Concentrations and Health Risk Assessment of Potentially Toxic Elements in Medicinal Herbs from Northern Nigeria

Mohammad Bashir Sulaiman[a*], Aishatu Hussein Santuraki[b], Auwal M. Adamu[c], Uzoamaka Virginia Ezenobi[d], Abdullahi Muhammad Gimba[e], Oluyinka Omoyeni Akinlotan[f]

[a]*Department of Pure and Industrial Chemistry, University of Nigeria, Nsukka, Enugu State, Nigeria*

[b]*Department of Chemical Sciences, Federal University Kashere, Gombe State, Nigeria*

[c]*Department of Pharmaceutical and Medicinal Chemistry, Gombe State University, Gombe State, Nigeria*

[d]*Department of Chemistry, Michael Okpara University of Agriculture, Umudike, Nigeria*

[e]*Department of Science Laboratory Technology, Gombe State Polytechnic, Bajoga, Gombe State, Nigeria*

[f]*Department of Chemistry, Kogi State College of Education (Technical) Kabba, Kogi State, Nigeria*

sulaimanmuhammadbashir@gmail.com mohammad.sulaiman.pg01935@unn.edu.ng

Keywords: *assessment, concentration, potentially toxic elements, health risk, medicinal herbs*

The concentrations of potentially toxic elements (Fe, Cd, Pb, Cu, Ni, Cr, and Zn) in most consumed medicinal herbs in Northern Nigeria were analyzed using Atomic Absorption Spectrometry (AAS). Twenty medicinal herbs were selected and purchased from the local markets. The findings of the study revealed that the investigated herb samples contained considerable levels of elements; Cu, Fe, Pb, Cd, and Cr above the permissible limits. The health risk observed as hazard index (HI) indicated that values were >1, in some samples. Therefore, the consumption of these studied medicinal herbs should be monitored to prevent the health implication due to a high level of these elements in the medicinal herbs.

Introduction

Herbs are traditional medicine used for the prevention and treatment of illnesses formulated from herbal plants. Herbal plants are used and represent a vital group of diverse traditional medicine and they are progressively increasing in primary health care intercession in both developing and developed countries in recent years [1]. According to World Health Organization (WHO), the global population of about 70-80% is estimated to still rely on non-conventional medications, generally derivatives from medicine plants [2, 3]. Nearly 80% population of Asians and Africans use traditional medicines mostly from herbal sources [2]. Herbal plants being from natural sources are chosen to compare to modern synthetic medicines by a foremost part of the globe [4].

There is a misconception widespread that herbs from natural sources are inherently safe; however, there have been an outsized number of incidences reported of adverse effects and toxicity linked to herbs in various parts of the globe [5]. These toxicities could be a result of the mineral contents present in various plants or contamination in the cause of formulations [6]. Among these contaminant substances, the occurrence of potentially toxic elements that are omnipresent could be a source of serious harmful effects on living organisms [7]. The possibility of potentially toxic elements being transferred to humans in the route use of herbs grown in contaminated areas is one of the fears for herbal and traditional medicine [8].

Potentially toxic elements pollution of herbs has been earlier reported in numerous studies [1]. The potentially toxic element contamination in herbs could be due to the contaminated environment in which the plants are raised [9-11]. The contaminated environment in which the plants are dried up, processed, and their storage or even adulterated tenaciously by the producer of the products in the finishing dosage [12]. The World Health Organization persists in ensuring the need to assert the quality of plant products, particularly analytical control of potentially toxic elements in medicinal herbs [10, 13]

However, this necessitated the World Health Organization (WHO), institutes, and regulatory agencies to introduce guidelines for the permissible limits of potentially toxic elements in consumable herbal and medicinal plants [14]. The study aimed to determine the concentrations and assess the health risk of potentially toxic elements (iron, cadmium, lead, copper, nickel, chromium, and zinc) in commonly consumed used medicinal herbs in Northern Nigeria.

Experimental part

Material and methods

A total of 60 liquid medicinal herbs samples prepared for oral administration of commonly consumed were randomly selected from herbal medicine vendors in local markets and were purchased from six selected cities in Northern Nigeria namely; Gombe, Maiduguri, Kano, Kaduna, Jos, and Kogi. All the medicinal plants used in the formulations were grown and harvested locally. The samples were selected from 20 types of medicinal herbs with different therapeutic agents. The herbs were divided into four clusters (PL) pile herbs; (TP) typhoid herbs; (YF) yellow fever herbs and (PD) power drink herbs based on their advertised therapeutic effects in **Table 1**. A total of five brands were chosen in each cluster and sampled three times at intervals of a month to ensure true sample representation.

Sample Digestion

The digestion of samples was done using nitric acid and perchloric acid in a ratio of (HNO_3:$HClO_4$; 4:1) according to reported elsewhere [15].

Table 1. Names of the samples and advertised therapeutic effects

S/N	Name	Nature	Therapeutic effects	Sample ID
1	Ajigarau	Liquid	Pile herb	PL_1
2	Na Gombe	Liquid	Pile herb	PL_2
3	Akurkura	Liquid	Pile herb	PL_3
4	Koko	Liquid	Pile herb	PL_4
5	Nagari	Liquid	Pile herb	PL_5
6	Maikwaka	Liquid	Typhoid herb	TP_1
7	ISN	Liquid	Typhoid herb	TP_2
8	Sulfan	Liquid	Typhoid herb	TP_3
9	Abulbula	Liquid	Typhoid herb	TP_4
10	Inusa wanza	Liquid	Typhoid herb	TP_5
11	Dandarazau	Liquid	Yellow fever herb	YF_1
12	Al-maskur	Liquid	Yellow fever herb	YF_2
13	Shawara	Liquid	Yellow fever herb	YF_3
14	Inusa wanzan	Liquid	Yellow fever herb	YF_4
15	As-sulfan	Liquid	Yellow fever herb	YF_5
16	Najib herbal mixture	Liquid	Power drinks herb	PD_1
17	Bulugwai	Liquid	Power drinks herb	PD_2
18	Komai daruwanka	Liquid	Power drinks herb	PD_3
10	Gamagari	Liquid	Power drinks herb	PD_4
20	Nasara power	Liquid	Power drinks herb	PD_5

Quality control

All reagents and standards used were of analytical grade. For quality control, the detection limit was set at 0.001 ppm, and blank samples were also analyzed to cancel the background effects. The calibration of the Atomic Absorption Spectrophotometer (ASS model AA320N, Wincom Coy Ltd., China) instrument follows the preparation of a series of standards in the concentration range of 0.5-20 ppm from standard GFS Fisher's AAS reference standard stock solutions of the studied metals containing 1000 ppm, to obtain the calibration curves. All the sample analysis was done in three replicates with mean recovery percentages of the elements ranging from 97 to 103%.

Data analysis

The data obtained were subjected to simple descriptive statistics (mean and standard deviation), and analysis of variance (ANOVA), was executed using SPSS version 25.

Health Risk Assessment

The health risk assessment is a multi-step procedure for analyzing the location data related to human health [16]. The health risk of ingesting the elements in each sample was assessed by evaluating; Estimated Daily Intake (EDI), Target Hazard Quotient (THQ), and Hazard Index (HI).

Estimated Daily Intake (EDI)

The estimated daily intake (EDI) of metals was evaluated using the equation below [17].

$$EDI = \frac{C \times F_{IR}}{W_{AB}} \qquad \text{Eq. (1)}$$

Where: EDI = average daily intake (mg/kg body weight/day); C = element concentration in the disclosure medium (ppm); F_{IR} = daily consumption rate; W_{AB} is the body weight (kg). W_{AB} values employed in this study were obtained from WHO [18].

Target Hazard Quotient (THQ)

The health risk created by metal disclosure is characterized by the target hazard quotient (THQ) and is evaluated using the equation below [19].

$$THQ = \frac{EDI}{RfD} \qquad \text{Eq. (2)}$$

Where: THQ = target hazard quotient, EDI = average daily intake ($mg.kg^{-1}$ body weight/day) and RfD = oral reference dose. The oral RfDs were 0.7, 0.02, 0.003, 0.04, 0.004, 0.001 and 0.04 mg/kg/day for Fe, Ni, Cr, Cu, Pb, Cd and Zn respectively [20-22]

Hazard Index (HI)

The hazard index (HI) is the summation of the target hazard quotients of all studied elements to estimate the total non-carcinogenic health hazard. The hazard index is evaluated using the equation below USEPA, [23]

$$HI = THQ_1 + THQ_2 + - - - + THQ_n \qquad \text{Eq. (3)}$$

Where: HI = hazard index of multiple metals; THQ =target hazard quotient. If the HI is <1, the exposure dose is lower than the adverse health threshold, but when HI is >1, the exposure dose is more than the adverse health threshold, and likely to have harmful effects on human health.

Results and discussion

The result of potentially toxic elements obtained from the analysis of the studied samples is presented in **Figure 1**. The mean concentrations of iron in the sampled medicinal herbs ranged from 131.32 to 21.27 ppm. The values of iron obtained were above the 0.06 ppm permissible limit set by WHO/FAO [24] in 6 samples; PL_4, PD_2, PD_4, TP_2, TP_4, and TP_5, and the highest iron concentration was recorded in PD_4, while the lowest was recorded in PL_3. The high level of iron in this study could be a result of the use of an iron utensil where the high temperature was applied during the production process [25, 26]. Iron is an essential trace element and has a significant function in the metabolism of organisms [20]. However, the toxicity of iron has a difficult effect on cardiovascular systems and diverse metabolic functions [27], and also causes gastrointestinal disorders like cramps and bleeding [20]. The recorded values in this study are in line with values of a similar study in Egyptian, which range from 26.96 to 1046.25 ppm [28], but are higher than reported values of 0.97 to 6.07 ppm, 11.89 to 25.30 ppm, 4.52 to 70.12 ppm from Kisii Region, Southwest Kenya [29], Northwestern India [30], and Southern Nigeria [12] respectively, and lower than the values of 181.63 to 6796.88 ppm reported by Jabeen et al. in the Haripur basin, Pakistan [31].

Cadmium causes both persistent poisoning and acute, adverse health effect on the liver, kidney, immune and vascular system [11, 32, 33]. The mean concentration of cadmium ranges from 0.10 to 0.51 ppm. The highest cadmium level was recorded in PL_1. The permissible limit of cadmium (0.3 ppm) in herbs was set by the WHO, China, and Thailand [17]. Cadmium was above the WHO/FAO permissible limit in 5 samples; PL_1, PD_1, PD_5, TP_1, and YF_3. The concentration of cadmium in these samples is comparable to values reported in a similar study, in Nigeria [18] and the United Arab Emirates [1]. However, the values are lower when compared to the concentration of cadmium from Nigeria [34] with cadmium levels ranging from 0.55 to 4.75 ppm, 0.39 to 1.58 ppm from Ukraine [35], and Zaria, Nigeria [36].

The concentration of lead ranged from 0.10 to 7.21 ppm in the samples. Lead is a widely used element in industrial applications and is a generally known environmental contaminant [37]. Lead is highly toxic to humans with typical symptoms of headache, convulsions, hypertension, muscular, skeletal, colic, chronic nephritis, anemia, and central nervous system disorders [38, 39]. Lead exposures in early childhood and prenatally can cause low cognitive advancement, learning deficits, and numerous other sound effects [29]. The sample YF_5 recorded the highest level of lead and lowest in PL_1, the levels of lead in sample clusters PL_5, PD_3, YF_1, and YF_5 were above the permissible limit set by WHO/FAO for lead in herbal medicine at 0.005 ppm [23], while below the limit in the other samples. The result of findings was higher than earlier reported, 70.1 to 49.53 ppm in branded herbal drugs in Pakistan [40], 0.25 to 2.64 ppm from India [41], and 0.15 to 0.41 ppm from Kenya [29]. However, the result of this finding was in line with the lead concentrations reported in similar studies in Nigeria [15] and Malaysia [42].

Copper concentration ranged from 0.94 to 36.26 ppm in the samples. YF_3 recorded the highest level of copper whereas the PL_3 recorded the lowest level. Copper is a vital element in the metabolic system in humans that regulates different processes in the human body like; energy production, connective tissue formation, oxidation-reduction reactions, synthesis of neurotransmitters, iron metabolism, etc. [43, 44]. However, excessive intake of copper is capable of causing dermatitis, vomiting, irritation of the upper respiratory tract, diarrhea, abdominal pain, and liver damage [45-47]. The WHO permissible limit for medicinal herbs has not been established yet, but the limit set by FAO/WHO in edible plants is 3.00 ppm [24]. Though, the oral RfDs limit for herbal plants set by Singapore and China are 150 and 20 ppm, respectively [14]. Copper was above the WHO/FAO limit in edible plants in 4 studied samples; PD_1, PD_5, YF_3, and TP_2, but below the permissible limits set by Singapore in all studied samples. The result of this study is comparable with values earlier reported from Turkey [48] and Pakistan [31]. Maobe et al. also reported the copper level range of 0.31 to 1.44 ppm in medicinal plants [29] lower than the values obtained in this study.

The concentration of nickel in the samples ranged from 2.10 to 12.55 ppm. PL_3 recorded the lowest while YF_2 recorded the highest nickel level among the samples. Nickel is essential for iron metabolism but toxic in a higher concentration. The high exposure to nickel has been related to an increased risk of cardiovascular disease, neurological deficit, high blood pressure lung cancer, and developmental deficits in childhood [49]. The toxicity of nickel may be a result of its capability to substitute other ions in proteins and enzymes or to combine with cellular compounds containing nitrogen, oxygen, and sulphur atoms thus inhibiting their actions [50, 51]. It has been reported that nickel toxicity in humans is rare in occurrence due to its low absorption in humans [52]. The permissible limit for herbs has not yet been established by WHO. The concentrations of nickel in this present study are higher than the levels of nickel reported ranging from 0.09 to 1.6 ppm from Kenya [29], and 8.81 to 10.25 ppm from Baghdad, Iraq [53].

The chromium concentrations in the samples ranged from BDL to 1.50 ppm. The highest chromium level was recorded in YF_2, while the lowest was recorded in PD_5 and YF_5, and below the detectable limit in PL_1 and YF_3. Chromium regulates carbohydrates, lipoprotein metabolism, and nucleic acid. It also enhances the insulin's action and thus plays a role in glucose metabolism [54-56], but its high intake can reduce blood glucose, cardiovascular disorders and alimentary, etc. [14, 17, 57], and deficiency of chromium leads to disturbance of lipids and glucose metabolism in humans and animals [52]. The limit for chromium in raw is 2.00 ppm, for herbal materials, and 0.02 mg/day for finished products [52]. The comparison of this permissible limit with the results obtained indicated that the concentration of chromium was above the permissible limit except in PL_1, PL_2, and YF_3. However, the chromium concentrations of 0.57 to 2.04 ppm of herbs in similar studies from Kenya [29] and 0.73 to 4.79 ppm in some selected medicinal plants growing within the University of Ibadan Campus, Nigeria [58] were above the results obtained in this finding.

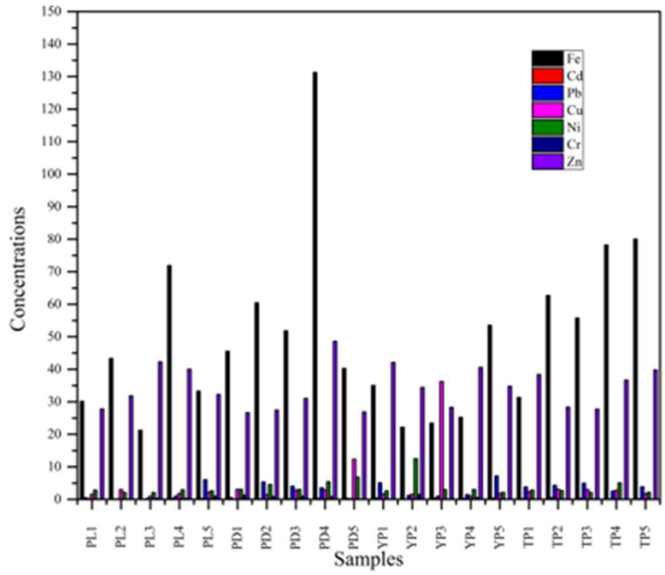

Figure 1. Mean concentrations of potentially toxic elements in medicinal herbs

Table 2. Estimated daily intakes (EDI) (ppm.bw/day) of potentially toxic elements in medicinal herbs from Northern Nigeria

Sample ID	EDI						
	Fe	**Cd**	**Pb**	**Cu**	**Ni**	**Cr**	**Zn**
PL_1	1.25E-02	2.10E-04	8.00E-05	6.40E-04	1.19E-03	0.00E-00	1.15E-02
PL_2	1.81E-02	5.00E-05	7.00E-05	1.25E-03	8.70E-04	4.00E-06	1.32E-02
PL_3	8.80E-03	4.00E-05	1.00E-04	3.90E-04	8.80E-04	1.30E-04	1.76E-02
PL_4	2.99E-02	13.0E-04	4.00E-04	7.50E-04	1.23E-03	1.10E-04	1.66E-02
PL_5	1.38E-02	1.00E-04	2.51E-03	9.00E-04	1.09E-03	4.10E-04	1.34E-02
PD_1	1.89E-02	2.00E-04	4.00E-05	1.29E-03	1.29E-03	5.40E-04	1.11E-02
PD_2	2.51E-02	5.00E-05	2.32E-03	6.10E-04	1.89E-03	3.60E-04	1.14E-02
PD_3	2.16E-02	9.00E-05	1.68E-03	1.19E-03	1.28E-03	4.10E-04	1.29E-02
PD_4	5.46E-02	1.40E-04	1.47E-03	1.22E-03	2.26E-03	3.70E-04	2.02E-02
PD_5	1.67E-02	1.40E-04	7.00E-05	5.15E-03	2.87E-03	1.20E-05	1.11E-02
YF_1	1.45E-02	1.70E-04	2.12E-03	7.00E-04	1.09E-03	2.50E-05	1.75E-02
YF_2	9.20E-03	4.00E-05	5.20E-04	6.50E-04	5.22E-03	6.20E-04	1.43E-02
YF_3	9.70E-03	1.70E-04	4.00E-04	1.51E-03	1.25E-03	0.00E-00	1.18E-02
YF_4	1.05E-02	1.00E-04	6.10E-04	4.00E-04	1.26E-03	2.20E-04	1.69E-02
YF_5	2.21E-02	1.50E-04	3.00E-03	7.80E-04	8.90E-04	1.20E-05	1.45E-02
TP_1	1.30E-02	9.00E-05	1.59E-03	9.90E-04	1.19E-03	2.00E-05	1.60E-02
TP_2	2.60E-02	2.00E-04	1.80E-03	1.29E-04	1.15E-03	1.60E-05	1.18E-02
TP_3	2.32E-02	1.30E-04	2.08E-03	1.25E-03	8.70E-04	5.00E-05	1.15E-02
TP_4	3.25E-02	4.00E-05	1.06E-03	1.17E-03	2.10E-03	3.00E-05	1.52E-02
TP_5	3.33E-02	8.00E-05	1.62E-03	7.40E-04	9.00E-04	3.00E-05	1.65E-02

Table 3. Target hazard quotient (THQ) and hazard index (HI) of potentially toxic elements in medicinal herbs from Northern Nigeria

Sample ID	**THQ**							**HI**
	Fe	**Cd**	**Pb**	**Cu**	**Ni**	**Cr**	**Zn**	
PL_1	1.78E-02	2.10E-01	2.00E-02	1.60E-02	5.95E-02	0.00E-00	2.89E-01	6.09E-01
PL_2	2.58E-02	5.00E-02	1.75E-02	3.12E-02	4.35E-02	0.00E-00	3.30E-01	4.98E-01
PL_3	1.25E-02	4.00E-02	2.50E-02	9.75E-03	4.40E-02	4.33E-02	4.40E-01	6.15E-01
PL_4	4.27E-02	1.30E-01	1.00E-01	1.87E-02	6.15E-02	3.66E-02	4.17E-01	8.06E-01
PL_5	1.97E-02	1.00E-01	6.27E-01	2.25E-02	5.54E-02	1.36E-01	3.36E-01	**1.29E +0**
PD_1	2.70E-02	2.00E-01	1,00E-02	3.22E-02	6.45E-02	1.80E-01	2.77E-01	7.91E-01
PD_2	3.58E-02	5.00E-02	5.55E-01	1.52E-02	9.45E-02	1.20E-01	2.86E-01	**1.19E +0**
PD_3	3.08E-02	9.00E-02	4.20E-01	2.97E-02	6.40E-02	1.36E-01	3.23E-01	**1.09E +0**
PD_4	7.80E-02	1.40E-01	3.67E-01	3.05E-02	1.13E-01	1.23E-01	5.06E-01	**1.35E +0**
PD_5	2.38E-02	1.40E-01	1.75E-02	1.28E-01	1.43E-01	3.30E-03	2.79E-01	7.36E-01
YF_1	2.07E-02	1.70E-01	5.30E-01	1.75E-02	5.45E-02	6.60E-03	4.38E-01	**1.23E +0**
YF_2	1.31E-02	4.00E-02	1.30E-01	1.62E-02	2.61E-02	2.06E-01	3.58E-01	7.90E-01
YF_3	1.38E-02	1.70E-01	1.00E-01	3.77E-02	6.25E-02	0.00E-00	2.95E-01	6.79E-01
YF_4	1.50E-02	1.00E-01	1.52E-01	1.00E-02	6.23E-02	7.33E-02	4.22E-01	**1.20E +0**
YF_5	3.15E-02	1.50E-01	7.50E-01	1.95E-02	4.45E-02	3.30E-03	3.62E-01	**1.83E +0**
TP_1	1.85E-02	9.00E-02	3.97E-01	2.47E-02	5.95E-02	6.60E-03	4.00E-01	9.96E-01
TP_2	3.71E-02	2.00E-01	4.50E-01	3.22E-02	5.75E-02	3.30E-03	2.95E-01	**1.07E +0**
TP_3	3.31F-02	1.30E-01	5.20E-01	3.12E-02	9.35E-02	1.66E-02	2.89E-01	**1.11E +0**
TP_4	4.64E-02	4.00E-02	2.65E-01	2.92E-02	1.05E-01	1.00E-02	3.81E-01	8.77E-01
TP_5	4.75E-02	8.00E-02	4.05E-01	1.85E-02	4.50E-02	1.00E-02	4.14E-01	6.15E-01

The concentrations of zinc ranged from 26.65 to 48.61 ppm medicinal herbs. Zinc is one of the most essential minerals in the human body [38], is known to manage the contractibility of muscles, and acts as a co-factor for enzymes in the body [52]. Nevertheless, elevated zinc intake above limits may result in toxic effects on the blood lipoprotein levels, copper levels, and immune system [17, 59]. Prolonged intake of drinks with elevated levels of potentially toxic elements can lead to skin irritation, decreased body weight, liver, and heart damage [25]. Kulhari et al. reported the level of zinc ranged from 2.42 to 8.93 ppm [30] and 0. 02 to 0.12 ppm and 0.20 to 3.95 ppm from Dubai, UAE [17] lower than the values recorded in the study. However, the concentrations of zinc in this study were also above the permissible limit of 0.06 ppm. The concentration of zinc is reported to be 12.65 to 146.67 ppm in traditional herbs commonly consumed in the United Arab Emirates [1] were higher than the values recorded in this study.

Health risk assessment

Potentially Toxic Elements Daily Intake: The EDIs of iron, cadmium, lead, copper, nickel, chromium, and zinc were calculated on the basic concentration of each potentially toxic element in the medicinal herb as presented in **Table 2**. The risk assessment was only for adults. The trend for daily intake was in the following order; Fe > Zn > Ni > Cu > Ni > Pb > Cr > Cd, this indicates that Fe was the maximum concentration between the daily intakes of potentially toxic elements. A similar study by Shadi et al. [20], also reported that the estimated daily intake (EDI) of Fe was the highest among the studied metals through the consumption of medicinal plants. The values of EDI in this finding were below the RfD values of all the studied samples, this suggests that the consumption of the analyzed medicinal herbs did not appear to pose a health risk to local adults.

Non-carcinogenic Risk: The HQs and HIs of potentially toxic elements of the medicinal herbs are presented in **Table 3**. The non-carcinogenic risk of medicinal herbs for adults was assessed based on the HQs. The HQ values of each metal through the ingestion of medicinal herbs were below one in all samples. The HI values range from 4.98E-01 to 1.837E+0 in the studied samples. HI, values in PL_5, PD_2, PD_3, PD_4, YF_4, YF_5, TP_2, and TP_3 samples were >1, indicating adverse health risks in those samples. A similar study by Mihreteab et al. [60], also reported that the HI was >1 in the traditional herbal from Ethiopia. These suggest that the consumption of these medicinal herb samples is unsafe, and not free of risks for all studied elements.

Conclusions

The study was carried out to determine the concentration and assess the health risk of potentially toxic elements in some medicinal herbs from northern Nigeria. The results of the study revealed that investigated herb samples contained considerable levels of elements; iron in PL_4, PD_2, PD_4, TP_2, TP_4, and TP_5, cadmium in PL_1, PD_1, PD_5, TP_1, and YF_3, lead in PL_5, PD_3, YP_1 and YP_5, copper in PD_1, PD_5, YF_3 and TP_2 and chromium in PL_1, PL_2, and YF_3 above the permissible limits (PL). The proclivity of the potentially toxic elements concentrations in the clusters were: Fe = PD > TP > PL > YF; Cd = PL > PD > TP > YF; Pb = PL > PD > YF > TP; Cu = YF > PD > TP > PL; Ni = YF > PD > TY > PL; Cr = PD > YF > PL > TP and Zn = PD > PL > YF > TP. The results of the health risk assessment in the study showed adverse human health risks in some samples, with HI values > 1. There is a need for constant monitoring of medicinal herbs sold in the market to be sure wholesome and safe herbs are sold for consumption by humans.

Acknowledgment

The authors are grateful to laboratory attendants of the faculty of pharmaceutical sciences, Gombe State University, and their research assistants.

Conflict of interest

The authors affirm that no conflict of interest.

References

[1] Dghaim R, Al Khatib S, Rasool H, Ali Khan M. Determination of Heavy Metals Concentration in Traditional Herbs Commonly Consumed in the United Arab Emirates. Journal of Environmental and Public Health 2015;2015:1-6.

[2] Sahoo N, Manchikanti P, Dey S. Herbal drugs: Standards and regulation. Fitoterapia 2010;81(6):462-471.

[3] WHO. Traditional Medicine Strategy (2002–2005), World Health Organization, Geneva, Switzerland. 2002.

[4] Kishan PS, Sanjib B, Pradeep S. Assessment of Heavy Metal Contents of Some Indian Medicinal Plants. American-Eurasian J Agric Environ Sci. 2014;14(10):1125-1129.

[5] Ernst E. Toxic heavy metals and undeclared drugs in Asian herbal medicines. Trends in Pharmacological Sciences 2002;23(3):136-139.

[6] Lekouch N, Sedki A, Nejmeddine A, Gamon S. Lead and traditional Moroccan pharmacopoeia. The Science of The Total Environment 2001;280(1-3):39-43.

[7] Nies D. Microbial heavy-metal resistance. Applied Microbiology and Biotechnology 1999;51(6):730-750.

[8] Yap CK, Fitri M, Mazyhar Y, Tan SG. Effects of Metal contaminated Soils on the accumulation of heavy metals in different parts of Centella asiatica: A Laboratory Study. Sains Malaysiana, 2010;39;347-52.

[9] Sayyed MRG, Sayadi MH. Variations in the heavy metal accumulation within the surface soils from the Chitgav Industrial area of Tehran. Proc. Int. Academy. Ecol Environ Sci. 2011;1(1):36-40.

[10] Zárate-Quiñones R, Custodio M, Orellana-Mendoza E, Cuadrado-Campó W, Grijalva-Aroni P, Peñaloza R. Determination of toxic metals in commonly consumed medicinal plants largely used in Peru by ICP-MS and their impact on human health. Chemical Data Collections 2021;33:100711.

[11] Jurowski K, Krośniak M. The Toxicological Assessment of Content and Exposure of Heavy Metals (Pb and Cd) in Traditional Herbal Medicinal Products with Marshmallow Root (Althaea officinalis L., radix) from Polish Pharmacies. Toxics 2022;10(4):188.

[12] Nkansah M, Hayford S, Borquaye L, Ephraim J. Heavy metal contents of some medicinal herbs from Kumasi, Ghana. Cogent Environmental Science 2016;2(1):1234660.

[13] WHO. Expert committee on specifications for pharmaceutical preparations. 2015.

[14] Ghani A. Estimation of macro and micro nutrients in some important medicinal plants of Soon Valley, District Khushab, Pakistan. African Journal Of Biotechnology 2012;11(78):14386-14391.

[15] Ekere NR, Ihedioha JN, Ayogu JI, Ogbefi-Chima FI, Onoja SU, Alum OL. Assessment of heavy metals content of some plant based medicines in parts of southern Nigeria, West Africa. Int J Pharm Sci Res. 2018;9(2):775-783.

[16] Sulaiman MB, Salawu A, Isa Z. Assessment of Potential Health Risks Associated with Remediated and Non-Remediated Soils at Illegal Mining compound in Dareta, Zamfara, Nigeria. Int. J Inno Sci Eng Techno. 2016;3(10):151-160.

[17] USEPA. Exposure factors handbook. Office of Research and Development, Washington. 1997.

[18] World Health Organization. WHO guidelines for

assessing quality of herbal medicines with reference to contaminants & residues Geneva. 2007;1-105.

[19] Pastorok P. Guidance manual for assessing human health risks from chemically contaminated fish and shellfish. PTI Environmental Service's submission to Battelle New England for EPA, Washington, DEC PTI Environ Draft Report C737-01 Bellevue, Washington, 1987; 91.

[20] Kohzadi S, Shahmoradi B, Ghaderi E, Loqmani H, Maleki A. Concentration, Source, and Potential Human Health Risk of Heavy Metals in the Commonly Consumed Medicinal Plants. Biological Trace Element Research 2018;187(1):41-50.

[21] Zhang J, Yang R, Chen R, Peng Y, Wen X, Gao L. Accumulation of Heavy Metals in Tea Leaves and Potential Health Risk Assessment: A Case Study from Puan County, Guizhou Province, China. International Journal of Environmental Research and Public Health 2018;15(1):133.

[22] Sulaiman MB, Maigari IA, Yahaya Y. Health Risk Assessment of Heavy Metals Accumulation in Tomatoes Irrigation Farms at Kwadon, Gombe, Nigeria. ATBU J Sci Techno Edu. 2019;**7**(2):271-280.

[23] PA USEPAUIRIS-dP Washington, DC. 2007.

[24] FAO/WHO, Contaminants, vol XVII. FAO/WHO, Rome. 1984.

[25] Maigari AU, Sulaiman MB, Maigari IA. Heavy Metals Contamination in Two Popular Local Drinks Consumed in Northern Nigeria. Int J Inno Sci Eng Techno. 2016;3(11):441-446.

[26] Jain P. Effects of cooking utensil of iron content of food. J Pub Health Catalog, 2018;1(4):89-92.

[27] Marin S, Griswold W. Human health effects of heavy metals, in Environmental Science and Technology Briefs for Citizens, Center for Hazardous Substance Research, Manhattan, Kan, USA. 2009;15:1-6.

[28] Ziarati P. Determination of Contaminants in Some Iranian Popular Herbal Medicines. Journal of Environmental & Analytical Toxicology 2012;2(1):1-3.

[29] Maobe MA, Gatebe E, Gitu L, Rotich H. Profile of heavy metals in selected medicinal plants used for the treatment of diabetes, malaria and pneumonia in Kisii region, southwest Kenya. Glob J Pharmacol. 2012;6(3):245-251.

[30] Kulhari A, Sheorayan A, Bajar S, Sarkar S, Chaudhury A, Kalia R. Investigation of heavy metals in frequently utilized medicinal plants collected from environmentally diverse locations of north western India. Springer Plus 2013;2(1):1.

[31] Jabeen S, Shah MT, Khan S, Hayat MQ. Determination of major and trace elements in ten important folk therapeutic plants of Haripur basin, Pakistan. J Med Pl Res. 2010;4(7):559-566.

[32] Hayes R. The Carcinogenicity of metals in humans. Cancer Causes and Control 1997;8(3):371-385.

[33] Sulaiman MB, Asegbeloyin JN, Ihedioha JN, Oyeka EE, Oji EO. Trace Metals Content of Soil around a Municipal Solid Waste Dumpsite in Gombe, Nigeria: Assessing the Ecological and Human Health Impact. J. Chem. Risk. 2019;9(3): 173-190.

[34] Hina BG, Rizwawi GG, Nasser S. Determination of toxic metals in some herbal drugs through AAS. Pak J Pharm Sci. 2001;24(3):313-58.

[35] Konieczynski P, Lysiuk R, Kopistecka M, Wesolowski M. Study of essential and toxic elements content in medicinal herbs harvested in Ukraine. Research Journal of Pharmacy and Technology 2021;14(11):6055-6060.

[36] Obiajunwa E, Adebajo A, Omobuwajo O. Essential and Trace Element Contents of Some Nigerian Medicinal Plants. Journal of Radioanalytical and Nuclear Chemistry 2002;252(3):473-476.

[37] Bidgoli SN, Mostafaii GR, Akbari H, Chimehi E, Miranzadeh MB. Determination of the Concentration of Heavy Metals and Their Assessment of Related Potential Health Risk for Dry Black Teas in Kashan, Iran. J Chem Health Risk. 2020;10(2):103-115.

[38] Khan SA, Khan LH, Marwat KB, Akhtar N. Profile of heavy metals in selected medicinal plants. Pak J Weed Sci Res. 2008;14(1-2):101-110.

[39] Edebi NV, Alade OO. Evaluation of pharmacognostical parameters and heavy metals in some locally manufactured herbal drugs. J Chem Pharm Res. 2011;3(2):88-97.

[40] Mohammed S, Naveed M, Harm K, Saeed AK. Analysis of Toxic heavy metals in Branded Pakistani, Herbal products. J Chem Soc Pak. 2010;32(4):471-475.

[41] Singh KP, Bhattacharya S, Sharma P. Assessment of heavy metal contents of some Indian medicinal plants. Am Eurasian J Agric Environ Sci. 2014;14(10):1125-1129.

[42] Uddin ABM, Khalid RS, Abbas SA. Determination of heavy metal concentration of different traditional medicine formulations available at the East Coast Region of Malaysia. African Journal of Pharmacy and Pharmacology 2012;6(2):1487-1491.

[43] JECFA. Joint IAO/WHO Expert Committee on Food and Diluted Evaluation of certain food additives and contaminants. 33.9. Report WHO technical report series No 776.WHO Geneva. 2000.

[44] Anke M, Angelow L, Glei M, Mueller M, Illing H. The biological importance of nickel in the food chain. Fresenius' Journal of Analytical Chemistry 1995;352(1-2):92-96.

[45] Dghaim R, Al Khatib S, Rasool H, Ali Khan M. Determination of Heavy Metals Concentration in Traditional Herbs Commonly Consumed in the United Arab Emirates. Journal of Environmental and Public Health 2015;2015:1-6.

[46] Ullah R, Khader JA, Hussain N, AbdElsalam NM, Talha M, Khan N. Investigation of macro and micro-nutrients in selected medicinal plants. African Journal of Pharmacy and Pharmacology 2012;6(25):1829-1832.

[47] Luo L, Wang B, Jiang J, Fitzgerald M, Huang Q, Yu Z, Li H, Zhang J, Wei J, Yang C, Zhang H, Dong L, Chen S. Heavy Metal Contaminations in Herbal Medicines: Determination, Comprehensive Risk Assessments, and Solutions. Frontiers in Pharmacology 2021;11:595335.

[48] Haci S, Tercan FA, Nadire PB. Determination of Heavy Metal Contents and Some Basic Aspects of Widely Used Herbal Teas in Turkey. Rev Chim (Bucharest). 2016;67(5):1019-1022.

[49] Jaya G, Amit G. Determination of trace metals in the leaves of Rauwolfia serpentine by using atomic absorption spectroscopy. Int J Chem Stu. 2016;4(3): 94-96.

[50] Chodak AD, Blaszczyk U. The impact of Nickel in human health. J Elementol. 2008;13(4):685-696.

[51] Coogan T, Latta D, Snow E, Costa M, Lawrence A. Toxicity and Carcinogenicity of Nickel Compounds. CRC Critical Reviews in Toxicology 1989;19(4):341-384.

[52] Adamu HM, Mshelia EH, Maigari AU, Umar HY, Balogun OL. Determination of Some Trace Elements and Macro Minerals in Grewia Mollis Plant Parts. Int J Pure App Sci Res. 2016;11(2):1-16.

[53] Raouf ALM, Hammud KK, Zamil SK. Macro-and trace metals in three medicinal herbs collected from Baghdad, Iraq market. Int J Pharm Sci Res. 2014;5(11):799-802.

[54] Maigari I, Auwal M, Sulaiman M, Nwankwo D. Determination and heavy metals some Nigerian medical plants. Bayero Journal of Pure and Applied Sciences 2021;13(1):153-157.

[55] Kishan PS, Sanjib B, Pradeep S. Assessment of Heavy Metal Contents of Some Indian Medicinal Plants. American-Eurasian J Agri Environ Sci. 2014;14(10):1125-1129.

[56] Kaplan L, Pesce A, Kazmierczak S, Clincal Chemistry-Theory, Analysis, Correlation, fourth ed. Mosby, London. 2003.

[57] WHO. Guidelines for Assessing Quality of Herbal Medicines with Reference to Contaminants and Residues. Geneva, Switzerland. 2007.

[58] Rufai S, Olaniyi M, Lawal I. Evaluation of heavy metals in some selected medicinal plants growing within the University of Ibadan Campus. Journal of Medicinal Plants for Economic Development 2019;3(1):a63.

[59] Fosmire G. Zinc toxicity. The American Journal of Clinical Nutrition 1990;51(2):225-227.

[60] Meseret M, Ketema G, Kassahun H. Health Risk Assessment and Determination of Some Heavy Metals in Commonly Consumed Traditional Herbal Preparations in Northeast Ethiopia. Journal of Chemistry 2020;2020:1-7.