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Concentration, Source, and Health Risk of Trace Metals in Some Liquid Herbal Medicine Sold in Nigeria

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Abstract
The ingestion of toxic metals through liquid herbal medicine over a long period of time, and in excessive dose, may result in chronic accumulation that could cause disorder to several organs of the body. This study evaluated the concentration, source, and probable health risk of 8 trace metals in liquid herbal medicines sold in Nigeria. Triplicate samples of 10 different brands of liquid herbal formulations were analyzed using flame atomic absorption spectrophotometer. Elemental concentrations (mg L^{-1}) ranged as < 0.00120 (nickel), 0.329–1.23 (zinc), < 0.00150–0.0750 (chromium), 0.565–6.94 (manganese), 1.75–19.4 (iron), < 0.00150–0.266 (cobalt), < 0.0018–3.01 (lead), and < 0.00900–0.0281 (copper). The estimated hazard quotient (HQ) and hazard index (HI) of trace metals (zinc, chromium, manganese, iron, cobalt, lead, and copper) were < 1.00, except for one of the herbal products which depicted a value of < 1.50, an indication that there is no major probable health effect due to exposure. Carcinogenic risks were lower than the threshold level of 10.0^{-6}–10.0^{-4}; this probably reflects non-existent carcinogenic risk in both age groups. The principal component analysis revealed the likelihood of geogenic and anthropogenic activities as indirect sources of trace metals in the herbs. Using hierarchical cluster analysis, AAB and AHM herbal mixtures showed strong similarities in cluster 1, while the remaining herbs reflected identical association within cluster 2. Based on the results of this study, there is need to periodically monitor levels of toxic metals in herbal medicine in order to ensure regulatory compliance and safeguard the health of its consumers.

Keywords Environmental health · Herbal medicine · Health risk · Trace metals · Carcinogenic risk · Hierarchical cluster analysis

Introduction

The intake of herbal medicine is a common practice in many developing countries including Nigeria. This practice is common among rural dwellers that use one or more plant parts for the preparation of medicinal concoctions. The herbal medicine is used for the treatment of many infectious and non-infectious diseases. In recent times, some of the herbal mixtures have been packaged and many have been duly registered with National Association of Traditional Medicine Practitioners of Nigeria (NATMPN) (a Nigerian agency regulating the activities of traditional medicine practitioners), and National Agency for Food, Drug and Administration and control (NAFDAC) (a Nigerian Agency regulating food and drug products). The agencies regulate the activities of traditional medicine practitioners in Nigeria [1, 2]. In spite of the institution of these agencies, several un-registered herbal medicines are still being marketed in some areas in Nigeria.

It is very important for consumer safety to control the quality of commercial herbal medicine which is commonly used in the treatment of diseases. The safety of these products is a source of concern among health care practitioners. In many urban areas, different herbal medicines are advertised in motor parks, garage, etc. Excessively ingested trace metal micro-pollutants are known to exacerbate adverse health effects in humans. Hence, there is the need to assess the cumulative toxic metal loading of

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herbal formulations [3]. Sometimes, potentially toxic metals are assimilated in herbal mixtures through unhygienic preparation procedures, or the contamination of cultivation soils from industrial processes or effluent discharges.

Herbal medicines are formulated from plants extracts, and are sold in powder and liquid forms. The liquid herbal formulations has water as its major diluent/constituent. Plants and potable water sources have been variously reported to contain trace metals at varying concentrations. Trace metals are known to be toxic when they exceed the threshold limit at which they are regarded to be essential. These include trace elements such as chromium, iron, zinc, and copper, whereas trace elements such as cadmium, lead, arsenic, and mercury have no known biological functions [4, 5].

Intake of toxic metals for a long period of time, and in high amounts via herbal medicine uptake route, can lead to chronic accumulation, culminating to deleterious health effects. This is particularly pronounced for metals that possess carcinogenic effects. Authors have reported metals such as cadmium, nickel, lead and chromium to portend carcinogenic risk [6–8]. This is because some of the compounds associated with these metals are carcinogenic. For instance, International Agency for Research on Cancer (IARC) has categorized some nickel compounds as human carcinogens. As such, metallic nickel could be carcinogenic to humans [9]. Also, Environmental Protection Agency (EPA) reported nickel refinery dust and nickel sub-sulfide as human carcinogens [9].

According to IARC, chromium, nickel and cadmium are classified as group 1 carcinogens [10]. The categorization, group 1 carcinogen, indicates the availability of adequate information to show carcinogenicity, and/or scientific evidence of their carcinogenicity in animal model, accompanied by strong proof in exposed humans. Also, lead compounds and its inorganic form are probably carcinogenic to humans (group 2A) [11]. This is due to insufficient proof of their carcinogenicity in humans, although with sufficient proof of their carcinogenic tendencies in animal model. The toxicity and carcinogenic mechanism of carcinogenic metals show inducement of oxidative stress, DNA damage, and cell death processes, which culminate to increased risk of cancer and cancer-related diseases [10]. The toxicity and diseases associated with these carcinogenic metals have been comprehensively documented by Izah et al. [4, 5], Kim et al. [10], and Sall et al. [12].

Several studies have been carried out with respect to determining trace metal levels in herbal medicine commonly produced and marketed in Nigeria [1, 2, 13–17]. However, these studies solely focused on the assessment of heavy metals with a view to regulatory compliance. According to Mohammad et al. [6] and Ogamba et al. [7], regulatory guidelines do not satisfactorily rank the toxicity of metals. They also do not reflect the actual associated risk index. Information about the human health risk of toxic metals is scarce in literature. Hence, this study focused on assessing the human health risk associated with ingestible trace metals found in liquid herbal medicine produced and marketed in some parts of Nigeria. The findings of this study will be useful to individuals that seek treatment of diseases using herbal medicine. It will also inform the decision of agencies that regulate the quality of herbal mixtures in Nigeria. The concentration of metals in liquid herbal medicines will be compared with potable water guidelines as previously applied by Igweze et al. [16]. Apart from the use of flame atomic absorption spectrometric (FAAS) method for the determination of trace elements in herbs, other analytical methods that have been applied to decipher trace metal levels in similar samples include inductively coupled plasma–optical emission spectrometry (ICP-OES) [18, 19]. In addition, previous studies have compared trace elements concentration in nutritional drinks with potable water guidelines [5, 20].

This study is aimed at determining the concentration of trace elements in locally sold herbal formulations, with a view to assessing the inherent health risks associated with its consumption by adult and undergraduate population within the study area.

Materials and Methods

Sample Collection

In this study, 10 different brands of liquid herbal medicines produced in Nigeria were purchased in triplicate batches from different commercial outlets in Yenagoa metropolis (Berger axis, Tombia junction, Opolo, Swali, and Azikoro) of Bayelsa State and Port Harcourt metropolis (Eleme junction, Oil-mill market, Elelenwo) of Rivers State, Nigeria. Overall, a total of 30 herbal mixtures were collected for trace metal analysis. Triplicate data was obtained for each of the 10 different products. Meanwhile, the constituents, expiration timeline, and diseases of cure are shown in Table 1, while all herbal products showed evidence of registration with national drug regulatory agencies (NAFDAC and NATMPN).

Sample Preparation and Trace Metal Analysis

The samples were prepared with slight modification to the method previously described by Aigberua [13, 22, 23]. Approximately 25.0 mL of the herbal formulations was transferred into glass beakers of 125 mL each; then, 10.0 mL mixture of concentrated HNO_3, 69.0% (v v^{-1}) Analar (BDH, Poole, UK) and HCl, 37.0% (v v^{-1}) (Sigma-Aldrich, Steinheim, Germany) was added in the ratio of 1:10. The acid-sample mixture was pre-digested at room temperature for 24 h. Afterwards, samples were thermally digested on a hotplate at low heat (50 °C) until the entire mixture was concentrated to about 5.00 mL. The pre-digestion and low heat application was used to avoid thermal loss of some volatile metals. The concentrated acid extract or clear solution produced was left to cool for 30 min. Thereafter, the acid solution was quantitatively transferred into 25.0 mL volumetric flask, and diluted to mark with distilled water [21]. The diluted acid extract was aspirated into the GBC 908PBMT atomic absorption spectrophotometer for elemental analysis, while reagent blanks consisting of digested acid mixtures, but excluding sample was first aspirated into the equipment. The reagent blank reading was used as correction factor for any likely chemical impurities. Apart from chromium which required a highly reducing flame type (fuel-rich), instrument operational conditions reflect the predominant use of oxidizing flame for the atomization of selected metals (Table 2). Meanwhile, spike recovery limits ranged between 92.6 and 98.8%, with limits of detection (LOD) and limits of quantification (LOQ) ranging between 0.000300–0.00500 mg L^{-1} and 0.000900–0.0152 mg L^{-1}, respectively for the different test metals (Table 3).

Health Risk Assessment

Risk assessment is a technique used in evaluating the probability of occurrence of toxicants such as trace metals over a period of time. Health risk was determined using chronic daily intake via oral route or ingestion, hazard quotient, hazard index (non-carcinogenic risks), and carcinogenic risk. These indices were calculated following methods previously utilized for drinking water quality assessment by Anyanwu and Nwachukwu [24] and Adeyemi and Ojekunle [25].

Chronic Daily Intake

$$\text{The chronic daily intake (CDI)(mg/kg/day) ingestion} = \frac{\text{Ch} \times \text{DI} \times \text{EF} \times \text{ED}}{\text{BW} \times \text{AT}}$$

where Ch is the concentration of herbal medicine in mg L^{-1}; DI is the daily intake (L day^{-1}) which is calculated based on the dosage and daily frequency of intake as recommended for different age groups by the manufacturer. The following daily intake values of 0.0400, 0.0400, 0.0890, 0.030, 0.0890, 0.120, 0.180, 0.0300, 0.120, and 0.133 L day^{-1} apply for sample codes MCA, OHC, SHM, AHM, GC, DRH, ARC, AAB, IHB, and GCB, respectively.

EF is the exposure frequency = 365 day per year [6, 8]. ED is exposure duration, which is the life expectancy rate. For Nigeria, the value is 48.9 years [22, 26, 27]. The minimum age was subtracted from the life expectancy values, hence the ED values used for this study were 30.9, 32.9, 40.9, 30.9, 36.9, 43.9, 32.9, 30.9, 32.9, 30.9 years for the consumption of herbal medicine bearing the following codes MCA, OHC, SHM, AHM, GC, DRH, ARC, AAB, IHB and GCB, respectively. The variable, body weight was calculated using two criteria, viz adult (body weight of 70.0 kg) and undergraduate individuals within the age range of 16–25 years (body weight of 65.0 kg) [22, 23, 28]. Meanwhile, AT is the Average time which is 365 × ED.

Hazard Quotient

Hazard quotient (HQ) is the ratio of chronic daily intake to reference oral dose of a trace element, all from the same exposure route [6, 7, 24, 25].

$$\text{Hazard quotient} = \frac{\text{CDI}}{\text{RFD}}$$

where the RFD is the reference oral dose of zinc = 0.300, chromium = 0.00300, manganese = 0.140, copper = 0.0400 [22, 26, 29], lead = 0.00350 [29, 30], iron = 0.700, and cobalt = 0.000300 [29, 31]. Both CDI and RFD are expressed in mg/kg/day. When HQ is < 1.00, it shows no potential harmful effects [8].

Hazard Index

Hazard index (HI) is the sum of hazard quotients [24, 25].

$$\text{Hazard index} = HQ_{Pb} + HQ_{Cr} + HQ_{Ni} + HQ_{Co} + HQ_{Cu} + HQ_{Zn} + HQ_{Mn} + HQ_{Fe}$$

If the HI is < 1.00, it is a reflection of non-considerable non-carcinogenic risk [8, 24, 25].

Carcinogenic Risk

Carcinogenic risk (CR) is used to show the probability of an individual developing any cancer over a life time [8]. CR is calculated by multiplying the CDI by the carcinogen slope factor (CSF) [25].

$$\text{Carcinogenicrisk} = \text{CDI} \times \text{CSF}$$

Here, CSF is the carcinogenic slope factor with value of 0.500 mg/day/mg for chromium [29, 32] and 0.00850 mg/kg/day for lead [29, 33]. The resulting values were compared with cancer risk standards previously described by Adeyemi and Ojekunle [25] and Joel et al. [34]. Thus, extremely low risk, totally acceptable ($< 10.0.0^{-6}$), low risk, showing no willingness to care about the risk or negligible risk (10.0^{-6}, 10.0^{-5}), low-medium risk, negligible risk (10.0^{-6}, 5×10.0^{-5}), medium risk, care about the risk (5×10.0^{-5}, 10.0^{-4}), medium–high risk, care about the risk and willing to invest (10.0^{-4}, 5×10.0^{-4}),

Table 1 Composition, uses, and dosage of some herbal medicine commonly used in the treatment of diseases in Nigeria

Name of herbal medicine	Uses	Composition	Year of expiration
MCA	Urinary tract infections, syphilis, *Staphylococcus aureus*, gonorrhoea, virginal discharge, weak erection of penis, stomach noise, menstrual pains, malaria, typhoid, hepatitis, moving objects in the body, chronic cough, reduction of high sugar level, tube blockage	*Zingiber officinale*, *Psidium guajava*, *Xylopia aethiopica*, *Cymbopogon citratus*, Aloe vera, Ginseng	2024
OHC	Ulcer, diabetes, high cholesterol, diarrhoea, general infertility, high blood pressure, arthritis, rheumatism, hepatitis A and B, menstrual disorder, *E.coli*, candidiasis, syphilis, gonorrhea	*Morinda lucida*, *Zingiber officinale*, *Vernonia amygdalina*, *Xylopia aethiopica*, *Cymbopogon citratus*, Aloe vera,	2023
SHM	Waist pain, vaginal discharge, menstrual pain, typhoid, stomach noise, syphilis, constant miscarriage, general body weakness, *E.coli*, candidiasis, body itching, *Staphylococcus aureus*, Gonorrhea	*Magnifera indica*, *Cymbopogon spp*, *Psidium guajava*, *Zingiber officinale*, *Citrus limon*, breadfruit, *Massularia acuminata*	2024
AHM	Sexually transmitted diseases	Magnifera indica, *Vernonia amygdalina*, water	2021
GC	Typhoid fever	*Vernonia amygdalina*, *Saccharum officinarum*, *Allium sativum*, *Cajanus cajan*, *Zingiber officinale*, caramel, water	2023
DRH	Malaria	*Cymbopogon citrates*, leaves of *Carica papaya*, *Moringa oleifera*, *Magnifera indica* bark, *Citrus limonia*, *Psidium guajava*, *Allium sativum*, water	2022
ARC	Gonorrhea, syphilis, *Staphylococcus aureus*, urinary tract infection, vaginal discharge, candidiasis, chlamydia, rheumatism, arthritis, waist pain, cramps and menstrual pain, pile, weak libido, malaria, typhoid, high blood pressure	*Moringa oleifera* Ginseng, *Carica papaya*, Aloe vera Honey, garlic, red grapes, ginger	2024
AAB	Fibroid	*Pterygrota macrocapa*, *Colocynthis citrullus*, *Strophanthus* species, *Nauclea latifolia*, Cascara, water	2024
IHB	Gonorrhea, syphilis, *Staphylococcus*, rheumatism, lower and higher blood, noisy stomach, typhoid, cholesterol, reduction of blood sugar, ulcer, pile	*Moringa oleifera*, *Carica papaya*, ginseng, Aloe vera, honey, garlic, red grapes	2022
GCB	Diabetes	Leaves of *Citrus aurantifolia*, *Mangifera indica*, *Vernonia amydgalina* and *Saccharum officinarum*, *Allium sativum*, *Moringa oleifera*, caramel, water	2023

Table 2 Operational conditions of the FAAS

Metals	Slit width (nm)	Wave-length (nm)	Lamp current (mA)	Flame composition		
				Acetylene (L min^{-1})	Air (L min^{-1})	Type
Lead, Pb	1.00	217	5.00	1.60	12.0	Oxidizing
Chromium, Cr	0.200	358	6.00	3.20	12.0	Highly reducing
Nickel, Ni	0.200	232	4.00	1.60	12.0	Oxidizing
Cobalt, Co	0.200	241	6.00	1.60	12.0	Oxidizing
Copper, Cu	0.500	325	3.00	1.60	12.0	Oxidizing
Zinc, Zn	0.500	214	0.500	1.60	12.0	Oxidizing
Manganese, Mn	0.200	280	5.00	1.60	12.0	Oxidizing
Iron, Fe	0.200	248	7.00	1.60	12.0	Oxidizing

high risk, paying attention to the risk and taking action to resolve it (5×10.0^{-5}, 10.0^{-3}), extremely high risk, reject the risk, and must solve it ($>10.0^{-3}$).

Statistical Analysis

Statistical Package for Social Sciences was used for the data analysis. Data was expressed as mean ± standard deviation. One-way analysis of variance was carried out at $p=0.05$. Waller-Duncan statistics was used to discern the source of the observed significant differences between the herbal medicine for each of the trace metals. Pearson correlation and Hierarchical cluster analysis (HCA) using squared Euclidean Distance and Ward Linkage was used to reveal the relationship among different herbs. Principal component analysis (PCA) was used to determine disparity in the properties and source of trace elements in herbal medicine.

Results

Toxic Metal Concentration

The concentration of selected toxic metals in herbal medicine commonly used for the treatment of diseases in Nigeria is presented in Table 4, while the Pearson correlation of the toxic metals is highlighted in Table 5. The concentration of nickel was below the detection limit of 0.00120 mg L^{-1}. The concentration of zinc, chromium, manganese, iron, cobalt, lead, and copper was in the range of 0.329–1.23 mg L^{-1}, < 0.00150–0.0750 mg L^{-1}, 0.566–6.94 mg L^{-1}, 1.75–19.4 mg L^{-1}, < 0.00150–0.266 mg L^{-1}, < 0.0018–3.01 mg L^{-1}, and < 0.00900–0.0281 mg L^{-1}, respectively. There was statistical variation ($p<0.05$) in the concentration of trace metals among the various herbs. Furthermore, Waller-Duncan test statistics showed no significant variation ($p>0.05$) between the mean concentrations of heavy metals contained in some of the herbs.

Very strong positive significant correlations ($p<0.01$) exist between zinc with chromium, iron, lead, and copper; chromium with lead and copper; manganese with cobalt; iron with cobalt, lead, and copper; and lead with copper. In addition, chromium also showed strong significant correlation ($p<0.05$) between manganese and iron.

Figures 1 and 2 show the hierarchical cluster analysis using Squared Euclidean Distance and Ward Linkage of the trace metal variables and individual (cases) liquid herbal medicine used in the treatment of several diseases in Nigeria, respectively. For trace metal variables, two main clusters

Table 3 Spike recovery limits for trace elements

Metals	LOD (mg L^{-1})	LOQ (mg L^{-1})	Concentration of spike standard(mg L^{-1})	Pre-spike concentration of sample (mg L^{-1})	Post-spike concentration of sample (mg L^{-1})	Percentage recovery (%)
Lead, Pb	6.00E-4	1.80E-3	2.00	< LOQ	1.85	92.6
Chromium, Cr	5.00E-4	1.50E-3	0.500	0.0310	0.506	95.3
Nickel, Ni	4.00E-4	1.20E-3	0.500	< LOQ	0.476	95.2
Cobalt, Co	5.00E-4	1.50E-3	1.00	0.234	1.20	97.5
Copper, Cu	3.00E-4	9.00E-4	0.500	< LOQ	0.494	98.8
Zinc, Zn	8.00E-4	2.40E-3	0.500	0.379	0.856	97.4
Manganese, Mn	2.00E-3	6.10E-3	2.00	1.34	3.25	97.5
Iron, Fe	5.00E-3	1.52E-2	1.50	1.36	2.77	97.0

Table 4 Concentration of selected toxic metals in herbal medicine commonly used in the treatment of diseases in Nigeria

Herbs codes	Zn (mg L^{-1})	Cr (mg L^{-1})	Mn (mg L^{-1})	Fe (mg L^{-1})	Co (mg L^{-1})	Pb (mg L^{-1})	Cu (mg L^{-1})
MCA	0.557 ± 0.0100d	0.0540 ± 0.00200 g	6.94 ± 0.00900e	5.33 ± 0.0400e	0.189 ± 0.00200e	< 0.00180 ± < 0.00180a	0.0210 ± 0.00400b
OHC	0.974 ± 0.00800f	0.0280 ± 0.00100e	4.44 ± 0.0180d	2.63 ± 0.0330b	0.0570 ± 0.00100b	< 0.00180 ± < 0.00180a	0.0220 ± 0.00200b
SHM	0.373 ± 0.0150ab	0.0130 ± 0.00100c	1.35 ± 0.0110b	4.17 ± 0.0150d	0.0890 ± 0.00200c	< 0.00180 ± < 0.00180a	< 0.000900 ± < 0.000900a
AHM	1.23 ± 0.0310 g	0.0750 ± 0.00500 h	1.15 ± 0.0720b	17.8 ± 0.574 g	0.0830 ± 0.00300b	3.01 ± 0.00600c	0.281 ± 0.0190d
GC	0.380 ± 0.00100b	0.0180 ± 0.00100d	0.565 ± 0.0210a	4.21 ± 0.0420d	< 0.00150 ± < 0.00150a	< 0.00180 ± < 0.00180a	< 0.000900 ± < 0.000900a
DRH	0.504 ± 0.00600c	0.00200 ± 0.000a	1.15 ± 0.144b	6.81 ± 0.13f	0.00500 ± 0.000a	< 0.00180 ± < 0.00180a	< 0.000900 ± < 0.000900a
ARC	0.329 ± 0.0330a	< 0.00150 ± < 0.00150a	0.566 ± 0.0290a	1.75 ± 0.174a	0.113 ± 0.0110d	< 0.00180 ± < 0.00180a	< 0.000900 ± < 0.000900a
AAB	0.845 ± 0.0510e	0.00900 ± 0.00100bc	3.60 ± 0.102c	19.4 ± 0.396 h	0.266 ± 0.0320f	0.334 ± 0.00700b	< 0.000900 ± < 0.000900a
IHB	0.370 ± 0.0260ab	0.0320 ± 0.00100f	1.28 ± 0.264b	5.10 ± 0.0560e	0.0750 ± 0.00400bc	< 0.00180 ± < 0.00180a	< 0.000900 ± < 0.000900a
GCB	0.380 ± 0.0220ab	0.00700 ± 0.0010b	0.748 ± 0.0500a	3.43 ± 0.400c	0.0850 ± 0.00400c	< 0.00180 ± < 0.00180a	0.0500 ± 0.00200c

Data is expressed as mean ± standard deviation (n=3); different letters along the column indicates significant difference (p=0.05) according to Waller-Duncan statistics

were formed, iron in cluster 1, with the other trace metals (manganese, lead, zinc, copper, cobalt, and chromium) in cluster 2. In the cluster two, sub-clusters were formed, with each sub-cluster having equal distances (Fig. 1). For the herbal medicine variables, two main clusters were formed, with AAB and AHM being within the same cluster (cluster 1), while the other herbs were grouped in cluster 2. Within cluster 2, sub-clusters were formed, consisting of MCA and OHC, while the remaining herbs are contained in the second sub-cluster (DRH, ARC, IHB, GCB, SHM, and GC), with each of the clusters showing equal distances (Fig. 2).

Table 6 summarizes the PCA results for trace metals in some liquid herbal medicine sold in Nigeria. There is a total variance of 79.5% for the two principal components (PCs). PC-1 contributed 54.7% to the variance which correlates with zinc ($r=0.885$), chromium ($r=0.812$), iron ($r=0.781$), lead ($r=0.929$), and copper ($r=0.854$), while PC-2 contributed 24.8% to the variance which correlates with manganese (r=0.854) and cobalt (r=0.837).

Health Risk Assessment

Table 7 shows the chronic daily intake (mg/kg/day) of selected toxic metals in liquid herbal medicine commonly used for the treatment of diseases in Nigeria. Apart from samples with concentration below equipment detectable level, the CDI for adult and undergraduates (UG) respectively was in the order: 10.0^{-4} and 10.0^{-4}–10.0^{-3} (zinc), and 10.0^{-6}–10.0^{-4} and 10.0^{-5}–10.0^{-4} (copper). Furthermore, the CDI for chromium, manganese, iron, cobalt, and lead was in the order: 10.0^{-5}–10.0^{-4}, 10.0^{-4}–10.0^{-3}, 10.0^{-3}–10.0^{-2}, 10.0^{-6}–10.0^{-4}, and 10.0^{-4}–10.0^{-3} respectively, for both adult and UG respectively. The HQ of zinc, chromium, manganese, iron, cobalt, and zinc was in the order: 10.0^{-3}, 10.0^{-3}–10.0^{-2}, 10.0^{-3}–10.0^{-2}, 10.0^{-3}–10.0^{-2}, 10.0^{-1}–10.0^{-1}, 10.0^{-2}–10.0^{-1}, and 10.0^{-4}–10.0^{-3} respectively, except where sample concentration was below equipment detectable level LOQ, in which case it portends non-existent toxicity for both adults and UG. In addition, cobalt toxicity in ARC2 was calculated as (1.05E + 00) for adults, while ARC1 and 2 recorded (1.05E + 00) and (1.14E + 00), respectively for undergraduates (Table 8). The HI value of toxic metals was in the order: 10.0^{-2}–10.0^{-1}, apart from ARC2 (1.07E + 00) for adults and ARC1 (1.07E + 00) and 2 (1.16E + 00) for UG (Table 9).

The carcinogenic risk of selected toxic metals in liquid herbal medicine commonly used for the treatment of diseases in Nigeria is shown in Table 10. For lead, the CR was in the order 10.0^{-6} for AAB and 10^{-5} for AHM, while there was no CR for the other herbal medicines studied. This is mainly because the metals were below LOQ. For chromium, CR was in the range of 10.0^{-6}–10.0^{-5}, except for ARC that contained no chromium. Of these, 50.0%, 40.0%, and 10.0% was 10.0^{-6}, 10.0^{-5}, and non-existent respectively. Overall, the CR of the toxic metals for adult and UG were in the order 10.0^{-6}–10.0^{-5}.

Discussion

Plant part extracts and water are the major constituents of many liquid herbal medicine used for the treatment of several type of diseases including hepatitis, typhoid fever, ulcer, malaria, diabetes, and fibroid. Meanwhile, trace metals are common constituents of plants and water resources. In this study, nickel was below LOQ, an indication that the toxicity associated with it is non-existent; hence, the concentration in the herbal medicine were in conformance with the guideline limit of 0.0200 mg L^{-1} specified by WHO [16]. Apart from MCA, the concentration of chromium was lower than WHO and SON permissible limit of 0.0500 mg/L [35, 36]. The values recorded for zinc, manganese and iron were higher than the guideline limit of 3.00 mg/L, 0.200 mg L^{-1} and 0.300 mg L^{-1} respectively, as recommended by SON [36].

Table 5 Pearson correlation of selected toxic metals in herbal medicine commonly used in the treatment of diseases in Nigeria

Parameters	Zn	Cr	Mn	Fe	Co	Pb	Cu
Zn	1.00						
Cr	0.626**	1.00					
Mn	0.324	0.375*	1.00				
Fe	0.691**	0.386*	0.0920	1.00			
Co	0.219	0.0990	0.567**	0.504**	1.00		
Pb	0.747**	0.721**	−0.145	0.684**	0.0240	1.00	
Cu	0.711**	0.748**	−0.125	0.551**	−0.0520	0.969**	1.00

*Correlation is significant at the 0.05 level (2-tailed) (strong)

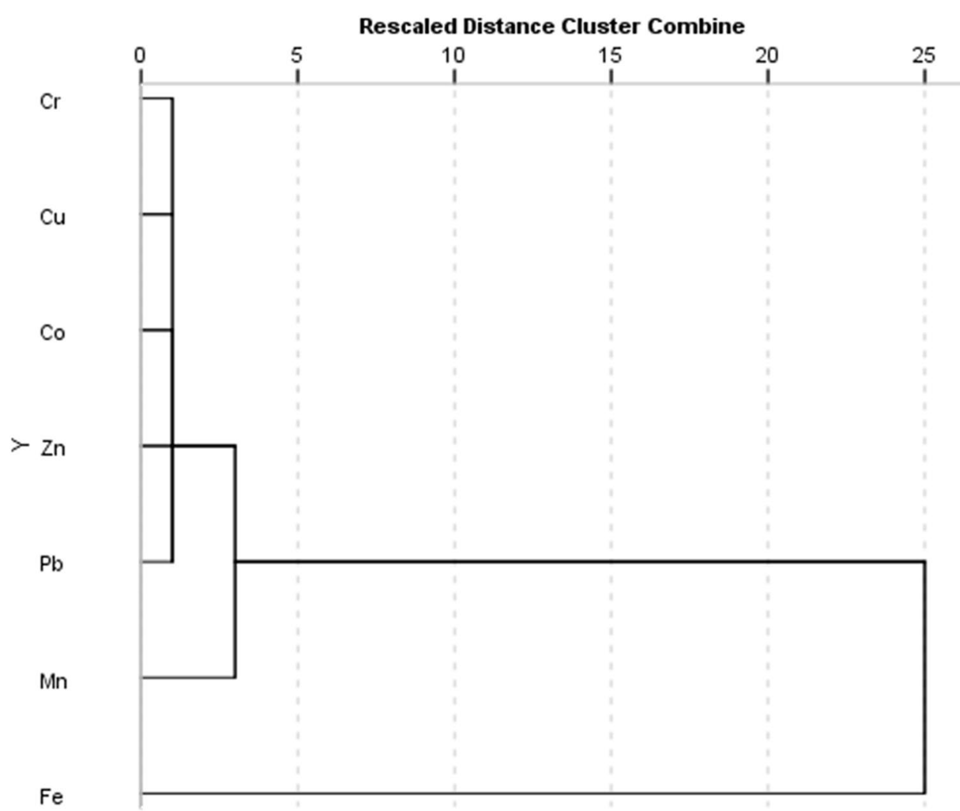
**Correlation is significant at the 0.01 level (2-tailed) (very strong)

n=30

In the two samples that lead was detected (AAB and AHM), concentration exceeded the WHO limit of 0.0100 mg L^{-1} [16]. In the four samples that copper was detected (MCA, OHC, AHM and GCB), concentrations were lower than 1.00 mg L^{-1} and 2.00 mg L^{-1} as recommended by SON and WHO, respectively [4]. Also, the concentration of cobalt was lower than the USEPA limit of 0.500 mg L^{-1} [16]. The concentration of toxic metals such as manganese, iron and lead, where detected, were predominantly higher than the recommended standard limits. This provides preliminary information about their toxicity.

The values recorded in this study are not in consonance with previous studies. For instance, Aigberua and Izah [1] reported the non-existence of nickel and lead, while zinc, iron, and cobalt had concentration of < 0.001–0.231 mg kg^{-1}, 6.82–15.3 mg kg^{-1}, and < 0.001–0.0149 mg kg^{-1} respectively in powdered herbal medicine produced in Ghana and Nigeria and commonly sold in Port Harcourt, Nigeria. Aigberua [13] reported chromium concentration of 0.0490–0.143 mg kg^{-1}, while copper and manganese were below instrument detection limit in powdered herbal medicine sold in Port Harcourt, Nigeria. The author further reported copper and manganese concentrations in the range of < 0.001–2.54 mg L^{-1} and 0.0410–0.982 mg L^{-1}, respectively, whereas chromium was observed to be below equipment detectable limit in liquid herbal medicine. Aigberua and Izah

Fig. 1 Hierarchical cluster analysis using Squared Euclidean Distance and Ward Linkage of the trace metal variables in liquid herbal medicine



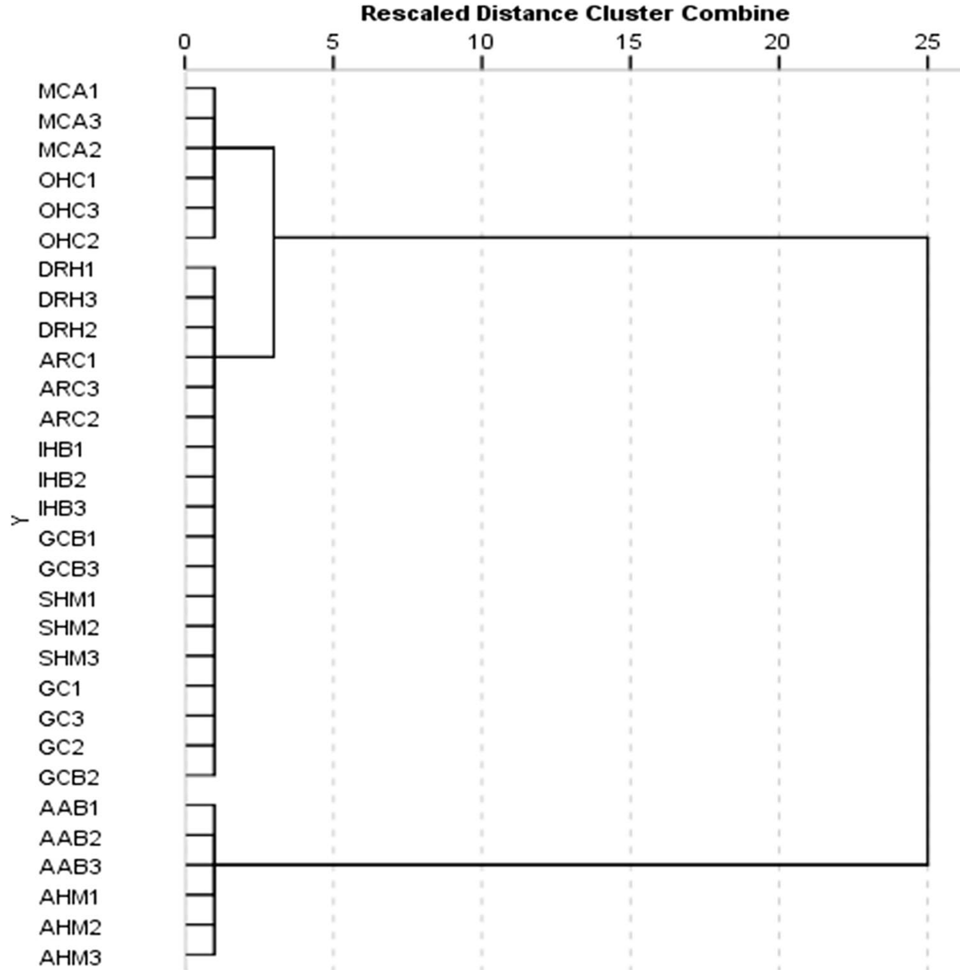


Fig. 2 Hierarchical cluster analysis using Squared Euclidean Distance and Ward Linkage of the individual liquid herbal medicine

[2] recorded < 0.001–0.0680 mg L^{-1}, < 0.001–0.0240 mg L^{-1}, < 0.001–0.177 mg L^{-1}, 1.30–27.1 mg L^{-1}, and < 0.001 mg L^{-1} for nickel, zinc, cobalt, iron, and lead, respectively in liquid herbal medicine produced in Nigeria. Onwordi et al. [17] reported trace metals in some herbal medicine in Lagos, Nigeria, within the range of 1.54–33.8 mg kg^{-1} (lead), 0.480–3.08 mg kg^{-1} (cadmium), and 0.730–54.0 mg kg^{-1} (nickel). Odoh and Ajiboye [37] recorded chromium, lead, nickel, cobalt, iron, and zinc concentrations within the range of 2.35–21.7 mg kg^{-1}, 6.44–25.1 mg kg^{-1}, 4.72–15.5 mg kg^{-1}, 0.640–5.56 mg kg^{-1}, 61.9–230 mg kg^{-1}, and 16.0–24.1 mg kg^{-1}, respectively in herbal medicine sold in Wukari metropolis, Taraba State, Nigeria. The author also reported no cadmium in herbal medicines. Ekeanyanwu et al. [15] reported chromium, nickel, and cadmium as non-existent in some herbal medicine (ATU wonder), Goodwill herbal, Jalin powder, Rinbacin Forte, Omega, THUJA 1000 powder, Aloe vera dental powder, tropical herbal mixture, and Virgy–virgy, except for a concentration of 0–0.702 ppm observed for manganese, and 0.0250–1.12 ppm for copper in herbal medicine sold in Port Harcourt, Nigeria. Afieroho et al. [14] reported trace metals concentration of 3.20–45.8 ppm (cadmium), 0–75.0 ppm (lead), and < 0.001 ppm (chromium) in herbal bitters preparation sold in Benin city, Southern Nigeria. Igweze et al. [16] recorded 0.000590–0.0337 mg L^{-1} (cadmium), 0.000660–0.0506 mg L^{-1} (chromium),

Table 6 Principal components for the selected trace metals in some liquid herbal medicine sold in Nigeria

Heavy metals	PC-1	PC-2
Total	3.83	1.74
% of variance	54.7	24.8
Cumulative %	54.7	79.5
Zn	**0.885**	0.107
Cr	**0.812**	0.0200
Mn	0.201	**0.854**
Fe	**0.781**	0.190
Co	0.268	**0.837**
Pb	**0.929**	− 0.338
Cu	**0.894**	− 0.382

The dominant trace metals in each PC are reported in bold

Table 7 Chronic daily intake (mg/kg/day) of selected toxic metals in herbal medicine commonly used for the treatment of diseases in Nigeria

Herbs codes	Zn		Cr		Mn		Fe		Co		Pb		Cu	
	Adult	UG	Adult	UG	Adult	UG	Adult	UG	Adult	UG	Adult	UG	Adult	UG
MCA1	3.14E-04	3.39E-04	3.03E-05	3.26E-05	3.97E-03	4.27E-03	3.03E-03	3.26E-03	1.09E-04	1.18E-04	0.00E+00	0.00E+00	1.26E-05	1.35E-05
MCA2	3.25E-04	3.50E-04	3.20E-05	3.45E-05	3.96E-03	4.27E-03	3.07E-03	3.31E-03	1.09E-04	1.17E-04	0.00E+00	0.00E+00	9.71E-06	1.05E-05
MCA3	3.15E-04	3.40E-04	2.97E-05	3.20E-05	3.96E-03	4.26E-03	3.04E-03	3.27E-03	1.07E-04	1.15E-04	0.00E+00	0.00E+00	1.37E-05	1.48E-05
OHC1	5.57E-04	5.99E-04	1.54E-05	1.66E-05	2.54E-03	2.73E-03	1.50E-03	1.62E-03	3.20E-05	3.45E-05	0.00E+00	0.00E+00	1.20E-05	1.29E-05
OHC2	5.53E-04	5.95E-04	1.66E-05	1.79E-05	2.54E-03	2.74E-03	1.52E-03	1.64E-03	3.31E-05	3.57E-05	0.00E+00	0.00E+00	1.26E-05	1.35E-05
OHC3	5.61E-04	6.04E-04	1.54E-05	1.66E-05	2.52E-03	2.72E-03	1.49E-03	1.60E-03	3.26E-05	3.51E-05	0.00E+00	0.00E+00	1.37E-05	1.48E-05
SHM1	4.81E-04	5.18E-04	1.65E-05	1.78E-05	1.70E-03	1.83E-03	5.31E-03	5.72E-03	1.14E-04	1.23E-04	0.00E+00	0.00E+00	0.00E+00	0.00E+00
SHM2	4.53E-04	4.87E-04	1.53E-05	1.64E-05	1.71E-03	1.84E-03	5.32E-03	5.73E-03	1.11E-04	1.19E-04	0.00E+00	0.00E+00	0.00E+00	0.00E+00
SHM3	4.90E-04	5.27E-04	1.65E-05	1.78E-05	1.73E-03	1.86E-03	5.28E-03	5.69E-03	1.16E-04	1.25E-04	0.00E+00	0.00E+00	0.00E+00	0.00E+00
AHM1	5.41E-04	5.83E-04	3.21E-05	3.46E-05	4.76E-04	5.13E-04	7.77E-03	8.36E-03	3.56E-05	3.83E-05	1.29E-03	1.39E-03	1.20E-04	1.30E-04
AHM2	5.15E-04	5.54E-04	3.39E-05	3.65E-05	5.28E-04	5.68E-04	7.80E-03	8.40E-03	3.64E-05	3.92E-05	1.29E-03	1.39E-03	1.29E-04	1.39E-04
AHM3	5.25E-04	5.65E-04	3.00E-05	3.23E-05	4.72E-04	5.08E-04	7.36E-03	7.93E-03	3.43E-05	3.69E-05	1.29E-03	1.39E-03	1.12E-04	1.21E-04
GC1	4.83E-04	5.20E-04	2.29E-05	2.47E-05	7.17E-04	7.72E-04	5.40E-03	5.82E-03	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
GC2	4.83E-04	5.20E-04	2.42E-05	2.60E-05	7.46E-04	8.04E-04	5.30E-03	5.70E-03	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
GC3	4.84E-04	5.22E-04	2.29E-05	2.47E-05	6.93E-04	7.46E-04	5.34E-03	5.76E-03	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
DRH1	8.64E-04	9.31E-04	3.43E-06	3.69E-06	1.94E-03	2.08E-03	1.17E-02	1.26E-02	8.57E-06	9.23E-06	0.00E+00	0.00E+00	0.00E+00	0.00E+00
DRH2	8.54E-04	9.19E-04	3.43E-06	3.69E-06	2.23E-03	2.40E-03	1.15E-02	1.23E-02	8.57E-06	9.23E-06	0.00E+00	0.00E+00	0.00E+00	0.00E+00
DRH3	8.74E-04	9.42E-04	3.43E-06	3.69E-06	1.74E-03	1.87E-03	1.19E-02	1.28E-02	8.57E-06	9.23E-06	0.00E+00	0.00E+00	0.00E+00	0.00E+00
ARC1	8.28E-04	8.92E-04	0.00E+00	0.00E+00	1.48E-03	1.59E-03	4.44E-03	4.79E-03	2.93E-04	3.16E-04	0.00E+00	0.00E+00	0.00E+00	0.00E+00
ARC2	9.39E-04	1.01E-03	0.00E+00	0.00E+00	1.37E-03	1.48E-03	4.97E-03	5.36E-03	3.16E-04	3.41E-04	0.00E+00	0.00E+00	0.00E+00	0.00E+00
ARC3	7.74E-04	8.34E-04	0.00E+00	0.00E+00	1.52E-03	1.63E-03	4.09E-03	4.40E-03	2.60E-04	2.80E-04	0.00E+00	0.00E+00	0.00E+00	0.00E+00
AAB1	3.56E-04	3.83E-04	4.29E-06	4.62E-06	1.54E-03	1.66E-03	8.37E-03	9.02E-03	1.15E-04	1.24E-04	1.45E-04	1.56E-04	0.00E+00	0.00E+00
AAB2	3.87E-04	4.16E-04	4.29E-06	4.62E-06	1.59E-03	1.71E-03	8.47E-03	9.12E-03	1.27E-04	1.37E-04	1.45E-04	1.57E-04	0.00E+00	0.00E+00
AAB3	3.44E-04	3.71E-04	3.43E-06	3.69E-06	1.50E-03	1.61E-03	8.14E-03	8.76E-03	1.00E-04	1.08E-04	1.40E-04	1.51E-04	0.00E+00	0.00E+00
IHB1	6.26E-04	6.74E-04	5.31E-05	5.72E-05	2.22E-03	2.39E-03	8.65E-03	9.32E-03	1.30E-04	1.40E-04	0.00E+00	0.00E+00	0.00E+00	0.00E+00
IHB2	6.82E-04	7.35E-04	5.49E-05	5.91E-05	2.63E-03	2.83E-03	8.59E-03	9.25E-03	1.22E-04	1.31E-04	0.00E+00	0.00E+00	0.00E+00	0.00E+00
IHB3	5.93E-04	6.39E-04	5.66E-05	6.09E-05	1.72E-03	1.85E-03	8.78E-03	9.45E-03	1.35E-04	1.46E-04	0.00E+00	0.00E+00	0.00E+00	0.00E+00
GCB1	7.33E-04	7.90E-04	1.33E-05	1.43E-05	1.40E-03	1.51E-03	6.49E-03	6.99E-03	1.62E-04	1.74E-04	0.00E+00	0.00E+00	9.50E-05	1.02E-04
GCB2	6.76E-04	7.28E-04	1.14E-05	1.23E-05	1.53E-03	1.64E-03	7.30E-03	7.86E-03	1.67E-04	1.80E-04	0.00E+00	0.00E+00	9.69E-05	1.04E-04
GCB3	7.56E-04	8.14E-04	1.33E-05	1.43E-05	1.34E-03	1.44E-03	5.78E-03	6.23E-03	1.54E-04	1.66E-04	0.00E+00	0.00E+00	9.12E-05	9.82E-05

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Table 8 Hazard quotient of selected toxic metals in herbal medicine commonly used for the treatment of diseases in Nigeria

Herbs codes	Zn		Cr		Mn		Fe		Co		Pb		Cu	
	Adult	UG	Adult	UG	Adult	UG	Adult	UG	Adult	UG	Adult	UG	Adult	UG
MCA1	1.05E-03	1.13E-03	1.01E-02	1.09E-02	2.84E-02	3.05E-02	4.33E-03	4.66E-03	3.64E-01	3.92E-01	0.00E+00	0.00E+00	3.14E-04	3.39E-04
MCA2	1.08E-03	1.17E-03	1.07E-02	1.15E-02	2.83E-02	3.05E-02	4.39E-03	4.73E-03	3.62E-01	3.90E-01	0.00E+00	0.00E+00	2.43E-04	2.62E-04
MCA3	1.05E-03	1.13E-03	9.91E-03	1.07E-02	2.83E-02	3.05E-02	4.34E-03	4.67E-03	3.56E-01	3.84E-01	0.00E+00	0.00E+00	3.43E-04	3.69E-04
OHC1	1.86E-03	2.00E-03	5.14E-03	5.54E-03	1.81E-02	1.95E-02	2.15E-03	2.31E-03	1.07E-01	1.15E-01	0.00E+00	0.00E+00	3.00E-04	3.23E-04
OHC2	1.84E-03	1.98E-03	5.52E-03	5.95E-03	1.82E-02	1.96E-02	2.18E-03	2.35E-03	1.11E-01	1.19E-01	0.00E+00	0.00E+00	3.14E-04	3.39E-04
OHC3	1.87E-03	2.01E-03	5.14E-03	5.54E-03	1.80E-02	1.94E-02	2.12E-03	2.29E-03	1.09E-01	1.17E-01	0.00E+00	0.00E+00	3.43E-04	3.69E-04
SHM1	1.60E-03	1.73E-03	5.51E-03	5.93E-03	1.22E-02	1.31E-02	7.59E-03	8.17E-03	3.81E-01	4.11E-01	0.00E+00	0.00E+00	0.00E+00	0.00E+00
SHM2	1.51E-03	1.63E-03	5.09E-03	5.48E-03	1.22E-02	1.32E-02	7.60E-03	8.19E-03	3.69E-01	3.97E-01	0.00E+00	0.00E+00	0.00E+00	0.00E+00
SHM3	1.63E-03	1.76E-03	5.51E-03	5.93E-03	1.24E-02	1.33E-02	7.55E-03	8.13E-03	3.86E-01	4.15E-01	0.00E+00	0.00E+00	0.00E+00	0.00E+00
AHM1	1.80E-03	1.94E-03	1.07E-02	1.15E-02	3.40E-03	3.66E-03	1.11E-02	1.20E-02	1.19E-01	1.28E-01	3.69E-01	3.98E-01	3.01E-03	3.24E-03
AHM2	1.72E-03	1.85E-03	1.13E-02	1.22E-02	3.77E-03	4.06E-03	1.12E-02	1.20E-02	1.21E-01	1.31E-01	3.68E-01	3.96E-01	3.21E-03	3.46E-03
AHM3	1.75E-03	1.88E-03	1.00E-02	1.08E-02	3.37E-03	3.63E-03	1.05E-02	1.13E-02	1.14E-01	1.23E-01	3.69E-01	3.98E-01	2.81E-03	3.02E-03
GC1	1.61E-03	1.73E-03	7.63E-03	8.22E-03	5.12E-03	5.52E-03	7.72E-03	8.31E-03	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
GC2	1.61E-03	1.73E-03	8.05E-03	8.67E-03	5.33E-03	5.74E-03	7.57E-03	8.15E-03	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
GC3	1.62E-03	1.74E-03	7.63E-03	8.22E-03	4.95E-03	5.33E-03	7.63E-03	8.22E-03	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
DRH1	2.88E-03	3.10E-03	1.14E-03	1.23E-03	1.38E-02	1.49E-02	1.67E-02	1.80E-02	2.86E-02	3.08E-02	0.00E+00	0.00E+00	0.00E+00	0.00E+00
DRH2	2.85E-03	3.07E-03	1.14E-03	1.23E-03	1.59E-02	1.71E-02	1.64E-02	1.76E-02	2.86E-02	3.08E-02	0.00E+00	0.00E+00	0.00E+00	0.00E+00
DRH3	2.91E-03	3.14E-03	1.14E-03	1.23E-03	1.24E-02	1.34E-02	1.70E-02	1.83E-02	2.86E-02	3.08E-02	0.00E+00	0.00E+00	0.00E+00	0.00E+00
ARC1	2.76E-03	2.97E-03	0.00E+00	0.00E+00	1.06E-02	1.14E-02	6.35E-03	6.84E-03	9.77E-01	1.05E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
ARC2	3.13E-03	3.37E-03	0.00E+00	0.00E+00	9.81E-03	1.06E-02	7.10E-03	7.65E-03	1.05E+00	1.14E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
ARC3	2.58E-03	2.78E-03	0.00E+00	0.00E+00	1.08E-02	1.17E-02	5.84E-03	6.29E-03	8.66E-01	9.32E-01	0.00E+00	0.00E+00	0.00E+00	0.00E+00
AAB1	1.19E-03	1.28E-03	1.43E-03	1.54E-03	1.10E-02	1.19E-02	1.20E-02	1.29E-02	3.83E-01	4.12E-01	4.14E-02	4.46E-02	0.00E+00	0.00E+00
AAB2	1.29E-03	1.39E-03	1.43E-03	1.54E-03	1.13E-02	1.22E-02	1.21E-02	1.30E-02	4.24E-01	4.57E-01	4.15E-02	4.47E-02	0.00E+00	0.00E+00
AAB3	1.15E-03	1.24E-03	1.14E-03	1.23E-03	1.07E-02	1.15E-02	1.16E-02	1.25E-02	3.34E-01	3.60E-01	3.99E-02	4.30E-02	0.00E+00	0.00E+00
IHB1	2.09E-03	2.25E-03	1.77E-02	1.91E-02	1.58E-02	1.71E-02	1.24E-02	1.33E-02	4.34E-01	4.68E-01	0.00E+00	0.00E+00	0.00E+00	0.00E+00
IHB2	2.27E-03	2.45E-03	1.83E-02	1.97E-02	1.88E-02	2.02E-02	1.23E-02	1.32E-02	4.06E-01	4.37E-01	0.00E+00	0.00E+00	0.00E+00	0.00E+00
IHB3	1.98E-03	2.13E-03	1.89E-02	2.03E-02	1.23E-02	1.32E-02	1.25E-02	1.35E-02	4.51E-01	4.86E-01	0.00E+00	0.00E+00	0.00E+00	0.00E+00
GCB1	2.45E-03	2.63E-03	4.43E-03	4.77E-03	1.00E-02	1.08E-02	9.28E-03	9.99E-03	5.38E-01	5.80E-01	0.00E+00	0.00E+00	2.38E-03	2.56E-03
GCB2	2.26E-03	2.43E-03	3.80E-03	4.09E-03	1.09E-02	1.17E-02	1.04E-02	1.12E-02	5.57E-01	6.00E-01	0.00E+00	0.00E+00	2.42E-03	2.61E-03
GCB3	2.52E-03	2.72E-03	4.43E-03	4.77E-03	9.55E-03	1.03E-02	8.26E-03	8.90E-03	5.13E-01	5.53E-01	0.00E+00	0.00E+00	2.28E-03	2.46E-03

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Table 9 Hazard index of selected toxic metals in herbal medicine commonly used for the treatment of diseases in Nigeria

Sample code	Adult	UG
MCA1	4.08E-01	4.39E-01
MCA2	4.07E-01	4.38E-01
MCA3	4.00E-01	4.31E-01
OHC1	1.34E-01	1.45E-01
OHC2	1.39E-01	1.49E-01
OHC3	1.36E-01	1.47E-01
SHM1	4.08E-01	4.40E-01
SHM2	3.95E-01	4.26E-01
SHM3	4.13E-01	4.45E-01
AHM1	5.18E-01	5.58E-01
AHM2	5.20E-01	5.60E-01
AHM3	5.12E-01	5.51E-01
GC1	2.21E-02	2.38E-02
GC2	2.26E-02	2.43E-02
GC3	2.18E-02	2.35E-02
DRH1	6.32E-02	6.80E-02
DRH2	6.48E-02	6.98E-02
DRH3	6.20E-02	6.68E-02
ARC1	9.97E-01	1.07E+00
ARC2	1.07E+00	1.16E+00
ARC3	8.85E-01	9.53E-01
AAB1	4.50E-01	4.84E-01
AAB2	4.92E-01	5.30E-01
AAB3	3.99E-01	4.30E-01
IHB1	4.82E-01	5.19E-01
IHB2	4.57E-01	4.93E-01
IHB3	4.97E-01	5.35E-01
GCB1	5.67E-01	6.11E-01
GCB2	5.87E-01	6.32E-01
GCB3	5.40E-01	5.82E-01

Undergraduate

0.000570–0.0206 mg/L (lead), 0.000580–0.216 mg L^{-1} (cobalt), and 0.000274–0.0401 mg L^{-1} (nickel) in some herbal medicines sold in the Niger Delta region of Nigeria.

7The significant variation observed in different herbal medicines may be due to differences in bioaccumulation tendencies of trace elements by various plants utilized for the formulation of herbal medicines. Similarly, trace elements, if contained in the formulation water may have accounted for the observed variation as well. Pearson correlation statistics showed most of the trace metals to emanate from similar source, showing mutual dependence and identical behavior during transport [7]. Ward Cluster analysis also showed that many of the herbal medicines have equal distances. However, close distance cluster indicates significant relationship, while distance cluster shows the degree of disassociation of the metals in herbal medicine [7].

Based on principal component analysis (PCA) result, all trace metals were discretely located apart from iron, whereas, all the different herbs showed discrete localization. The reasonable dispersion of iron (Fe) from other trace metals is due to its outlier concentration in the different herbal mixtures. The significantly high concentration of trace elements in MCA, OHC, AHM and AAB herbal formulations are responsible for the variance and slight dispersion from the predominant cluster (Fig. 3). The detected metals (zinc, chromium, manganese, iron, cobalt, lead, and copper) could be influenced by the concentration of trace elements in plants and water used during the herbal formulation process. Studies have shown that trace metal micro-pollutants are found in plants and water [4, 7, 23, 38]. Thus, the trace metals detected in test herbs may have resulted from both geogenic and anthropogenic sources, particularly from farmlands where the plants were cultivated. In the same vein, the source of water used in formulating the herbal concoction may have contributed to the reported metal concentration.

The health risks were assessed based on two perspectives, viz carcinogenic risk and non-carcinogenic risk. Information on the health risk of toxic metals in herbal formulation is scarce in literature. Health risk was determined for the concentration of toxic metals in herbal formulations. To assess the risk, there is need to develop systemic impact due to chronic exposure to toxic metals by ingestion [8]. The CDI, HQ and HI were calculated for two groups (adults and UG), and the values recorded were < 1.00 for both groups, except for HQ of cobalt and HI of ARC2 for adults, as well as ARC1 and 2 for UG with a value in the order of > 1.00. According to Razaei et al. [8], HQ of less than (< 1.00) indicates non-carcinogenic risk due to oral intake of liquid herbal formulations. Conversely, a value higher than 1.00 (> 1.00) indicates probability of non-cancer causing effects on human health [25]. However, similar trends have been reported in potable water. Adeyemi and Ojekunle [25], Anyanwu and Nwachukwu [24] reported that HQ of some trace metals in potable water were higher than 1.00 (> 1.00).

The HI which shows the overall probability for non-carcinogenic effects by multiple toxic metals [8] was less than 1.00 (< 1.00). This indicates that there is no possibility of cumulative deleterious health concern [8] for both groups that ingest these herbal formulations. However, it is pertinent to note that trace metals toxicity in humans is related to their intake [6]. Overall, the HI value from this study was less than those reported in some drinking water sources in some parts of Nigeria [24, 25].

Table 10 Carcinogenic risk of selected toxic metals in herbal medicine commonly used for the treatment of diseases in Nigeria

Sample code	Cr		Pb		Total carcinogenic risk	
	Adult	UG	Adult	UG	Adult	UG
MCA1	1.51E-05	1.63E-05	0.00E+00	0.00E+00	1.51E-05	1.63E-05
MCA2	1.60E-05	1.72E-05	0.00E+00	0.00E+00	1.60E-05	1.72E-05
MCA3	1.49E-05	1.60E-05	0.00E+00	0.00E+00	1.49E-05	1.60E-05
OHC1	7.71E-06	8.31E-06	0.00E+00	0.00E+00	7.71E-06	8.31E-06
OHC2	8.29E-06	8.92E-06	0.00E+00	0.00E+00	8.29E-06	8.92E-06
OHC3	7.71E-06	8.31E-06	0.00E+00	0.00E+00	7.71E-06	8.31E-06
SHM1	8.26E-06	8.90E-06	0.00E+00	0.00E+00	8.26E-06	8.90E-06
SHM2	7.63E-06	8.22E-06	0.00E+00	0.00E+00	7.63E-06	8.22E-06
SHM3	8.26E-06	8.90E-06	0.00E+00	0.00E+00	8.26E-06	8.90E-06
AHM1	1.61E-05	1.73E-05	1.10E-05	1.18E-05	2.71E-05	2.91E-05
AHM2	1.69E-05	1.82E-05	1.09E-05	1.18E-05	2.79E-05	3.00E-05
AHM3	1.50E-05	1.62E-05	1.10E-05	1.18E-05	2.60E-05	2.80E-05
GC1	1.14E-05	1.23E-05	0.00E+00	0.00E+00	1.14E-05	1.23E-05
GC2	1.21E-05	1.30E-05	0.00E+00	0.00E+00	1.21E-05	1.30E-05
GC3	1.14E-05	1.23E-05	0.00E+00	0.00E+00	1.14E-05	1.23E-05
DRH1	1.71E-06	1.85E-06	0.00E+00	0.00E+00	1.71E-06	1.85E-06
DRH2	1.71E-06	1.85E-06	0.00E+00	0.00E+00	1.71E-06	1.85E-06
DRH3	1.71E-06	1.85E-06	0.00E+00	0.00E+00	1.71E-06	1.85E-06
ARC1	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
ARC2	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
ARC3	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
AAB1	2.14E-06	2.31E-06	1.23E-06	1.33E-06	3.37E-06	3.63E-06
AAB2	2.14E-06	2.31E-06	1.24E-06	1.33E-06	3.38E-06	3.64E-06
AAB3	1.71E-06	1.85E-06	1.19E-06	1.28E-06	2.90E-06	3.13E-06
IHB1	2.66E-05	2.86E-05	0.00E+00	0.00E+00	2.66E-05	2.86E-05
IHB2	2.74E-05	2.95E-05	0.00E+00	0.00E+00	2.74E-05	2.95E-05
IHB3	2.83E-05	3.05E-05	0.00E+00	0.00E+00	2.83E-05	3.05E-05
GCB1	6.65E-06	7.16E-06	0.00E+00	0.00E+00	6.65E-06	7.16E-06
GCB2	5.70E-06	6.14E-06	0.00E+00	0.00E+00	5.70E-06	6.14E-06
GCB3	6.65E-06	7.16E-06	0.00E+00	0.00E+00	6.65E-06	7.16E-06

Undergraduate

The estimated carcinogenic risk was in the order: 10.0^{-6}–10.0^{-5}. Studies have indicated that the threshold limit for assessing risk of heavy metals is 10.0^{-6}–10.0^{-4}, which indicates the probability of 1 in 1,000,000 and 1 in 10,000 persons developing cancer [6, 7, 23, 24, 32, 39]. However, based on the Cancer Risk Assessment Standards by Adeyemi and Ojekunle [25], and Joel et al. [34], the CR depicts low risk; not willing to care about the risk or negligible risk (10.0^{-6}, 10.0^{-5}). Hence, the findings of this study revealed that CR did not exceed the threshold limit of concern to consumers of liquid herbal medicine within the study areas. As such, the risk associated with these carcinogenic metals in liquid herbal formulations is considered insignificant for individuals residing in the study area. However, it is important to note that long term exposure to low amounts of carcinogenic metals could result in divergent types of cancer [6].

Conclusion

This study was carried out to assess the health risk associated with carcinogenic metals (chromium, lead, cadmium, and nickel) that are ingested from the intake of liquid herbal formulations during the treatment of infectious and non-infectious diseases. Health risk index calculations helps to effectively rank the toxicity of trace metals, thereby vividly portraying the human health risk associated to its exposure. The risk assessment relevant to the study includes the carcinogenic and non-carcinogenic risk. Overall, the concentration of trace metals in herbal concoctions was in the order: copper < cobalt < lead < zinc < manganese < iron, while nickel was not detected in any of the herbal medicines. The HQ was less than 1.00 (< 1.00), except for cobalt in ARC of both groups (adults and UG). Also, HI was mostly less than 1.00 (< 1.00), except for sample ARC. The CR value showed

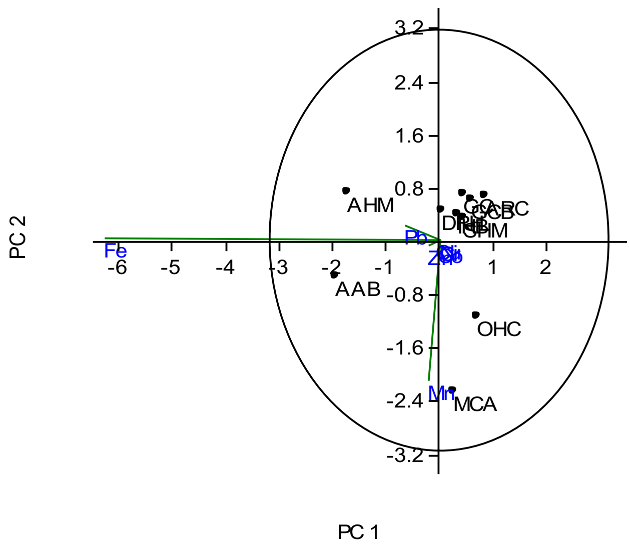

Fig. 3 Principal component analysis of trace metals and the different herbs

that the ingestion of carcinogenic metals via herbal consumption is negligible. However, lead and chromium showed carcinogenic tendencies for both groups of people (adult and undergraduates). Hence, there is need to routinely monitor the level of trace elements in herbal mixtures in order to ensure detection when abnormalities that could endanger consumer health occurs.

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Availability of Data and Material Raw data available on request.

Code Availability Not applicable.

Declarations

Ethics Approval Ethical approved was obtained from the research and ethics committee of Bayelsa Medical University, Yenagoa, Bayelsa State, Nigeria.

Consent to Participate Not applicable.

Consent for Publication Not applicable.

Conflict of Interest The authors declare no competing of interest.

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