	22.0	21.0	21.6 ± 0.6	22.2	21.0	67.9
Pb	Nd	Nd	Nd	Nd	Nd	Nd	Nd	Nd	Nd	10.0
Se	Nd	Nd	Nd	Nd	Nd	Nd	Nd	Nd	Nd	
Si	161.8 ± 4.4	166.0	157.0	1165.8 ± 9.6	1175.6	1156.2	1298.8 ± 7.2	1307.2	1294.6	-
Sn	34.6 ± 1.4	35.4	33.0	93.6 ± 0.2	93.6	93.4	84.2 ± 1.0	85.4	83.6	-
Zn	42.0 ± 0.0	42.0	42.0	50.6 ± 0.2	50.8	50.4	42.6 ± 0.2	42.8	42.6	100.0

Key: WFL = WHO / FAO limit, [] = concentration, Nd = not detected, Max = maximum, Min = minimum

Potassium levels are also significant, particularly in the stem (17.563 mg/kg), and this element is essential for maintaining fluid balance, muscle contraction, and nerve signalling [28]. With EDI values of 4.70 mg/day for the root, 15.05 mg/day for the stem, and 7.07 mg/day for the leaf, *S. cocculoides* could serve as a valuable supplementary source of potassium in the diet. Similarly, magnesium concentrations are moderate, especially in the leaf (6412.6 mg/kg), and this mineral supports many enzymatic processes, including energy production and protein synthesis [29]. The high EDI of 5.50 mg/day in the leaf reflects its importance in preventing magnesium deficiency.

Sodium and phosphorus concentrations are relatively lower, which is beneficial in preventing excessive sodium intake while still providing

Table 3
Estimated Daily Intake (EDI, mg/day) of nutrients and heavy metals in the root, stem, and leaf of *S. cocculoides*.

	Root	Stem bark	Leaf	WHO/FAO Limit
Nutrient				
Ca	16.817	42.220	17.727	-
K	4.702	15.054	7.066	-
Mg	1.991	3.380	5.497	-
Na	1.209	1.458	1.240	-
P	1.069	1.279	1.538	-
S	0.850	1.129	1.929	-
Heavy metals				
Ag	0.177	0.031	0.019	0.025
Al	22.669	3.240	1.697	1.0
As	Nd	Nd	Nd	-
Cd	0.002	0.002	0.003	0.0025
Co	0.008	0.007	0.010	0.05
Cr	0.052	0.026	0.027	0.025–0.035
Cu	0.130	0.046	0.129	0.5
Fe	13.228	1.518	1.219	8.0
Mn	0.325	0.825	1.773	1.8–2.3
Ni	0.024	0.018	0.019	1.0
Pb	Nd	Nd	Nd	-
Se	Nd	Nd	Nd	-
Si	0.139	0.999	1.113	-
Sn	0.030	0.080	0.072	14.0
Zn	0.036	0.043	0.037	1.0

Table 4

Hazard Quotient (HQ), and Hazard Index of the root, stem, and leaf of *S. coccuroides*.

Metal	Target Hazard Quotient		
	Root	Stem bark	Leaf
Ag	35.486	6.240	3.771
Al	22.669	3.272	1.697
As	Nd	Nd	Nd
Cd	2.400	2.400	2.571
Co	27.429	22.286	32.571
Cr	0.035	0.017	0.018
Cu	3.244	1.153	3.236
Fe	18.898	2.169	1.741
Mn	2.324	5.896	12.667
Ni	0.026	0.020	0.020
Pb	Nd	Nd	Nd
Se	Nd	Nd	Nd
Si	Nd	Nd	Nd
Sn	0.049	0.1337	0.120
Zn	0.120	0.1446	0.122
Hazard index (HI)	112.680	43.731	58.537

Table 5

Cancer risk (CR) of the root, stem, and leaf of *S. coccuroides*.

	Root	Stem bark	Leaf
Al	4.534	0.654	0.339
Cd	0.015	0.015	0.016
Cr	2.123	1.047	1.125
Ni	0.020	0.015	0.016
Σ CR (Al, Cd, Cr, Ni)	6.691	1.732	1.495

enough of these nutrients to support important physiological functions such as fluid balance (sodium) and cellular energy metabolism (phosphorus) [30,31]. Sulfur, found in considerable amounts, particularly in the leaf (2250.6 mg/kg), plays a key role in synthesizing amino acids and vitamins essential for metabolism [32]. Thus, the sulfur levels across plant parts further enhance its medicinal value. While this study found significant amounts of essential nutrients, a recent comparable study reported relatively low levels of calcium (Ca), potassium (K), magnesium (Mg), sodium (Na), phosphorus (P), and sulfur (S) in *S. siame* leaves. As a result, *S. coccuroides* is considered more nutritious than *S. siame* in this study [33].

However, when evaluating the heavy metal concentrations in *S. coccuroides*, some significant health risks emerge, especially regarding heavy metal exposure. Al, for instance, is found in high concentrations, particularly in the root (26,447.6 mg/kg) and stem (3817.4 mg/kg), far exceeding the WHO/FAO safe limit of 1.0 mg/kg for medicinal plants. In contrast to the current study, a similar investigation found significantly lower aluminum concentrations, ranging from 30.983 to 368.877 mg/kg, in various parts of medicinal plants collected from the eastern Mediterranean region of Turkey [34]. Al is a concern due to its potential neurotoxic effects, especially with long-term consumption [35]. The Target Hazard Quotient (THQ) values for Al in the root (22.669) and stem (3.272) indicate a significant health risk from regular consumption (Table 4), with a corresponding cancer risk (CR) of 4.534 for the root and 0.654 for the stem (Table 5). This highlights the potential carcinogenic danger associated with aluminum exposure [36].

Similarly, Cd concentrations, though relatively low (2.8 mg/kg in both the root and stem), exceed the WHO limit of 0.3 mg/kg. Cd exposure is linked to kidney damage and bone demineralization [37], and the THQ values for Cd in the root (2.4) suggest a notable non-carcinogenic risk. Though the cancer risk (CR) values for Cd (0.015 for both the root and stem) remain within acceptable limits, Cd exposure remains a concern. Cr concentrations, especially in the root (60.4 mg/kg), also exceed safe limits. However, unlike the current study, some study reported lower levels of both Cd and Cr in medicinal herbs marketed in

Malawi [38]. While Cr in its trivalent form is beneficial for glucose metabolism, hexavalent chromium (CrVI) is toxic [39]. The THQ values for chromium (0.035 in the root and 0.017 in the stem) suggest moderate non-carcinogenic risks, while the CR values (2.123 for the root and 1.047 for the stem) indicate a significant potential for carcinogenic effects. However, it may suffice to add that Cr exists in several oxidation states, with the two most prevalent forms in environmental contexts being trivalent chromium Cr³⁺ and hexavalent Cr⁶⁺ [39]. Cr³⁺ is generally considered less toxic and is an essential micronutrient for some organisms, whereas Cr⁶⁺ is highly toxic, soluble, and mobile in alkaline conditions, making it a significant environmental contaminant [40]. The speciation of Cr can significantly influence its bioavailability and potential toxicity. Factors such as soil pH, organic matter content, and the presence of competing ions play crucial roles in determining the form of Cr that plants uptake [41]. Recent studies have shown that Cr⁶⁺ can be readily absorbed by plant roots and translocated to aerial parts, leading to oxidative stress and phytotoxicity [41]. Conversely, Cr³⁺ tends to bind more strongly to soil particles and organic matter, reducing its bioavailability and uptake [42]. Given these differences, assessing total Cr concentrations without accounting for speciation could lead to misinterpretations of ecological risk and health implications. Future investigations should prioritize Cr speciation analysis to enable a more accurate evaluation of its environmental impact and inform guidelines for safe soil and water quality.

Nickel concentrations are relatively low (27.8 mg/kg in the root and 21.4 mg/kg in the stem), well below the WHO/FAO safe limit of 67.9 mg/kg. A study in India indicated that various plants accumulated Ni at levels ranging from 75.7 to 156.4 mg/kg of dry weight, which exceeds the concentrations of Ni found in the current study [43]. Although nickel is essential in trace amounts, excessive exposure can cause allergic reactions and respiratory issues [44]. The THQ values for nickel (0.026 in the root and 0.020 in the stem) are minimal, indicating a low health risk. In contrast, a study in India reported much higher HQ values for nickel in *Calotropis procera* (3.003) and *Pteridium latiusculum* (2.618) [43]. Lead and arsenic were not detected in any of the samples, which is advantageous, as these heavy metals are known to cause severe health issues, including neurological damage and carcinogenicity [45]. While Pb and As were not detected in the current study, a previous investigation reported levels of 1.13 mg/kg of Pb in *Mondia whitei*, 1.02 mg/kg in *Moringa oleifera*, and 1.05 mg/kg in *Azadirachta indica*. Additionally, that study quantified As levels at 0.060 mg/kg in *Mondia whitei*, 0.048 mg/kg in *Moringa oleifera*, and 0.078 mg/kg in *Azadirachta indica* [38].

Iron and manganese concentrations are also significant. The root contains high iron levels (15,433 mg/kg), which, while beneficial for oxygen transport and enzyme functions, can lead to iron overload and oxidative stress when consumed in excess [46,47]. The THQ for iron in the root (18.898) is notably high, indicating a potential risk for iron toxicity. Manganese concentrations are highest in the leaf (2069 mg/kg), and while manganese is essential for bone formation and metabolism, excessive intake can lead to neurological issues [48]. The THQ for manganese in the leaf (12.667) suggests a considerable health risk.

The overall hazard index (HI), which sums all THQs for the various metals, is particularly high for the root (112.680), indicating significant potential for non-carcinogenic risks, primarily due to high levels of Al and Fe. The stem (HI = 43.731) and leaf (HI = 58.537) also exceed the threshold for safety, signalling potential health risks with consumption of these plant parts. Previous studies have reported Health Index (HI) values greater than one. For instance, a study examining the potential health risks of Chinese herbal medicines found an HI of 11.9 for *Toxicodendron resinosa* [49]. Additionally, the total cancer risk (CR) from heavy metal exposure, particularly Al, Cd, Cr, and Ni, is highest in the root (6.691), followed by the stem (1.732) and leaf (1.495). These values suggest that consuming *S. coccuroides*, particularly the root, could result in significant carcinogenic risks over time.

While *S. cocculoides* provides considerable medicinal benefits, especially as a source of nutrients such as Ca, K, and Mg, its high concentrations of potentially toxic heavy metals, particularly Al, Cr, and Fe, pose significant health risks. Regular consumption of these plant parts could lead to both non-carcinogenic and carcinogenic effects, especially for individuals with prolonged exposure. Therefore, careful consideration and monitoring of metal concentrations in *S. cocculoides* are necessary, and appropriate processing methods should be employed to mitigate the associated health risks.

The root accumulates substantial amounts of Al, Cr, Fe, Ni, and Ag, suggesting these metals are likely linked to environmental contamination or adaptation to stress conditions [50,51]. While the stem and leaf tissues also show accumulation of metals such as Fe and Cr, they demonstrate a stronger association with nutrients such as Mg, phosphorus (P), and S, which are crucial for both plant growth and human nutrition [52].

The high concentrations of Al, Cr, Fe, and Ni in the root indicate that *S. cocculoides* may have potential in phytoremediation, as it could be effective in absorbing excess metals from contaminated soils [20,53]. Although the stem and leaf tissues exhibit moderate levels of these metals, their primary function may be more related to nutrient distribution and physiological processes, rather than metal absorption. However, the presence of bioavailable metals such as Ca, K, Mg, Na, P, and S in the plant tissues underscores its potential medicinal value. However, the detection of toxic heavy metals such as Cr, Cd, and Ni, albeit within permissible safety limits, warrants caution when considering the use of this plant in medicinal or dietary applications. This analysis underscores the dual role of *S. cocculoides*, highlighting both its medicinal benefits and its potential application in environmental remediation through metal absorption from soils.

3.4. Toxicity predictions for toxic heavy metals

In the current study, many criteria, including LD50, predicted hepatotoxicity, neurotoxicity, nephrotoxicity, respiratory toxicity, cardiotoxicity, carcinogenicity, immunotoxicity, mutagenicity, cytotoxicity, clinical toxicity, and nutritional toxicity were taken into account for the toxicity analysis of toxic heavy metals (Al, Cd, Cr, and Ni) in the current study. Table 6 shows toxicity analysis of toxic heavy metals (Al, Cd, Cr, and Ni) from *S. cocculoides*.

I = Inactive, A = active

The toxicity analysis of the toxic heavy metals - Al, Cd, Cr, and Ni

Table 6
Toxicity analysis of toxic heavy metals in *S. cocculoides*.

Tested toxicities	Toxic Heavy Metals			
	Al	Cd	Cr	Ni
Predicted LD50 (mg/kg)	5000	890	440	780
Predicted toxicity class	5	4	3	4
Hepatotoxicity (prediction/ probability)	I/0.97	I/0.98	I/0.98	I/0.97
Neurotoxicity (prediction/ probability)	A/ 0.59	A/ 0.59	A/ 0.59	A/ 0.59
Nephrotoxicity (prediction/ probability)	A/ 0.84	I/0.84	I/0.84	I/0.84
Respiratory toxicity (prediction/ probability)	A/ 0.77	I/0.77	I/0.77	A/ 0.77
Cardiotoxicity (prediction/probability)	I/0.98	I/0.99	I/0.92	I/0.98
Carcinogenicity (prediction/ probability)	I/0.69	I/0.62	I/0.65	I/0.83
Immunotoxicity (prediction/probability)	I/0.99	A/ 0.99	I/0.99	A/ 0.99
Mutagenicity (prediction/ probability)	I/0.75	I/0.76	I/0.76	I/0.76
Cytotoxicity (prediction/ probability)	I/0.74	I/0.79	I/0.79	I/0.79
BBB-Barrier	A/1.0	A/1.0	A/1.0	A/1.0
Ecotoxicity	A/ 0.85	A/ 0.85	A/ 0.85	A/ 0.85
Clinical toxicity (prediction/ probability)	I/0.83	I/0.84	I/0.84	I/0.84

from *S. cocculoides* reveals several important health and environmental implications. While Al appears to have relatively low acute toxicity with a high LD50 of 5000 mg/kg, it is still of concern due to its predicted neurotoxicity, nephrotoxicity, and respiratory toxicity [54]. The fact that Al can cross the blood-brain barrier (BBB) increases its potential to cause neurological damage, which may lead to chronic issues over time [55]. Moreover, Al is predicted to be ecotoxic, suggesting that its presence in the environment could have harmful effects on ecosystems.

Cd, despite showing inactivity for hepatotoxicity and some other forms of toxicity, is predicted to be a neurotoxin, immunotoxin, and ecotoxic agent. Its moderate toxicity classification (class 4) and lower LD50 (890 mg/kg) indicate a greater risk to human health compared to Al, particularly with chronic exposure [54]. Cd's ability to impair immune function and its potential to damage ecosystems through bioaccumulation highlight the need for strict monitoring of this metal, especially since it is a well-known environmental contaminant [56].

Cr, predicted to have a significant toxicity (class 3) with an LD50 of 440 mg/kg, is especially concerning for its neurotoxic potential and its ability to cross the BBB. While the analysis indicates low risk for nephrotoxicity and respiratory toxicity, Cr (particularly in its hexavalent form, Cr (VI)) is a well-established carcinogen in humans, making its presence in *S. cocculoides* noteworthy for both medicinal and environmental considerations [57]. Ni also poses a moderate toxicity risk (class 4) with an LD50 of 780 mg/kg, and it shares similar concerns with Al and Cd regarding its neurotoxic, respiratory toxic, and immunotoxic effects. Similar to the other metals, Ni's ability to cross the BBB and its predicted ecotoxicity present a dual concern for both human health and environmental safety.

It may suffice to stress that, while *S. cocculoides* may offer medicinal benefits, the presence of these toxic heavy metals raises health risk concerns. Their potential for neurotoxicity, respiratory damage, and ecotoxicity, alongside the fact that they can cross the blood-brain barrier, suggests a need for caution in medicinal use. Additionally, the environmental risks associated with the metals point to the importance of monitoring their levels, especially in phytoremediation or ecological restoration efforts.

3.5. Implications for traditional medicine

The findings on *S. cocculoides* highlight both the potential and the risks associated with its use in traditional medicine. On one hand, the plant's tissues are rich in nutrients such as Ca, K, and Mg, which contribute positively to its medicinal value and may support health when consumed in moderation [58]. However, the presence of toxic heavy metals such as Al, Cd, Cr, and Ni poses significant health risks, particularly due to their neurotoxic, immunotoxic, and ecotoxic effects. These metals' potential to accumulate in the human body, cross the blood-brain barrier, and cause long-term damage raises concerns about the safety of using *S. cocculoides* as a regular medicinal plant [22]. The elevated levels of these contaminants suggest the need for caution, proper processing, or regulation when incorporating the plant into traditional remedies, especially to prevent toxic exposure over time. Additionally, while *S. cocculoides* shows some promise for phytoremediation due to its metal accumulation capabilities, careful consideration must be given to its environmental impact and the implications of reintroducing these metals into the food chain.

4. Conclusion

In conclusion, the metal analysis of *S. cocculoides* reveals a dual role for the plant in both medicine and environmental applications, though it also highlights significant health risks. The plant exhibits high concentrations of nutrients such as Ca, K, and Mg, which contribute positively to its potential medicinal uses. However, the presence of toxic heavy metals such as Al, Cd, Cr, and Ni in the plant's tissues raises concerns due to their neurotoxic, immunotoxic, and ecotoxic potential, as well as their

ability to cross the blood-brain barrier. These metals, found in concentrations exceeding recommended limits, pose health risks if the plant is consumed frequently or in large quantities, especially in traditional medicinal practices. Although *S. cocculoides* shows promise in absorbing heavy metals from the soil, its role in phytoremediation must be approached cautiously to prevent further environmental contamination or food chain exposure. Overall, while *S. cocculoides* holds potential in traditional medicine and environmental management, the risks associated with heavy metal toxicity necessitate careful regulation, monitoring, and possibly detoxification methods before its broader application. It is recommended that the consumption of *S. cocculoides* be limited, particularly in regions with known soil contamination. Additionally, implementing protocols for heavy metal testing and establishing safety thresholds for medicinal use would be beneficial in mitigating health risks associated with this plant. Implementing agricultural practices that reduce heavy metal uptake could also enhance the safety of *S. cocculoides* for medicinal and environmental purposes.

Future research perspectives

Future research on *S. cocculoides* should focus on several key areas to expand understanding of its medicinal, and environmental potential. Firstly, more in-depth studies on the bioavailability of both nutrients and toxic heavy metals in the plant are crucial to assess how these metals are absorbed, distributed, and metabolized in the human body. Investigating how traditional preparation methods, such as boiling or drying, influence the concentrations of toxic heavy metals could provide strategies to reduce their levels and make the plant safer for medicinal and dietary use. Additionally, further toxicological profiling, including in vivo and in vitro studies, should be conducted to validate the predicted toxic effects, such as neurotoxicity, immunotoxicity, and ecotoxicity, and to determine the long-term health impacts of consuming the plant. Exploring detoxification techniques, whether through bioremediation, selective breeding of low-metal-accumulating varieties, or phytochemical treatments, could also be valuable in mitigating the risks associated with heavy metal contamination. In the environmental sphere, future studies should investigate the potential of *S. cocculoides* for phytoremediation on a larger scale, particularly in soils contaminated with heavy metals. Understanding its metal uptake mechanisms and tolerance thresholds would be beneficial in developing effective strategies for cleaning up polluted environments. Finally, research should explore the plant's interactions with soil microbiota and other environmental factors that influence its metal absorption, which could offer insights into optimizing its use for both environmental restoration and safe traditional medicinal practices.

CRediT authorship contribution statement

Monyai Mokgaetji: Visualization, Validation, Resources, Methodology, Investigation. **Chimuka Luke:** Writing – review & editing, Validation, Supervision, Resources, Methodology, Funding acquisition. **Sen Singh Indra:** Writing – review & editing, Supervision. **Chibuye Bitwell:** Writing – review & editing, Writing – original draft, Software, Project administration, Methodology, Investigation, Formal analysis.

Consent for publication

All authors consent to publish this manuscript.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

References

- [1] G.R. Willsky, R.W. Bussmann, M.L. Ganoza-Yupanqui, G. Malca-Garcia, I. Castro, D. Sharon, Integrating traditional and modern medicine: perspectives from ethnobotany, medical anthropology, microbiology, and pharmacy, *Transform. Glob. Health: Interdiscip. Chall., Perspect., Strateg.* (2020) 301–314, https://doi.org/10.1007/978-3-030-32112-3_19.
- [2] A. Joshi, S. Kaur, S.K. Taneja, R. Mandal, Review article on molecular mechanism of regulation of hypertension by macro-elements (Na, K, Ca and Mg), micro-elements/trace metals (Zn and Cu) and toxic elements (Pb and As), *Biol. Trace Elem. Res.* 202 (2024) 1477–1502, <https://doi.org/10.1007/s12011-023-03784-z>.
- [3] K. Jomova, M. Makova, S.Y. Alomar, S.H. Alwasel, E. Nepovimova, K. Kuca, et al., Essential metals in health and disease, 367, *Chem. Biol. Inter.* 367 (2022) 1–28, <https://doi.org/10.1016/J.CBI.2022.110173>.
- [4] V.O. Adimula, P.C. Onianwa, O. Ilupeju, E. Ayom, A.A. Baba, Assessment of heavy metals in foods and adult dietary intake estimates, *Afr. J. Sci., Technol., Innov. Dev.* 11 (2019) 261–268, <https://doi.org/10.1080/20421338.2018.1556455>.
- [5] L. Tariq, B.A. Bhat, S.S. Hamdani, R.A. Mir, Phytochemistry, pharmacology and toxicity of medicinal plants, *Med. Aromat. Plant. Healthc. Ind. Appl.* (2021) 217–240, https://doi.org/10.1007/978-3-030-58975-2_8.
- [6] E.E. Golia, The impact of heavy metal contamination on soil quality and plant nutrition. Sustainable management of moderate contaminated agricultural and urban soils, using low cost materials and promoting circular economy, *Sustain Chem. Pharm.* 33 (2023), <https://doi.org/10.1016/j.scp.2023.101046>.
- [7] D.A. Hines, K. Eckman, *Indigenous Multipurpose Trees of Tanzania. Uses and Economic Benefits for People, Food and Agricultural organization*, 1993, pp. 1–221. FO:Misc/93/9 Working Paper.
- [8] B. Kříbek, I. Nyambe, O. Sracek, M. Mihaljevič, I. Kněsl, Impact of mining and ore processing on soil, drainage and vegetation in the zambian copperbelt mining districts: a review, *Minerals* 13 (3) (2023), <https://doi.org/10.3390/min13030384>.
- [9] M. Moghimi Dehkordi, Z. Pournuroz Nodeh, K. Soleimani Dehkordi, H. salmanvandi, R. Rasouli Khorjastan, M. Ghaffarzadeh, Soil, air, and water pollution from mining and industrial activities: sources of pollution, environmental impacts, and prevention and control methods, *Results Eng.* 23 (2024) 1–21, <https://doi.org/10.1016/J.RINENG.2024.102729>.
- [10] L.I. Ezemonye, P.O. Adebayo, A.A. Enuneku, I. Tongo, E. Ogbomida, Potential health risk consequences of heavy metal concentrations in surface water, shrimp (*Macrobrachium macrobrachion*) and fish (*Brycinus longipinnis*) from Benin River, Nigeria, *Toxicol. Rep.* 6 (2019) 1–9, <https://doi.org/10.1016/J.TOXREP.2018.11.010>.
- [11] M.M. Ghuniem, N. Gad, M.A. Tahon, L. Ryad, Exposure assessment of pesticide residues, heavy metals, and veterinary drugs through consumption of Egyptian fish samples, *Toxicol. Rep.* 13 (2024) 1–14, <https://doi.org/10.1016/J.TOXREP.2024.101724>.
- [12] C.E. Ugwu, A.M. Igboke, S.M. Suru, C.C. Dike, A.N. Mbachu, H.C.C. Maduka, Evaluating the human health risks of heavy metal contamination in copper and steel factory effluents in Nnewi, Anambra State, Nigeria, *Toxicol. Rep.* 12 (2024) 614–621, <https://doi.org/10.1016/J.TOXREP.2024.05.009>.
- [13] N.O. Eliaza, S.B. Malamla, Y.R. Mabula, A.V. Ntarisa, Human health risk assessment of heavy metals in beer brands from Tanzania market, *Toxicol. Rep.* 13 (2024) 101820, <https://doi.org/10.1016/J.TOXREP.2024.101820>.
- [14] B. Kaninga, R.M. Lark, B.H. Chishala, K.K. Maseka, G.M. Sakala, S.D. Young, A. Tye, E.M. Hamilton, M.J. Watts, Crop uptake of heavy metals in response to the environment and agronomic practices on land near mine tailings in the Zambian Copperbelt Province, *Environ. Geochem Health* 43 (2021), <https://doi.org/10.1007/s10653-021-00849-7>.
- [15] N. Galli, D.D. Chiarelli, M. D'Angelo, M.C. Rulli, Socio-environmental impacts of diamond mining areas in the Democratic Republic of Congo, *Sci. Total Environ.* 810 (2022) 152037, <https://doi.org/10.1016/J.SCTOTENV.2021.152037>.
- [16] J.N. Pieters, N.S. Ndaba, S. Ngcobo, Exploring prioritization of wellbeing and health impacts for mining communities during the mining life cycle within the sub-Saharan Africa context: a systematic review, *BMC Public Health* 25 (2025) 1432, <https://doi.org/10.1186/s12889-025-22691-7>.
- [17] M. M. Pretty, K. O. Odeku, Harmful mining activities, environmental impacts and effects in the mining communities in South Africa: a critical perspective, *Environ. Econ.* 8 (2017), [https://doi.org/10.21511/ee.08\(4\).2017.02](https://doi.org/10.21511/ee.08(4).2017.02).
- [18] L. Chen, M. Zhou, J. Wang, Z. Zhang, C. Duan, X. Wang, S. Zhao, X. Bai, Z. Li, Z. Li, L. Fang, A global meta-analysis of heavy metal(loid)s pollution in soils near copper mines: evaluation of pollution level and probabilistic health risks, *Sci. Total Environ.* 835 (2022) 155441, <https://doi.org/10.1016/J.SCTOTENV.2022.155441>.
- [19] J. Hou, A. Pugazhendhi, R. Sindhu, V. Vinayak, N.C. Thanh, K. Brindhadevi, et al., An assessment of biochar as a potential amendment to enhance plant nutrient uptake, *Environ. Res.* 214 (2022) 113909, <https://doi.org/10.1016/j.envres.2022.113909>.
- [20] Y. Zhu, H. Gu, H. Li, S.S. Lam, M. Verma, H.S. Ng, et al., Phytoremediation of contaminants in urban soils: a review, *Environ. Chem. Lett.* 22 (2024) 355–371, <https://doi.org/10.1007/s10311-023-01663-6>.

- [21] M. Adnan, B. Xiao, M.U. Ali, P. Xiao, P. Zhao, H. Wang, S. Bibi, Heavy metals pollution from smelting activities: a threat to soil and groundwater, *Ecotoxicol. Environ. Saf.* 274 (2024) 116189, <https://doi.org/10.1016/j.ecoenv.2024.116189>.
- [22] B. Chibuye, I.S. Singh, L. Chimuka, K.K. Maseka, Metabolite profiling, phytochemical studies, heavy metal determination and health risk assessment of *Entandrophragma deleuyoi* De Wild in Zambia, *South Afr. J. Bot.* 172 (2024) 663–677, <https://doi.org/10.1016/j.sajb.2024.07.053>.
- [23] B. Chibuye, I.S. Singh, L. Chimuka, M. Mokgaetji, K.K. Maseka, Determination of metals in *Diplorhynchus condylocarpon* (Müll.Arg.) Pichon (Apocynaceae) using ICP OES and health risk assessment, *Toxicol. Environ. Chem.* (2024) 1–26, <https://www.tandfonline.com/doi/full/10.1080/02772248.2024.2419088>.
- [24] Y.F. Chen, M.X. He, H.M. Feng, Q. Liu, J.X. Chen, T. Li, Health risk study of cadmium, chromium, lead and arsenic in reservoir water of Changzhou, China, *J. Environ. Sci. Health A Tox Hazard Subst. Environ. Eng.* 58 (2023) 680–693, <https://doi.org/10.1080/10934529.2023.2206772>.
- [25] USEPA. Regional Screening Levels - USEPA. United States Environmental Protection Agency. 2015. (<http://www.epa.gov/reg3hwmd/risk/human/rb-concentration-table/index.htm>).
- [26] USEPA. Regional Screening Level (RSL) Summary Table: November 2021. Usepa. 2021, 2020 (November). (<http://www.epa.gov/regshwmd/risk/human/Index.Htm>).
- [27] U. Okpanachi, K.A. Yusuf, M.K. Ikubaje, G.C.A. Okpanachi, Effects of egg shell meal on the performance and haematology of layers and their egg quality, *Afr. J. Sci., Technol., Innov. Dev.* 13 (2021) 204–215, <https://doi.org/10.1080/20421338.2020.1838111>.
- [28] R. Ketritz, J. Loffin, Potassium homeostasis – physiology and pharmacology in a clinical context, *Pharmacol. Ther.* 249 (2023) 1–23, <https://doi.org/10.1016/j.pharmthera.2023.108489>.
- [29] S. Ashique, S. Kumar, A. Hussain, N. Mishra, A. Garg, B.H.J. Gowda, et al., A narrative review on the role of magnesium in immune regulation, inflammation, infectious diseases, and cancer, *J. Health, Popul. Nutr.* 42 (2023) 1–14, <https://doi.org/10.1186/s41043-023-00423-0>.
- [30] M.A. Farag, B. Abib, Z. Qin, X. Ze, S.E. Ali, Dietary macrominerals: updated review of their role and orchestration in human nutrition throughout the life cycle with sex differences, *Curr. Res Food Sci.* 6 (2023) 1–14, <https://doi.org/10.1016/j.crf.2023.100450>.
- [31] A.-A.-H. Ali, Overview of the vital roles of macro minerals in the human body, *J. Trace Elem. Miner.* 4 (2023) 1–11, <https://doi.org/10.1016/J.JTEMIN.2023.100076>.
- [32] A.W. Hansen, K.V. Venkatachalam, Sulfur-element containing metabolic pathways in human health and crosstalk with the microbiome, *Biochem. Biophys. Rep.* 35 (2023) 1–14, <https://doi.org/10.1016/j.bbrep.2023.101529>.
- [33] A.O. Ogunniran, O.S. Dauda, D. Rotimi, F.C. Jegede, D.J. Falodun, P.O. Adekunle, Nutritional, phytochemical, and antimicrobial properties of *Senna siamea* leaves, *Toxicol. Rep.* 13 (2024) 101793, <https://doi.org/10.1016/J.TOXREP.2024.101793>.
- [34] F. Karahan, I.I. Ozyigit, I.A. Saracoglu, I.E. Yalcin, A.H. Ozyigit, A. Ilcim, Heavy metal levels and mineral nutrient status in different parts of various medicinal plants collected from eastern mediterranean region of Turkey, *Biol. Trace Elem. Res.* 197 (2020), <https://doi.org/10.1007/s12011-019-01974-2>.
- [35] S. Ahmed, M.F. Uddin, M.S. Hossain, A. Jubair, M.N. Islam, M. Rahman, Heavy metals contamination in shrimp and crab from southwest regions in Bangladesh: possible health risk assessment, *Toxicol. Rep.* 10 (2023) 580–588, <https://doi.org/10.1016/J.TOXREP.2023.05.001>.
- [36] S.J. Mandriota, Aluminum and its carcinogenic traits, *Pers. Care Prod. Hum. Health* (2023) 331–360, <https://doi.org/10.1016/B978-0-323-99684-6.00006-9>.
- [37] C. Singh, R. Singh, A. Shekhar, Oxidative stress in cadmium toxicity in animals and its amelioration, *Cadmium Toxic. Mitig.* (2024) 391–411, https://doi.org/10.1007/978-3-031-47390-6_15.
- [38] A.T. Mlangeni, Health risk assessment of toxic metal(oids) (As, Cd, Pb, Cr, and Co) via consumption of medicinal herbs marketed in Malawi, *Toxicol. Rep.* 11 (2023) 145–152, <https://doi.org/10.1016/J.TOXREP.2023.07.004>.
- [39] A. Saouli, O. Adjroud, M. Ncir, A. Bachir, F.A. El, Attenuating effects of selenium and zinc against hexavalent chromium-induced oxidative stress, hormonal instability, and placenta damage in preimplanted rats, *Environ. Sci. Pollut. Res.* 30 (2023) 60050–60079, <https://doi.org/10.1007/s11356-023-26700-3>.
- [40] M.M. Islam, A.A. Mohana, M.A. Rahman, M. Rahman, R. Naidu, M.M. Rahman, A comprehensive review of the current progress of chromium removal methods from aqueous solution, *Toxics* 11 (2023), <https://doi.org/10.3390/toxics11030252>.
- [41] S. Ullah, Q. Liu, S. Wang, A.U. Jan, H.M.A. Sharif, A. Ditta, G. Wang, H. Cheng, Sources, impacts, factors affecting Cr uptake in plants, and mechanisms behind phytoremediation of Cr-contaminated soils, *Sci. Total Environ.* 899 (2023) 165726, <https://doi.org/10.1016/J.SCITOTENV.2023.165726>.
- [42] S. Samrana, A. Ali, U. Muhammad, A. Azizullah, H. Ali, M. Khan, S. Naz, M. D. Khan, S. Zhu, J. Chen, Physiological, ultrastructural, biochemical, and molecular responses of glandless cotton to hexavalent chromium (Cr6+) exposure, *Environ. Pollut.* 266 (2020) 115394, <https://doi.org/10.1016/J.ENVPOL.2020.115394>.
- [43] A. Naz, A. Chowdhury, R. Chandra, B.K. Mishra, Potential human health hazard due to bioavailable heavy metal exposure via consumption of plants with ethnobotanical usage at the largest chromite mine of India, *Environ. Geochem Health* 42 (2020), <https://doi.org/10.1007/s10653-020-00603-5>.
- [44] W. Begum, S. Rai, S. Banerjee, S. Bhattacharjee, M.H. Mondal, A. Bhattarai, A. et al., A comprehensive review on the sources, essentiality and toxicological profile of nickel, *RSC Adv.* 12 (2022) 9139–9153, <https://doi.org/10.1039/d2ra00378c>.
- [45] K. Renu, R. Chakraborty, H. Myakala, R. Koti, A.C. Famurewa, H. Madhyastha, et al., Molecular mechanism of heavy metals (Lead, Chromium, Arsenic, Mercury, Nickel and Cadmium) - induced hepatotoxicity – A review, *Chemosphere* 271 (2021), <https://doi.org/10.1016/j.chemosphere.2021.129735>.
- [46] L. dos Santos, S.R. Bertoli, R.A. Ávila, V.B. Marques, Iron overload, oxidative stress and vascular dysfunction: evidences from clinical studies and animal models, *Biochim Biophys. Acta Gen. Subj.* 1866 (2022) 1–10, <https://doi.org/10.1016/j.bbagen.2022.130172>.
- [47] J. Wan, H. Ren, J. Wang, Iron toxicity, lipid peroxidation and ferroptosis after intracerebral haemorrhage, *Stroke Vasc. Neurol.* 4 (2019) 93–95, <https://doi.org/10.1136/svn-2018-000205>.
- [48] N.D.R.O. Ijere, I.O. JN, M. IC, O. OI, Bioaccumulation of PAHs and heavy metals by waterleaf and fluted pumpkin harvested in four communities around hairdressing salon facilities in Abia State, Nigeria, *J. Environ. Sci. Public Health* 06 (2022) 281–298, <https://doi.org/10.26502/jesph.96120174>.
- [49] C.M. Yang, M.Y. Chien, P.C. Chao, C.M. Huang, C.H. Chen, Investigation of toxic heavy metals content and estimation of potential health risks in Chinese herbal medicine, *J. Hazard Mater.* 412 (2021), <https://doi.org/10.1016/j.jhazmat.2021.125142>.
- [50] N.H. Ghorji, T. Ghorji, M.Q. Hayat, S.R. Imadi, A. Gul, V. Altay, et al., Heavy metal stress and responses in plants, *Int. J. Environ. Sci. Technol.* 16 (2019) 1807–1828, <https://doi.org/10.1007/s13762-019-02215-8>.
- [51] S. Dubey, M. Shri, A. Gupta, V. Rani, D. Chakraborty, Toxicity and detoxification of heavy metals during plant growth and metabolism, *Environ. Chem. Lett.* 16 (2018) 1169–1192, <https://doi.org/10.1007/s10311-018-0741-8>.
- [52] S. Kumar, S. Kumar, T. Mohapatra, Interaction between macro- and micro-nutrients in plants, *Front. Plant Sci.* 12 (2021) 1–9, <https://doi.org/10.3389/fpls.2021.665583>.
- [53] H.W. Tan, Y.L. Pang, S. Lim, W.C. Chong, A state-of-the-art of phytoremediation approach for sustainable management of heavy metals recovery, *Environ. Technol. Innov.* 30 (2023) 1–24, <https://doi.org/10.1016/j.eti.2023.103043>.
- [54] B. Chibuye, I.S. Singh, L. Chimuka, K.K. Maseka, In silico and ADMET molecular analysis targeted to discover novel anti-inflammatory drug candidates as COX-2 inhibitors from specific metabolites of *Diospyros batokana* (Ebenaceae), *Biochem Biophys. Rep.* 39 (2024) 1–13, <https://doi.org/10.1016/j.bbrep.2024.101758>.
- [55] D. Wu, Q. Chen, X. Chen, F. Han, Z. Chen, Y. Wang, The blood–brain barrier: structure, regulation, and drug delivery, *Signal Transduct. Target. Ther.* 8 (2023) 1–26, <https://doi.org/10.1038/s41392-023-01481-w>.
- [56] Z. Wang, Y. Sun, W. Yao, Q. Ba, H. Wang, Effects of cadmium exposure on the immune system and immunoregulation, *Front. Immunol.* 12 (2021) 1–15, <https://doi.org/10.3389/fimmu.2021.695484>.
- [57] A. Pathak, V. Asediya, P. Anjaria, S.P. Singh, Health risk linked to Cr toxicity in food and environment, *Environ. Sci. Eng.* F1975 (2023), https://doi.org/10.1007/978-3-031-44029-8_10.
- [58] R. Nieder, D.K. Benbi, F.X. Reichl, Macro- and secondary elements and their role in human health, *Soil Compos. Hum. Health* (2018) 257–315, https://doi.org/10.1007/978-94-024-1222-2_6.