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# Metals and metalloid in medicinal plants: occurrence and risk assessment to human health

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# Abstract

**Aim:** This study was aimed at determining the levels of trace elements in six medicinal plants of tropical origin.

**Methods:** The levels of As, Cd, Co, Cu, Fe, Mn, Ni, Pb, and Zn in *Albizia glaberrima* (AG), *Aristolochia ringens* (AR), *Brysocarpus coccineus* (BC), *Ipomoea asarifolia* (IA), *Sansevieria liberica* (SL), and *Telfairia occidentalis* (TO) were determined using an inductively coupled plasma-mass spectrometry. The estimated dietary intakes of the metals, hazard quotients (HQ), and hazard index (HI) were calculated.

**Results:** The highest levels of Cd, Pb, Zn, and Fe were detected in IA. BC had the highest levels of Mn and Ni while AR had the highest levels of Cu, Co, and As. However, the levels of the metals were mostly below the permissible limits in the plants. The estimated dietary weekly intakes (EWIs) were below the provisional tolerable weekly intake for each chemical element. The EWIs range values were  $21.566-643.114 \mu g/kg$  per day (kg is the unit of body weight),  $0.008-1.529 \mu g/kg$  per day,  $0.6-7.815 \mu g/kg$  per day,  $67.569-215.889 \mu g/kg$  per day,  $4.305-185.451 \mu g/kg$  per day,  $0.225-1.704 \mu g/kg$  per day,  $1.03-10.2 \mu g/kg$  per day,  $0.933-2.286 \mu g/kg$  per day, and  $62.554-854.4 \mu g/kg$  per day for Cu, Cd, Pb, Zn, Mn, Co, Ni, As, and Fe, respectively. The HQ values of the elements were less than 1 except for Cu in AR (1.321). The values of lifetime cancer risks exceeded the permissible limit in all the plant materials.

**Conclusions:** The findings from the study revealed that the consumption of TO, SL, and AG for medicinal purposes has no inherent non-carcinogenic toxicity while the consumption of AR, IA, and BC has some risks of non-carcinogenic toxic. However, the six plant materials showed inherent risks of carcinogenic events, as

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such their use for medicinal purposes must be cautious, maybe by reducing both the ingestion rate and the frequency of intake.

# **Keywords**

Traditional medicine, medicinal plants, toxic elements contamination, health risk assessment, inductively coupled plasma-mass spectrometry

# Introduction

The awareness of medicinal plants' potential in treating several human ailments has increased considerably over the years [1, 2]. The increased acceptance of medicinal plants in human treatments could be partly due to their availability, cost-effectiveness, and potency, with little or no side effects, compared to orthodox medicines that are often associated with certain side effects [3, 4]. Traditionally, herbal medicines are taken as a decoction in which the bioactive ingredients in the plant materials are extracted in solvents such as water or ethanol [5].

The tropical and subtropical climates support the cultivation of important botanicals that exhibit medicinal properties [6–8]. The pharmacological properties of these botanicals have been attributed to certain bioactive constituents and secondary metabolites such as flavonoids, polyphenols, saponins, and tannins [9, 10]. The potential of plant materials has been optimally explored in some countries, especially in Asia, where plant-based traditional medicine and herbal remedies are quite popular [11, 12].

The six plant materials being considered in this study have demonstrated ample medicinal properties. The different parts of *Sansevieria liberica* (SL, Agavaceae), commonly referred to as the "African bowstring hemp", have shown to be promising in treating human diseases. The juice extracted from its leaf has been used to treat venereal diseases, including gonorrhea. The leaf sap is used for treating ulcers, and when topically applied, it is used for treating toothache. The fermented rhizome has also been used for malaria treatment, and root decoction has been used to treat convulsions [13, 14]. Similarly, the various leaf extracts have demonstrated anticancer potentials both *in vitro* and *in vivo* [15]. *Ipomoea asarifolia* (IA, Convolvulaceae), commonly known as "morning glory", has been used to treat malaria, diabetes, rheumatism, elephantiasis, and syphilis [16]. The leaf extracts of *Brysocarpus coccineus* (BC) are analgesic, anti-inflammatory, and antipyretic [17]. Also, the extracts of *Albizia glaberrima* (AG) have analgesic, anti-inflammatory and antipyretic properties [18]. The leaf extracts of *Telfairia occidentalis* (TO) were anti-inflammatory and antinociceptive [19], while the root extract of *Aristolochia ringens* (AR) had anticancer activity [20].

Notwithstanding the numerous health benefits of medicinal plants, their inherent contamination with toxic chemical elements is a public health concern. Some studies have reported elevated levels of toxic elements in medicinal plants from different parts of the world. Luo et al. [21] detected Cd, Pb, As, and Hg in Chinese medicinal herbs at levels that pose serious risks to human health. In a study on Indian medicinal plants, the levels of Cd and Hg were detected at concentrations that exceeded the permissible levels for the elements in medicinal plants [22]. In Brazilian medicinal plants, the detected levels of most elements were within the acceptable limits except for Cd which was present at levels higher than the acceptable limit [23]. The contamination of medicinal herbs with toxic elements has been linked to various human anthropogenic activities, which release the toxic chemical elements (including toxic metals and metalloids) into the environment and are subsequently uptake by the plants from the soil [24]. The literature is rich on the adverse effects of toxic chemical elements on humans such as carcinogenicity, immunotoxicity, oxidative stress, organ damage, and competition with essential elements such as Zn and Gu, thus limiting their bioavailability [25–28].

The regulation of contaminants (toxic metals, in particular) in medicinal plants is lacking or poorly enforced in several countries, especially in Africa [29, 30]. Given the evidence that toxic metals sometimes accumulate within the plant tissues and the wide consumption of medicinal plants for health purposes, studies on health risk assessment of contaminants in medicinal plants become imperative. Therefore, this

study aimed to determine the levels of some metals and metalloids in six Nigerian medicinal plants and perform a risk assessment of the elements through the consumption of these plants.

# **Materials and methods**

# **Collection and preparation of plant materials**

The plant materials used in the study were the roots of AR and SL, the leaves of BC, IA, and TO, and the stem bark of AG. The plant materials were obtained from different parts of Nigeria; the details, including classification, source, and reported medical benefits, are shown in Table 1. The plant materials were identified and authenticated at the Forestry Research Institute of Nigeria (FRIN), Ibadan, Nigeria, and the Department of Botany, Faculty of Science, University of Lagos, Lagos, Nigeria.

Medicinal plant	Common name	Family	Collection site	Medicinal uses	References	
AG	White nongo	Leguminosae	Abatadu village, Ikire Osun State, Nigeria (7°30'0"N, 4°30'0"E)	Fever, pain, epilepsy, rheumatism, and inflammation	[18, 50]	
AR	Dutchman's pipe or Snakework	Aristolochiaceae	Mushin, Lagos State, Nigeria (6°32'0"N, 3°21'0"E)	Cancer, asthma, skin diseases, typhoid, sores, snake poison, diabetes, parasitic infections, inflammation	[20, 51–53]	
BC	Crimson thyme	e Connaraceae	lju-Ogundimu, Ifako- ljaiye, Lagos State, Nigeria (6°39'50"N, 3°20'17"E)	Swellings, tumors, hemorrhage, pain, diarrhea, skin and mouth disorders, German measles, jaundice, gonorrhea, urinary problems, impotence, anemia, primary and secondary sterility	[17, 50, 54– 56]	
IA	Morning glory Convolvulaceae		Akinmorin Town, Oyo State, Nigeria (7°46'59"N, 3°57'0"E)	Malaria, diabetes, rheumatism, elephantiasis, syphilis, neuralgia, arthritic pain, and stomach ache	[16, 57]	
SL	African bowstring hemp	Agavaceae	Mushin, Lagos State, Nigeria (6°32'0"N, 3°21'0"E)	Cancer, gonorrhea, ulcer, toothache, malaria, convulsion	[13–15]	
ТО	Fluted pumpkin	Cucurbitaceae	Oshodi, Lagos, Nigeria (6°30'51"N, 3°18'31"E)	Cancer, diabetes, cardiovascular diseases, infertility, anaemia, inflammation	[19, 58]	

Table 1. Some details about the medicinal plants used in the study

N: northern latitude; E: east longitude

The roots of AR and SL, and the stem bark of AG were chopped into small pieces and allowed to air-dry in the laboratory until constant weights were obtained. Also, fresh leaves of BC, IA, and TO were air-dried at room temperature until constant weights were obtained. The dried plant materials were pulverized into powder using a blender. The plant powder was digested following the methods reported by Adeyemi et al. [31]. A portion of 100 mg of each powder was weighed in triplicate into a polypropylene tube of 15 mL, followed by the addition of 1 mL of nitric acid (20% v/v, CAS: 7697-37-2, Sigma-Aldrich) and 2 mL of hydrogen peroxide (30% v/v, CAS: 7722-84-1, Sigma-Aldrich). The mixture was placed in a microwave oven (Ethos D, Milestone, Sorisole, Italy) for 40 min to effect digestion. The digests were allowed to cool and made up to 10 mL with ultrapure water (Milli-Q System).

# Determination of levels of elements in the plant materials

The levels of the following elements, As, Cd, Co, Cu, Fe, Mn, Ni, Pb, and Zn were determined in the digests of the plant materials using an inductively coupled plasma mass spectrometer (ICP-MS) equipped with a reaction cell (DRC-ICP-MS ELAN DRCII, PerkinElmer, Sciex, Norwalk, CT, USA). The equipment was operated with high-purity argon (99.999%, Praxair, Brazil). The samples were introduced into the equipment through a quartz cyclonic spray chamber and a Meinhard nebulizer connected by Tygon<sup>®</sup> tubes to the ICP-MS's peristaltic pump (set at 35 r/min). The ICP-MS was operated with a Perkin Elmer platinum sampler and skimmer cones. The standards were prepared by the multi-element stock solution containing 10 mg/L of each element. The internal standard (10 mg/L Rh, CAS: 7440-16-6, Perkin Elmer) was added online. Before each run, 0.005% (v/v) Triton X-100 (CAS: 9036-19-5, Sigma-Aldrich) in 2% (v/v) nitric acid (HNO<sub>3</sub>, CAS: 7697-37-2, Sigma-Aldrich) was prepared and applied as the rinse solution.

#### Quality control of data

The accuracy of the method used for the elemental analyses was checked by determining the levels of elements in a standard reference material, SRM 8415 whole egg powder, which was obtained from the National Institute of Standards and Technology (NIST). The whole egg powder was digested along with the plant powders, and the digests were quantified for elemental composition. The measured concentrations of the elements were compared to the targeted values for each element, and the measured and targeted values were similar (Table 2). The method limit of detection (LOD) was determined using the equation formula:

## $LOD = 3.3 \times (SD/slope)$

Where SD represents the standard deviation of twenty consecutive measurements of the blanks, and the slope was determined from the calibration curve. The LODs were 0.034 ng/g, 0.008 ng/g, 0.006 ng/g, 0.479 ng/g, 2,081 ng/g, 0.096 ng/g, 0.507 ng/g, 0.059 ng/g, and 7.302 ng/g for As, Cd, Co, Cu, Fe, Mn, Ni, Pb, and Zn, respectively. The method's precision for between- and within-batch analyses for the element was less than 14% and 5%, respectively (n = 10, SRM 8415 whole egg powder).

Analytes	Target value	Detected value	
As (ng/g)	10	14 ± 0.1	
Cd (ng/g)	5	4 ± 0.2	
Co (ng/g)	12 ± 5	17 ± 3	
Cu (µg/g)	2.7 ± 0.35	3.1 ± 0.3	
Mg (µg/g)	305 ± 27	290 ± 21	
Mn (µg/g)	1.78 ± 0.38	1.74 ± 0.3	
P (mg/g)	10.01 ± 0.32	9.74 ± 0.43	
Sb (µg/g)	2	1.73 ± 0.12	

 $1.44 \pm 0.15$ 

 $471 \pm 27$ 

66.2 ± 3.7

Table 2. The concentrations of elements in the NIST standard reference material (SRM 8415 egg powder)

The values are mean  $\pm$  SD of five replicates

Se (mg/g) V (µg/g)

Zn (µg/g)

#### Non-carcinogenic risk assessment of consumption of medicinal plants

#### Estimation of dietary intakes of metals/metalloid

The dietary intake of each element was calculated using the formula:

 $1.39 \pm 0.17$ 

459 ± 81

67.5 ± 7.6

 $EDI = C_m \times IR/body$  weight

In the equation, EDI corresponds to the estimated dietary daily intake  $\mu$ g/kg per day (kg is the unit of body weight), C<sub>m</sub> is the mean concentration of the element as determined in the samples ( $\mu$ g/g), and IR is the ingestion rate of the medicinal plant. The IR values in unfinished herbal products are lacking. However, the IR was assumed to be 200 g/day in this study, representing a worst-case scenario [32]. Subsequently, the estimated dietary weekly intakes (EWIs) were calculated by multiplying the EDI values by 3 (frequency of consumption per week). The EWI values were then compared with the provisional tolerable weekly intake (PTWI) values for each element obtained from the Joint Food and Agriculture Organization (FAO)/World Health Organization (WHO) Expert Committee on Food Additives (JECFA).

## Estimation of chronic dietary daily intake of metals/metalloids

The chronic dietary daily intake of the elements was calculated based on the reported study by Geronimo et al. [33] using the formula:

 $CDI = EDI \times EFr \times ED_T / AT$ 

Where CDI is the chronic dietary daily intake ( $\mu$ g/kg per day), EFr is the frequency of exposure, which is taken to be 90 days, the ED<sub>T</sub> is the total exposure duration, taken as 30 years for a non-carcinogenic chronic exposure in an adult while AT is the average exposure time (days) for a non-carcinogenic event in an adult, which is taken as 30 years × 365 days/year = 10,950 days.

#### Estimation of target hazard quotients and total hazard index

The target hazard quotients (HQ) for each element were determined using the formula:

HQ = CDI/RfD

RfD is the oral reference dose for each element. The RfD values ( $\mu$ g/kg per day) used were obtained from the United States Environmental Protection Agency as follows: Cu: 40, Cd: 0.5, Pb: 3.5, Rb: 5, Zn: 300, Mn: 140, Se: 5, Co: 0.3, Ni: 20, As: 0.3, and Fe: 700. A target HQ (THQ) value (< 1) is considered no risk while THQ values (> 1) are considered to have non-carcinogenic risks. The total hazard index (THI) was calculated by finding the summation of the THQs for all the elements of each plant material.

#### Estimation of lifetime cancer risks

The lifetime cancer risks (CR) of As, Cd, Ni, and Pb were estimated using the formula:

 $CR = (EDI \times EFr \times ED_T^* / AT^*) \times SF$ 

Wherethe  $ED_{T}^{*}$  is taken as 70 years for a carcinogenic chronic exposure in an adult while AT<sup>\*</sup> is the average exposure time (days) for a carcinogenic event in an adult, which is taken as 70 years × 365 days/year = 25,550 days, and SF is the slope factor taken as 1.5 mg/kg per day, 6.7 mg/kg per day, 0.91 mg/kg per day, and 0.0085 mg/kg per day for As, Cd, Ni, and Pb respectively.

#### **Statistical analyses**

The data on the levels of elements in the plant materials were first checked for normality using the Shapiro-Wilk test, and because the data did not fit the Gaussian distribution, significant differences in the mean concentrations were determined non-parametrically using the Kruskal-Wallis test. This was followed by Dunn's multiple comparison tests in circumstances of significant differences. The data were presented as mean  $\pm$  SD. Statistical analyses were performed with GraphPad Prism (version 8), and statistical significance was assumed at P < 0.05.

## Results

#### Levels of metals/metalloids in medicinal plants

The concentrations of the metals/metalloids in the plant materials are shown in Table 3. The mean levels of the elements differed significantly among the medicinal plants (P < 0.05). The highest Cd, Pb, Zn, and Fe levels were detected in IA. BC had the highest levels of Mn and Ni, while the highest Cu, Co, and As levels were detected in AR. Although several metals/metalloids were detected in the medicinal plants, however, the levels were mostly below the permissible limits for each of the elements set by the JECFA, except for Mn, As, and Fe in which the levels were above the permissible limits in some plants. The levels of detected Mn were above the permissible limit in five (BC, AG, AR, SL, and IA) of the six medicinal plants used in the study. The levels of As in IA were about 10-fold higher than the permissible limit, while the levels of detected Fe in AR, and IA were well above the allowable limit.

#### EWIs of metals/metalloids through consumption of medicinal plants

The EWIs values of the elements through the consumption of medicinal plants are shown in Table 4. The EWIs ranges were  $21.566-43.114 \mu g/kg$  per day,  $0.008-1.529 \mu g/kg$  per day,  $0.281-7.815 \mu g/kg$  per day,  $67.569-215.889 \mu g/kg$  per day,  $4.305-185.451 \mu g/kg$  per day,  $0.225-1.704 \mu g/kg$  per day,  $1.03-10.2 \mu g/kg$  per day,  $0.933-2.286 \mu g/kg$  per day, and  $62.554-854.4 \mu g/kg$  per day for Cu, Cd, Pb, Zn, Mn, Co, Ni, As, and Fe respectively. The highest EWIs of Cd, Pb, Zn, and Fe were detected in IA, BC had the highest EWIs of Mn and Ni, while the highest EWIs of Cu, Co, and As were detected in AR.

#### Non-carcinogenic and carcinogenic risk assessments

The CDI and HQ/hazard index (HI) for the elements in the medicinal plants are shown in Tables 5 and 6, respectively. The non-carcinogenic risk assessment of the metals/metalloids through the consumption of

Table 3. Levels of metals and metalloids (µg/g) in Nigerian medicinal plants

Elements	BC	AG	AR	то	SL	IA	PL
Cu	2.516 ± 0.121 <sup>ª</sup>	2.794 ± 0.249 <sup>a</sup>	75.03 ± 0.202 <sup>b</sup>	3.626 ± 0.49 <sup>a</sup>	3.065 ± 0.136 <sup>a</sup>	3.159 ± 0.321 <sup>ª</sup>	150
Cd	$0.002 \pm 0.000^{a}$	$0.001 \pm 0.000^{a}$	$0.008 \pm 0.001^{b}$	$0.003 \pm 0.000^{a}$	$0.008 \pm 0.000^{b}$	0.178 ± 0.000 <sup>c</sup>	0.3
Pb	0.254 ± 0.001 <sup>c</sup>	$0.033 \pm 0.002^{a}$	$0.379 \pm 0.034^{d}$	$0.084 \pm 0.004^{b}$	$0.07 \pm 0.000^{b}$	0.912 ± 0.118 <sup>e</sup>	10
Zn	$7.883 \pm 0.119^{a}$	$8.997 \pm 0.314^{a}$	$9.715 \pm 0.056^{a}$	$10.528 \pm 0.823^{a}$	13.709 ± 1.499 <sup>b</sup>	25.187 ± 0.063 <sup>c</sup>	50
Mn	$21.636 \pm 3.47^{d}$	$2.016 \pm 0.062^{b}$	3.397 ± 0.164 <sup>b</sup>	$0.502 \pm 0.013^{a}$	7.118 ± 0.033 <sup>c</sup>	$2.098 \pm 0.055^{b}$	2
Со	0.158 ± 0.005 <sup>c</sup>	$0.026 \pm 0.002^{a}$	$0.199 \pm 0.002^{\circ}$	$0.033 \pm 0.000^{a}$	$0.093 \pm 0.018^{b}$	$0.12 \pm 0.006^{b}$	0.48
Ni	1.19 ± 0.029 <sup>c</sup>	$0.298 \pm 0.017^{b}$	$0.748 \pm 0.02^{bc}$	$0.369 \pm 0.18^{b}$	$0.416 \pm 0.091^{b}$	$0.12 \pm 0.006^{a}$	1.5
As	$0.166 \pm 0.024^{b}$	$0.122 \pm 0.001^{a}$	$0.267 \pm 0.019^{b}$	$0.206 \pm 0.036^{a}$	$0.109 \pm 0.001^{a}$	$0.138 \pm 0.006^{a}$	10
Fe	$7.746 \pm 0.1585^{a}$	$7.298 \pm 0.024^{a}$	$33.53 \pm 0.427^{\text{b}}$	17.2 ± 1.46ª	$14.58 \pm 5.694^{a}$	$99.68 \pm 4.044^{\circ}$	20

Data with the same superscripts in the same row are not statistically different from one another. Values are mean  $\pm$  SD of three replicates. The SD values which are less than 0.0001 were written as 0.000 in this table. PL: permissible limits

Table 4. EWIs (µg/kg per day) of metals and metalloids in Nigerian medicinal plants

Medicinal plants	Cu	Cd	Pb	Zn	Mn	Со	Ni	As	Fe
BC	21.566	0.014	2.177	67.569	185.451	1.351	10.2	1.424	66.394
AG	23.949	0.008	0.281	77.117	17.28	0.225	2.555	1.043	62.554
AR	43.114	0.065	3.247	83.271	29.117	1.704	6.409	2.286	287.4
то	31.08	0.025	0.719	90.24	4.305	0.284	3.162	1.769	147.429
SL	26.271	0.073	0.6	117.506	61.011	0.797	3.567	0.933	124.971
IA	27.077	1.529	7.815	215.889	17.983	1.03	1.03	1.184	854.4
PTWI*	3,500	7	25	7,000	2,500	NE	35	15	5,600

\* Values are obtained from the JECFA. NE: not estimated

medicinal plants was performed by calculating the values of HQs and HIs for each element. The HQ and HI values (< 1) are considered safe and non-carcinogenic, while HQ and HI values (> 1) pose health risks to consumers [21]. The HQ values of the elements were less than one except for Cu in AR in which the HQ was 1.321. The THI values were 1.035, 0.454, 2.601, 0.705, 0.652, and 1.271 for BC, AG, AR, TO, SL, and IA respectively. The plant materials can therefore be arranged as AR > IA > BC > TO > SL > AG with the first three considered non-carcinogenic risky.

Table 5. Estimated CDI ( $\mu$ g/kg per day) of metals and metalloids in Nigerian medicinal plants

						-		-			
Plants	Cu	Cd	Pb	Rb	Zn	Mn	Se	Co	Ni	As	Fe
BC	1.773	0.001	0.179	7.022	5.554	15.243	2.983	0.111	0.838	0.117	5.457
AG	1.968	0.001	0.023	8.916	6.338	1.42	2.588	0.019	0.21	0.086	5.141
AR	52.859	0.005	0.267	8.786	6.844	2.393	1.444	0.14	0.527	0.188	23.622
то	2.555	0.002	0.059	16.559	7.417	0.354	2.177	0.023	0.26	0.145	12.117
SL	2.159	0.006	0.049	18.276	9.658	5.015	0.566	0.066	0.293	0.077	10.272
IA	2.226	0.126	0.642	17.744	17.744	1.478	1.544	0.085	0.085	0.097	70.225

Table 6. THQ and THI of metals and metalloids in Nigerian medicinal plants

Plants	Cu	Cd	Pb	Zn	Mn	Со	Ni	As	Fe	тні
BC	0.044	0.002	0.051	0.019	0.109	0.37	0.042	0.39	0.008	1.035
AG	0.049	0.001	0.007	0.021	0.01	0.062	0.011	0.286	0.007	0.454
AR	1.321	0.011	0.076	0.023	0.017	0.467	0.026	0.626	0.034	2.601
то	0.064	0.004	0.017	0.025	0.003	0.078	0.013	0.485	0.017	0.705
SL	0.054	0.012	0.014	0.032	0.036	0.218	0.015	0.256	0.015	0.652
IA	0.056	0.251	0.184	0.059	0.011	0.282	0.004	0.324	0.1	1.271

The estimation of lifetime CR of four known carcinogenic metals (As, Cd, Ni, and Pb) is shown in Table 7. The range values of estimated CR were 0.004–0.842, 0.002–0.382, 0.077–0.763, and 0.115–0.282 for Cd, Pb, Ni, and As respectively.

Table 7. Lifetime CR of metals and metalloids in Nigerian medicinal plants

Plants	Cd	Pb	Ni	As	
BC	0.007	0.002	0.763	0.176	
AG	0.004	0.014	0.191	0.129	
AR	0.036	0.159	0.479	0.282	
ТО	0.014	0.035	0.237	0.218	
SL	0.04	0.029	0.267	0.115	
IA	0.842	0.382	0.077	0.146	

# Discussion

The mean levels of the elements detected in the medicinal in this study were comparable to the levels determined for each element in studies from other countries of the world, such as Bangladesh, Brazil, Ghana, Turkey, and India [33–36]. The presence of metals in the plant tissues indicates possible contamination of the soils with toxic metals/metalloids, which were then taken up by the plants through the root [24, 37, 38].

Some elements were detected at levels lower than those detected in medicinal plants from other parts of the world. For example, the detected levels of cadmium in this study were about ten-fold lower than the values detected in medicinal plants from India (<  $LOD = 4 \times 10^{-4}$ ) and Brazil (<  $LOD = 7 \times 10^{-4}$ ) [33, 39]. The detection of metals in the plant materials at low levels in this study was due to the sensitivity of the equipment used for the elemental analyses (ICP-MS). The limits of detection for most of the elements were in the range of part per trillion. This was in contrast to the studies by Kulhari et al. [39] and Geronimo et al. [33], in which the sensitivity of the equipment for elemental analyses was low, and that could explain the reason why certain elements were detected even at low levels in this study.

Most of the elements detected in the medicinal plants in this study are essential elements known to play important physiological and biochemical roles in humans. In this context, Cu, Zn, and Mn are known to play essential roles in maintaining the redox homeostasis of the body through their potential to scavenge deleterious reactive oxygen species [40, 41]. Fe is an important component of hemoglobin, the molecule responsible for transporting oxygen and other nutrients within the body [42]. Co is a component of vitamin B12 required for red blood cell formation [43]. However, the plant materials also detected certain toxic elements such as Cd, Pb, As, and Ni. These elements are known to cause various physiological disorders in humans; Cd and Pb have been shown to be carcinogenic and nephrotoxic, causing damage to the kidney [44, 45]. They have also been able to cause oxidative stress in humans [46]. As has reportedly resulted in endocrine disruption, immune dysfunction, and disruption of cellular metabolism in humans [27, 28]. Ni is carcinogenic and causes damage to important body organs such as the lungs, stomach, and kidneys [26]. Comparing the EWI values of the elements in the plant materials to the PTWI values for each element revealed that the levels were below the limits for all the elements. Based on the PTWI values, the consumption of medicinal plants to treat ailments and diseases may not pose health risks to humans.

Although several studies have evaluated the risk assessment of toxic metals through the consumption of herbal medicines, however only one study has performed the risk assessment of AR of the six plant materials used in this study [47], while this is the first study to carry out a risk assessment of toxic metals in the remaining five plant materials. The use of HQ and hazard indices for risk assessments of toxicants in food or edible substances is quite popular [47, 48]. The data obtained from the calculation of the HQ alone implies that all six plant materials were safe for human consumption, considering their HQ values were less than 1. However, when considering the HI values, three plant materials were safe for consumption without risk of non-carcinogenic events. At the same time, the other three, AR, IA, and BC were found to have potential risks of non-carcinogenic toxicity. These findings were similar to the reports of Odukoya et al. [47], which also reported a high risk of non-carcinogenic toxicity due to the consumption of AR from Nigeria. In another study, Ghasemidehkordi et al. [49] reported an HQ value of less than 1 for Hg through consumption of herbs collected from Iran, which would imply a no risk of non-carcinogenic toxicity. However, this assumption could not be upheld when the HI value was considered. Hence, the risk assessment of non-carcinogenic toxicity of edible substances should include multiple parameters. Little is still known about the impacts of environmental contaminants in herbal products on human health probably due to the paucity of human biomonitoring studies on this topic, as such future research efforts should be geared in this direction, which will help to better understand the risks of environmental contaminants in herbal products.

The acceptable limits of CR of toxic metals ranged between  $10^{-6}$  to  $10^{-4}$  [21]. The estimated CR of the elements in all the six plants in the present study exceeded this range, hence there are potential risks of carcinogenic events through consumption of these medicinal plants. These findings are particularly unexpected since As, Cd, Ni, and Pb have been reported as carcinogens [21, 25–28].

In conclusion, the results from this study showed that the six medicinal plant materials used in this study contained the analyzed metals and metalloids at comparable levels or below those detected in medicinal plants from other parts of the world. More importantly, the elements were present at levels that were well below the permissible limits for each of the elements set by the Joint Committee of the FAO and WHO, except for occasional instances in a few plants where the levels of Mn, As, and Fe were above the permissible limits. The multi-parameter risk assessment of non-carcinogenic toxicity of the metals indicated that the consumption of TO, SL, and AG for medicinal purposes has no inherent non-carcinogenic toxic effects. Although, the obtained results suggest that the consumption of most of the plants did not pose serious risks of non-carcinogenic toxicity, however, there are inherent risks of carcinogenic toxicity through consumption of the plants for medicinal purposes, as such their use for medicinal purposes must be cautious maybe by reducing both the IR and the frequency of intake.

# **Abbreviations**

AG: Albizia glaberrima AR: Aristolochia ringens **BC: Brysocarpus coccineus** CDI: chronic dietary daily intake CR: cancer risks EDI: estimated dietary daily intake EWIs: estimated dietary weekly intakes HQ: hazard quotients IA: Ipomoea asarifolia ICP-MS: inductively coupled plasma mass spectrometer IR: ingestion rate JECFA: the Joint Food and Agriculture Organization/World Health Organization Expert Committee on Food Additives LOD: limit of detection PTWI: provisional tolerable weekly intake SD: standard deviation SL: Sansevieria liberica THI: total hazard index THQ: target hazard quotients TO: Telfairia occidentalis

# Declarations

# **Author contributions**

JAA: Conceptualization, Methodology, Formal analysis, Funding acquisition, Writing—original draft, Writing—review & editing. AJA: Conceptualization, Formal analysis, Data curation, Writing—original draft, Writing—review & editing. OSS, BAR, VCdOS, VOB, and MCOS: Methodology, Formal analysis, Data curation, Writing—original draft, Writing—review & editing. COA: Conceptualization, Formal analysis, Writing—review & editing, Supervision. FBJ: Conceptualization, Formal analysis, Funding acquisition, Writing—review & editing, Supervision.

### **Conflicts of interest**

Bruno A. Rocha is the GE of Exploration of Foods and Foodomics, but he had no involvement in the journal review process of this manuscript. The authors declare that they have no conflicts of interest.

**Ethical approval** 

Not applicable.

**Consent to participate** 

Not applicable.

**Consent to publication** 

Not applicable.

#### Availability of data and materials

The raw data supporting the conclusions of this manuscript will be made available by the author (Joseph A. Adeyemi, jaadeyemi@futa.edu.ng), without undue reservation, to any qualified researcher.

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# References

- 1. Kasilo OMJ, Wambebe C, Nikiema JB, Nabyonga-Orem J. Towards universal health coverage: advancing the development and use of traditional medicines in Africa. BMJ Glob Health. 2019;4:e001517.
- 2. Khan MSA, Ahmad I. Herbal medicine: current trends and future prospects. In: Khan MSA, Ahmad I, Chattopadhyay D, editors. New look to phytomedicine. Florida: Academic Press; 2019. pp. 3–13.
- Anand U, Jacobo-Herrera N, Altemimi A, Lakhssassi N. A comprehensive review on medicinal plants as antimicrobial therapeutics: potential avenues of biocompatible drug discovery. Metabolites. 2019;9: 258.
- 4. Süntar I. Importance of ethnopharmacological studies in drug discovery: role of medicinal plants. Phytochem Rev. 2020;19:1199–209.
- 5. Lezoul NE, Belkadi M, Habibi F, Guillén F. Extraction processes with several solvents on total bioactive compounds in different organs of three medicinal plants. Molecules. 2020;25:4672.
- 6. Moyo M, Aremu AO, Van Staden J. Medicinal plants: an invaluable, dwindling resource in sub-Saharan Africa. J Ethnopharmacol. 2015;174:595–606.

- 7. de Santana BF, Voeks RA, Funch LS. Ethnomedicinal survey of a maroon community in Brazil's Atlantic tropical forest. J Ethnopharmacol. 2016;181:37–49.
- 8. Bibi F, Abbas Z, Harun N, Perveen B, Bussmann RW. Indigenous knowledge and quantitative ethnobotany of the Tanawal area, Lesser Western Himalayas, Pakistan. Plos One. 2022;17:e0263604.
- 9. Bouyahya A, Belmehdi O, Benjouad A, El Hassani RA, Amzazi S, Dakka N, et al. Pharmacological properties and mechanism insights of Moroccan anticancer medicinal plants: what are the next steps? Ind Crops Prod. 2020;147:112198.
- 10. Ma RH, Ni ZJ, Zhu YY, Thakur K, Zhang F, Zhang YY, et al. A recent update on the multifaceted health benefits associated with ginger and its bioactive components. Food Funct. 2021;12:519–42.
- 11. Elahee SF, Mao H, Shen X. Traditional Indian medicine and traditional Chinese medicine: a comparative overview. Chin Med Cult. 2019;2:105–13.
- 12. Salvilla RCM, Faller EM. Indian and Chinese traditional medicine on COVID-19: a review and perspective. Int J Sci Res Publ. 2021;11:77–81.
- 13. Watt JM, Breyer-Brandwijk MG. The medicinal and poisonous plants of Southern and Eastern Africa. Berlin: Springer; 1962.
- 14. Orabueze IC, Uzor SC, Ndiaye B, Uba D, Ota DA, Agbedahusi J. Antimalarial, antioxidant activities and chemoprofile of *Sansevieria liberica* Gerome and Labroy (Agavaceae) leaf extract. Adv Pharmacol Pharm Sci. 2021;2021:9053262.
- 15. Akindele AJ, Wani ZA, Sharma S, Mahajan G, Satti NK, Adeyemi OO, et al. *In vitro* and *in vivo* anticancer activity of root extracts of *Sansevieria liberica* Gerome and Labroy (Agavaceae). Evid Based Complementary Altern Med. 2015;2015:560404.
- 16. Meira M, Silva EP, David JM, David JP. Review of the genus *Ipomoea*: traditional uses, chemistry and biological activities. Rev Bras Farmacogn. 2012;22:682–713.
- 17. Akindele AJ, Eksioglu EA, Kwan JC, Adeyemi OO, Liu C, Luesch H, et al. Biological effects of *Byrsocarpus coccineus in vitro*. Pharm Biol. 2011;49:152–60.
- 18. Ogbiti VM, Akindele AJ, Adeyemi OO. Analgesic, anti-inflammatory, and antipyretic activities of hydroethanolic stem bark extract of *Albizia glaberrima*. J Herbs Spices Med Plants. 2017;23:44–67.
- 19. Akindele AJ, Oladimeji-Salami JA, Usuwah BA. Antinociceptive and anti-inflammatory activities of *Telfairia occidentalis* hydroethanolic leaf extract (Cucurbitaceae). J Med Food. 2015;18:1157–63.
- 20. Akindele AJ, Wani Z, Mahajan G, Sharma S, Aigbe FR, Satti N, et al. Anticancer activity of *Aristolochia ringens* Vahl. (Aristolochiaceae). J Tradit Complement Med. 2014;5:35–41.
- Luo L, Wang B, Jiang J, Fitzgerald M, Huang Q, Yu Z, et al. Heavy metal contaminations in herbal medicines: determination, comprehensive risk assessments, and solutions. Front Pharmacol. 2021;11: 595335.
- 22. Sadhu A, Upadhyay P, Singh PK, Agrawal A, Ilango K, Karmakar D, et al. Quantitative analysis of heavy metals in medicinal plants collected from environmentally diverse locations in India for use in a novel phytopharmaceutical product. Environ Monitor Assess. 2015;187:542.
- 23. Tschinkel PF, Melo ES, Pereira HS, Silva K, Arakaki DG, Lima NV, et al. The hazardous level of heavy metals in different medicinal plants and their decoctions in water: a public health problem in Brazil. BioMed Res Int. 2020;2020:1465051.
- 24. Vinogradova N, Glukhov A, Chaplygin V, Kumar P, Mandzhieva S, Minkina T, et al. The content of heavy metals in medicinal plants in various environmental conditions: a review. Horticulturae. 2023;9:239.
- 25. Rafati Rahimzadeh M, Rafati Rahimzadeh M, Kazemi S, Moghadamnia A. Cadmium toxicity and treatment: an update. Caspian J Intern Med. 2017;8:135–45.
- 26. Rizvi A, Parveen S, Khan S, Naseem I. Nickel toxicology with reference to male molecular reproductive physiology. Reprod Biol. 2020;20:3–8.

- 27. Sabir S, Akash MS, Fiayyaz F, Saleem U, Mehmood MH, Rehman K. Role of cadmium and arsenic as endocrine disruptors in the metabolism of carbohydrates: inserting the association into perspectives. Biomed Pharmacother. 2019;114:108802.
- 28. Rahaman MS, Rahman MM, Mise N, Sikder MT, Ichihara G, Uddin MK, et al. Environmental arsenic exposure and its contribution to human diseases, toxicity mechanism and management. Environ Pollut. 2021;289:117940.
- 29. Adeoye I, Etuk V. Prevalence, predictors and pregnancy outcomes of unprescribed and herbal medicine use in Ibadan, Nigeria. BMC Complement Med Ther. 2023;23:17.
- 30. Usai J, Ekeocha Z, Byrn S, Clase K. Herbal medicines registration process for Zimbabwe overview of the process. BIRS Africa Technical Report Papers; 2021 Nov. Report No.: TR-BIRSAFRICA-2021-8.
- 31. Adeyemi JA, Adedire CO, Paulelli AC, Martins-Junior AC, Ileke KD, Barbosa Jr F. Levels and dietary intake of lead (Pb) and six essential elements in gari samples from Ondo States, Southwest Nigeria: a potential risk factor of health status. J Food Compost Anal. 2016;45:34–8.
- 32. Kenny CR, Ring G, Sheehan A, Mc Auliffe MAP, Lucey B, Furey A. Novel metallomic profiling and noncarcinogenic risk assessment of botanical ingredients for use in herbal, phytopharmaceutical and dietary products using HR-ICP-SFMS. Sci Rep. 2022;12:17582.
- 33. Geronimo ACR, Melo ESP, Silva KRN, Pereira HS, Nascimento VA, Machate DJ, et al. Human health risk assessment of heavy metals and metalloids in herbal medicines used to treat anxiety: monitoring of safety. Front Pharmacol. 2021;12:772928.
- Bakar MA, Bhattacherjy SC. Assessment of heavy metals concentration in some selected medicinal plants collected from BCSIR, Chittagong cultivation area in Bangladesh. Hamdard Med. 2012;55: 26–32.
- 35. Annan K, Dickson RA, Amponsah IK, Nooni IK. The heavy metal contents of some selected medicinal plants sampled from different geographical locations. Pharmacognosy Res. 2013;5:103–8.
- 36. Karahan F. Evaluation of trace element and heavy metal levels of some ethnobotanically important medicinal plants used as remedies in Southern Turkey in terms of human health risk. Biol Trace Elem Res. 2023;201:493–513.
- 37. Roy M, McDonald LM. Metal uptake in plants and health risk assessments in metal-contaminated smelter soils. Land Degrad Develop. 2015;26:785–92.
- 38. Mohamed BA, Ellis N, Kim CS, Bi X. The role of tailored biochar in increasing plant growth, and reducing bioavailability, phytotoxicity, and uptake of heavy metals in contaminated soil. Environ Pollut. 2017;230:329–38.
- 39. Kulhari A, Sheorayan A, Bajar S, Sarkar S, Chaudhury A, Kalia RK. Investigation of heavy metals in frequently utilized medicinal plants collected from environmentally diverse locations of northwestern India. Springerplus. 2013;2:676.
- 40. Silva CS, Moutinho C, Ferreira da Vinha A, Matos C. Trace minerals in human health: iron, zinc, copper, manganese and fluorine. Int J Sci Res Methodol. 2019;13:57–80.
- 41. Giménez VM, Bergam I, Reiter RJ, Manucha W. Metal ion homeostasis with emphasis on zinc and copper: potential crucial link to explain the non-classical antioxidative properties of vitamin D and melatonin. Life Sci. 2021;281:119770.
- 42. Vogt AC, Arsiwala T, Mohsen M, Vogel M, Manolova V, Bachmann MF. On iron metabolism and its regulation. Int J Mol Sci. 2021;22:4591.
- 43. Osman D, Cooke A, Young TR, Deery E, Robinson NJ, Warren MJ. The requirement for cobalt in vitamin B<sub>12</sub>: a paradigm for protein metalation. Biochim Biophys Acta Mol Cell Res. 2021;1868:118896.
- 44. Rani A, Kumar A, Lal A, Pant M. Cellular mechanisms of cadmium-induced toxicity: a review. Int J Environ Health Res. 2014;24:378–99.
- 45. Orr SE, Bridges CC. Chronic kidney disease and exposure to nephrotoxic metals. Int J Mol Sci. 2017;18: 1039.

- 46. Kiziler AR, Aydemir B, Onaran I, Alici B, Ozkara H, Gulyasar T, et al. High levels of cadmium and lead in seminal fluid and blood of smoking men are associated with high oxidative stress and damage in infertile subjects. Biol Trace Elem Res. 2007;120:82–91.
- 47. Odukoya JO, Odukoya JO, Ndinteh DT. Elemental measurements and health risk assessment of sub-Saharan African medicinal plants used for cardiovascular diseases' and related risk factors' treatment. J Trace Elem Med Biol. 2021;65:126725.
- 48. Liu H, Tang J, Chen T, Zhu P, Sun D, Wang W. Assessment of heavy metals contamination and human health risk assessment of the commonly consumed medicinal herbs in China. Environ Sci Pollut Res. 2023;30:7345–57.
- 49. Ghasemidehkordi B, Malekirad AA, Nazem H, Fazilati M, Salavati H, Shariatifar N, et al. Concentration of lead and mercury in collected vegetables and herbs from Markazi province, Iran: a non-carcinogenic risk assessment. Food Chem Toxicol. 2018;113:204–10. Erratum in: Food Chem Toxicol. 2018;121:717–8.
- 50. Burkill HM. The useful plants of west tropical Africa. Econ Bot. 1986;40:176.
- 51. Soladoye MO, Adetayo MO, Chukwuma EC, Adetunji AN. Ethnobotanical survey of plants used in the treatment of haemorrhoids in South-Western Nigeria. Ann Biol Res. 2010;1:1–15.
- 52. Aigbe FR, Adeyemi OO. The aqueous root extract of Aristolochia ringens (Vahl) prevents chemically induced inflammation. Planta Med. 2011;77:PF28.
- 53. Van Wyk BE, Wink M, editors. Medicinal plants of the world. Oxfordshire: CABI; 2017.
- 54. Neuwinger HD. African ethnobotany: poisons and drugs; chemistry, pharmacology and toxicology. J Nat Prod. 1997;60:864–5.
- 55. Yakubu MT, Atoyebi AR. *Brysocarpus coccineus* (Schum & Thonn) root reinstates sexual competence and testicular function in paroxetine-induced sexual dysfunction in male Wistar rats. Andrologia. 2018;50:e12980.
- 56. Sunday EA, Onyeyili PA, Saganuwan SA. Therapeutic effects of *Byrsocarpus coccineus* root bark extract on bacterially and chemically induced diarrhea in the Wistar albino rat (*Rattus norvegicus domestica*). Animal Model Exp Med. 2019;2:312–25.
- 57. Akindele AJ, Unachukwu EG, Osiagwu DD. 90 Days toxicological assessment of hydroethanolic leaf extract of *Ipomoea asarifolia* (Desr.) Roem. and Schult. (Convolvulaceae) in rats. J Ethnopharmacol. 2015;174:582–94.
- 58. Kayode AAA, Kayode OT. Some medicinal values of Telfeiria occidentalis: a review. Am J Biochem. 2011;1:30–8.