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Nigerian herbal remedies and heavy metals: violation of standard recommended guidelines

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ABSTRACT

Objective: The growing popularity of herbal remedies approved by the National Agency for Food and Drug Administration and Control (NAFDAC), in Nigeria necessitates a critical re–evaluation of the risks associated with their use. Arsenic, cadmium, chromium, cobalt, lead and nickel contents of were analysed to ascertain their compliance with the recommended limits of the World Health Organization, European Union and United States Environmental Protection Agency. **Methods:** Twenty four different Nigerian herbal remedies (NHR) in two types of pharmaceutical dosage forms – liquid and capsules, were sampled using basket market protocol in the Niger Delta, Nigeria, in December, 2010. The NHR were ashed before digestion using conc aqua regia HCL: HNO₃ (3:1) and arsenic, cadmium, chromium, cobalt, lead and nickel were assayed with Atomic Absorption Spectrophotometer, AAS 205A. Arsenic, cadmium, chromium, cobalt, lead and nickel contents of were compared with the recommended limits of the World Health Organization (WHO), European Union (EU) and United States Environmental Protection Agency (USEPA). **Results:** The highest concentrations of the heavy metals were found in the solid dosage forms whereas the lowest concentrations were found in the liquid preparations. Our study shows the percentage violation of the WHO and EU limits for the six metals were arsenic (0%); cadmium (58.3%); chromium (4.16%); cobalt (0%); lead (54.1%) and nickel (54.1%). **Conclusions:** This study highlights the need for pharmaco–vigilance especially with respect to metalo–toxicity of Nigerian herbal remedies and need for in–depth risk assessment to understand the extent of the problem.

1. Introduction

Over 80% of the populations in some Asian and African countries depend on traditional medicine for primary health care [1]. Herbal remedies often contain numerous different plant and animal–derived products that combine to act synergistically to affect a desired outcome [2, 3]. However, due to the proprietary nature of herbal remedies manufacture, coupled with a lack of industry regulation, the biological origin of contents can be difficult to determine with confidence, leading to questions regarding herbal remedies quality, efficacy and safety [4,5]. Undeclared or misidentified ingredients and adulterants can pose serious health risks to consumers [4,6,7,8].

Survey has shown that about 75 – 80% the global population still relies on herbal remedies especially in the developing

countries [9–10]. Almost all are available without prescription, easy to use and are thought by the consumers as “healthier” and safer than orthodox pharmaceutical substances [11]. The World Health Organization (WHO) stated that users of herbal remedies globally exceed that of conventional orthodox medicine by two to three times [12]. The Nigerian herbal remedies usually consists of several herbs and other ingredients only known to the manufacturer, dried and ground into powder, mixed and encapsulated as either soft or hard gelatin capsules, whereas the liquid preparation are either suspensions or filtered solution of a mixture of herbs. The extent of heavy metal contamination in registered Nigerian herbal remedies is not documented. Studies globally have demonstrated that most herbal remedies are not subjected to stringent drug approval processes.

Although the majority of published cases of heavy metal poisoning come from occupational exposures, some herbal remedies may also contain toxic amounts of heavy metals [13]. Also a prospective study showed that 25% of corneal

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ulcer in Tanzania and 26% of childhood blindness in Nigeria and Malawi were associated with the use of traditional eye medicine [14]. Heavy metals occur freely in soil and water and could easily contaminate food and herbal products. There is therefore a need to protect the total population [15]. Moreover lead, thallium, mercury, arsenic, copper and cadmium poisoning from consumption of such products have been widely reported [16, 17, 18].

Heavy metal contamination is a global challenge because herbal product contamination with heavy metals have also been reported from Africa [19], Europe [20, 21], South America [22, 23] [23].

This study has attempted to analyse and quantify the levels of arsenic, cadmium, chromium, cobalt, lead and nickel in commonly used herbal remedies and ascertain their compliance with stated limits by World Health organization (WHO), the European Union (EU) and United States Environmental Protection Agency (USEPA).

2. Materials and methods

Using a basket market protocol, twenty four different Nigerian Herbal supplements (NHS) randomly sampled at herbal medicines fair in the Niger Delta in December, 2010 were used for the study. They were analyzed for Arsenic, Cadmium, Chromium, Cobalt, Lead and Nickel contents and to ascertain their compliance with the recommended limits of the World Health Organization (WHO), European Union (EU).

The samples were ashed and digested in Teflon lab ware that had been cleaned in a high-efficiency particulate air (HEPA) filtered (class 100), trace-metal-clean laboratory to minimize contamination. This protocol involved sequential cleaning of the lab ware in a series of baths in solutions (1 week each) and rinses (five per deionized water rinses, then 6-NHCl (reagent grade) solutions and ultrapure water rinses, finally 7.5 N HNO₃ (trace metal grade) solution and ultrapure water rinses. The lab ware was then air dried in a polypropylene laminar air flow-exhausting hood. Dry ashing method was used by adding 30 ml of each sample into a conical flask and heated on a hot plate at 2000 °C, for 45min, then in a furnace at 500 °C until the volume was drastically reduced to near dryness. Digestion was done by addition of 10 ml conc. aqua regia (HCl:HNO₃, 3:1), it was then heated to dryness. About 20 ml deionized water was added, stirred and filtered. The filtrate was made up in standard volumetric flask and mercury, antimony and tin were assayed with Atomic Absorption Spectrophotometer 205A. The limit of detection for arsenic, cadmium, chromium, cobalt, lead and nickel was 0.0005ppm with blank values reading as 0.00 ppm for the three metals in deionized water with electrical

conductivity value of lower than 5 μ S/cm. Samples were analysed in triplicates.

3. Results

Tables 1– 6 shows the arsenic, cadmium, chromium, cobalt, lead and nickel levels in comparison with recommended guidelines of WHO, EU, and USEPA.

The liquid preparations did not violate the limits of the WHO, EU and USEPA. Almost all the solid samples violated the limits. The highest and lowest values for each of the metals in ppm were arsenic: <0.005 – <0.005; Cadmium: 0.00059–0.0337; Chromium: 0.00066 – 0.0506; Cobalt: 0.00058 –0.216; lead: 0.00057 – 0.0206 and Nickel: 0.000274 – 0.0401. All the samples had non-detectable levels of arsenic (<0.005ug/l) Table 1.

Table 2 shows the values for cadmium in the supplements. None of the liquid preparations violated the limits for WHO and EU although the WHO and EU had differing limits for cadmium. The solid samples were more contaminated with cadmium reaching a level of 1023% (of the WHO limit) and 514% (of the EU limit) in one sample (Smart herbal capsule).

Table 3 shows the values for chromium. All the samples except one (Elimax capsule) did not violate the limits for WHO and EU. The violation was however minimal – 1.2%.

Table 4 shows the values for cobalt. The USEPA limit for cobalt is 0.05 ug/l and none of the samples violated the limit. Table 5 shows the level of lead contamination in the herbal supplements. About 54.1% of the samples (all solids) violated the WHO and EU limits for lead. None of the liquid formulations violated the limits.

Table 6 shows the nickel contamination of the herbal supplements. None of the liquid formulations violated the limits. Also 54.1% of the samples (all solids) violated the WHO and EU limits for nickel except Ababio capsule. The violation ranged from 18.5% – 140%.

4. Discussion

Studies of heavy metal contamination of phytochemicals have taken a wider global interest [19–23]. We sought to examine the heavy metal contamination profile of Nigerian herbal remedies with a view of ascertaining degree of violations of standard recommended guidelines of WHO, EU and US EPA has provided some important pharmaco-vigilance data.

The study has revealed that almost all the capsules and soft get preparations were heavily contaminated with cadmium, lead and nickel. Although none of the liquid preparations violated the limits for WHO and EU and US EPA however

Table 1

ARSENIC LEVELS IN NIGERIAN HERBAL REMEDIES (LIQUID (nos 1–9) AND SOLID (nos 10–24) DOSAGE FORMS)

S/NO (NHS)	NIGERIAN HERBAL SUPPLEMENT BATCH NO.	NAFDAC NO.	ARSENIC LEVEL (mg/l)	WHO LIMIT (mg/l)	EU LIMIT (mg/l)	% VIOLATION WHO LIMIT	% Violation eu limit	USEPA LIMIT	% Violation usepa limit
1	EVANS BITTERS	9108	A7–0249L	<0.0005	0.01	0.01	0	0	
2	SUPER BITTERS	251210	A7–030L	<0.0005	0.01	0.01	0	0	
3	JIMJAD BITTERS	L3	0384L	<0.0005	0.01	0.01	0	0	
4	IJEBU HERBAL TONIC	010	04–9922L	<0.0005	0.01	0.01	0	0	
5	EMI BLOOD TONIC	067	04–6219L	<0.0005	0.01	0.01	0	0	
6	VENESTEN CLEANSER	068	04–6220L	<0.0005	0.01	0.01	0	0	
7	ALIVE ULCERFAST	001	N/A	<0.0005	0.01	0.01	0	0	
8	EROXIL 5000	241210	A7–0263L	<0.0005	0.01	0.01	0	0	
9	BAKER CLEANSER	BWBLO5	A7–0273	<0.0005	0.01	0.01	0	0	
10	RELIVA CAPLETS	SA046	A7–0285L	<0.0005	0.01	0.01	0	0	
11	REJUVER HERBAL ANTI–OXIDANT	SA058	A7–0292L	<0.0005	0.01	0.01	0	0	
12	SUPER CLEANER CAPSULE	001	04–9813L	<0.0005	0.01	0.01	0	0	
13	SUPER 24/7 CAPSULE	068	A7–0213L	<0.0005	0.01	0.01	0	0	
14	SUPER CLEAN CAPSULES	N/A	A7–0536L	<0.0005	0.01	0.01	0	0	
15	SUPA – A1	110	A7–0374L	<0.0005	0.01	0.01	0	0	
16	Me and you herbal formular capsules	012	04–9914L	<0.0005	0.01	0.01	0	0	
17	UNIC CAPSULES	001	04–9782L	<0.0005	0.01	0.01	0	0	
18	ELIMAX CAPSULES	0002	A7–0549L	<0.0005	0.01	0.01	0	0	
19	ABABIO CAPSULES	001	04–9782L	<0.0005	0.01	0.01	0	0	
20	VEROCIN CAPSULES	N/A	A7–0949L	<0.0005	0.01	0.01	0	0	
21	ALPHAM CAPSULES	001	A7–0816L	<0.0005	0.01	0.01	0	0	
22	AZOQ CAPSULES	AO4	A7–0408L	<0.0005	0.01	0.01	0	0	
23	HP CAPSULES	001	04–9782	<0.0005	0.01	0.01	0	0	
24	SMART HERBAL CAPSULES	002	A7–0860L	<0.0005	0.01	0.01	0	0	

Table 2

CADMIUM LEVELS IN NIGERIAN HERBAL REMEDIES (LIQUID (nos 1–9) AND SOLID (nos 10–24) DOSAGE FORMS)

S/NO (NHS)	NIGERIAN HERBAL SUPPLEMENT BATCH NO.	NAFDAC NO.	CADMIUM LEVEL (mg/l)	WHO LIMIT (mg/l)	EU LIMIT (mg/l)	% VIOLATION WHO LIMIT	% VIOLATION EU LIMIT	USEPA LIMIT	% VIOLATION USEPA LIMIT
1	EVANS BITTERS	9108	A7–0249L	0.00059	0.003	0.005	0	0	
2	SUPER BITTERS	251210	A7–030L	0.00086	0.003	0.005	0	0	
3	JIMJAD BITTERS	L3	0384L	0.00073	0.003	0.005	0	0	
4	IJEMU HERBAL TONIC	010	04–9922L	0.00050	0.003	0.005	0	0	
5	EMI BLOOD TONIC	067	04–6219L	0.00059	0.003	0.005	0	0	
6	VENESTEN CLEANSER	068	04–6220L	0.00077	0.003	0.005	0	0	
7	ALIVE ULCERFAST	001	N/A	0.00066	0.003	0.005	0	0	
8	EROXIL 5000	241210	A7–0263L	0.00087	0.003	0.005	0	0	
9	BAKER CLEANSER	BWBLO5	A7–0273	0.00084	0.003	0.005	0	0	
10	RELIVA CAPLETS	SA046	A7–0285L	0.00122	0.003	0.005	0	0	
11	REJUVER HERBAL ANTI–OXIDANT	SA058	A7–0292L	0.0225	0.003	0.005	650	350	
12	SUPER CLEANER CAPSULE	001	04–9813L	0.0179	0.003	0.005	496	240	
13	SUPER 24/7 CAPSULE	068	A7–0213L	0.0304	0.003	0.005	913	508	
14	SUPER CLEAN CAPSULES	N/A	A7–0536L	0.0227	0.003	0.005	656	354	
15	SUPA – A1	110	A7–0374L	0.0296	0.003	0.005	886	492	
16	Me and you herbal formular capsules	012	04–9914L	0.0225	0.003	0.005	650	350	
17	UNIC CAPSULES	001	04–9782L	0.0166	0.003	0.005	453	232	
18	ELIMAX CAPSULES	0002	A7–0549L	0.0306	0.003	0.005	920	512	
19	ABABIO CAPSULES	001	04–9782L	0.0209	0.003	0.005	596	318	
20	VEROCIN CAPSULES	N/A	A7–0949L	0.0207	0.003	0.005	590	314	
21	ALPHAM CAPSULES	001	A7–0816L	0.0168	0.003	0.005	460	236	
22	AZOQ CAPSULES	AO4	A7–0408L	0.0328	0.003	0.005	993	556	
23	HP CAPSULES	001	04–9782	0.0326	0.003	0.005	986	552	
24	SMART HERBAL CAPSULES	002	A7–0860L	0.0337	0.003	0.005	1023	574	

Table 3

CHROMIUM LEVELS IN NIGERIAN HERBAL REMEDIES (LIQUID (nos 1–9) AND SOLID (nos 10–24) DOSAGE FORMS)

S/NO	NIGERIAN HERBAL SUPPLEMENT (NHS)	BATCH NO.	NAFDAC NO.	CHROMIUM LEVEL (mg/l)	WHO LIMIT (mg/l)	EU LIMIT (mg/l)	% VIOLATION WHO LIMIT	% VIOLATION EU LIMIT	USEPA LIMIT	% VIOLATION USEPA LIMIT
1	EVANS BITTERS	9108	A7-0249L	0.00066	0.05	0.05	0	0		
2	SUPER BITTERS	251210	A7-030L	0.00073	0.05	0.05	0	0		
3	JIMJAD BITTERS	L3	0384L	0.00088	0.05	0.05	0	0		
4	IJEBU HERBAL TONIC	010	04-9922L	0.00087	0.05	0.05	0	0		
5	EMI BLOOD TONIC	067	04-6219L	0.00087	0.05	0.05	0	0		
6	VENESTEN CLEANSER	068	04-6220L	0.00088	0.05	0.05	0	0		
7	ALIVE ULCERFAST	001	N/A	0.00123	0.05	0.05	0	0		
8	EROXIL 5000	241210	A7-0263L	0.00124	0.05	0.05	0	0		
9	BAKER CLEANSER	BWBLO5	A7-0273	0.00165	0.05	0.05	0	0		
10	RELIVA CAPLETS	SA046	A7-0285L	0.00327	0.05	0.05	0	0		
11	REJUVER HERBAL ANTI-OXIDANT	SA058	A7-0292L	0.0257	0.05	0.05	0	0		
12	SUPER CLEANER CAPSULE	001	04-9813L	0.0338	0.05	0.05	0	0		
13	SUPER 24/7 CAPSULE	068	A7-0213L	0.0328	0.05	0.05	0	0		
14	SUPER CLEAN CAPSULES	N/A	A7-0536L	0.0307	0.05	0.05	0	0		
15	SUPA – A1	110	A7-0374L	0.0229	0.05	0.05	0	0		
16	Me and you herbal formular capsules	012	04-9914L	0.0336	0.05	0.05	0	0		
17	UNIC CAPSULES	001	04-9782L	0.0405	0.05	0.05	0	0		
18	ELIMAX CAPSULES	0002	A7-0549L	0.0506	0.05	0.05	1.2	1.2		
19	ABABIO CAPSULES	001	04-9782L	0.0363	0.05	0.05	0	0		
20	VEROCIN CAPSULES	N/A	A7-0949L	0.0389	0.05	0.05	0	0.05		
21	ALPHAM CAPSULES	001	A7-0816L	0.0387	0.05	0.05	0	0.05		
22	AZOQ CAPSULES	AO4	A7-0408L	0.0428	0.05	0.05	0	0.05		
23	HP CAPSULES	001	04-9782	0.0236	0.05	0.05	0	0.05		
24	SMART HERBAL CAPSULES	002	A7-0860L	0.0402	0.05	0.05	0	0.05		

Table 4

COBALT LEVELS IN NIGERIAN HERBAL REMEDIES(LIQUID (nos 1–9) AND SOLID (nos 10–24) DOSAGE FORMS)

S/NO	NIGERIAN HERBAL SUPPLEMENT (NHS)	BATCH NO.	NAFDAC NO.	COBALT LEVEL (mg/l)	WHO LIMIT (mg/l)	EU LIMIT (mg/l)	% VIOLATION WHO LIMIT	% VIOLATION EU LIMIT	USEPA LIMIT (mg /l)	% VIOLATION USEPA LIMIT
1	EVANS BITTERS	9108	A7-0249L	0.00058					0.50	0
2	SUPER BITTERS	251210	A7-030L	0.00126					0.50	0
3	JIMJAD BITTERS	L3	0384L	0.00094					0.50	0
4	IJEMBU HERBAL TONIC	010	04-9922L	0.00123					0.50	0
5	EMI BLOOD TONIC	067	04-6219L	0.00087					0.50	0
6	VENESTEN CLEANSER	068	04-6220L	0.00068					0.50	0
7	ALIVE ULCERFAST	001	N/A	0.00067					0.50	0
8	EROXIL 5000	241210	A7-0263L	0.00158					0.50	0
9	BAKER CLEANSER	BWBLO5	A7-0273	0.00091					0.50	0
10	RELIVA CAPLETS	SA046	A7-0285L	0.00068					0.50	0
11	REJUVER HERBAL ANTI-OXIDANT	SA058	A7-0292L	0.0135					0.50	0
12	SUPER CLEANER CAPSULE	001	04-9813L	0.0129					0.50	0
13	SUPER 24/7 CAPSULE	068	A7-0213L	0.0157					0.50	0
14	SUPER CLEAN CAPSULES	N/A	A7-0536L	0.0184					0.50	0
15	SUPA – A1	110	A7-0374L	0.0117					0.50	0
16	Me and you herbal formular capsules	012	04-9914L	0.0115					0.50	0
17	UNIC CAPSULES	001	04-9782L	0.0125					0.50	0
18	ELIMAX CAPSULES	0002	A7-0549L	0.0154					0.50	0
19	ABABIO CAPSULES	001	04-9782L	0.0117					0.50	0
20	VEROCIN CAPSULES	N/A	A7-0949L	0.0129					0.50	0
21	ALPHAM CAPSULES	001	A7-0816L	0.0113					0.50	0
22	AZOQ CAPSULES	AO4	A7-0408L	0.0158					0.50	0
23	HP CAPSULES	001	04-9782	0.0216					0.50	0
24	SMART HERBAL CAPSULES	002	A7-0860L	0.0167					0.50	0

Table 5

LEAD LEVEL OF NIGERIAN HERBAL REMEDIES (LIQUID (nos 1–9) AND SOLID (nos 10–24) DOSAGE FORMS)

S/NO	NIGERIAN HERBAL SUPPLEMENT (NHS)	BATCH NO.	NAFDAC NO.	LEAD LEVEL (mg/l)	WHO LIMIT (mg/l)	EU LIMIT (mg/l)	% VIOLATION WHO LIMIT	% VIOLATION EU LIMIT	USEPA LIMIT	% VIOLATION USEPA LIMIT
1	EVANS BITTERS	9108	A7-0249L	0.00057	0.01	0.01	0	0		
2	SUPER BITTERS	251210	A7-030L	0.00074	0.01	0.01	0	0		
3	JIMJAD BITTERS	L3	0384L	0.00095	0.01	0.01	0	0		
4	IJEBU HERBAL TONIC	010	04-9922L	0.00108	0.01	0.01	0	0		
5	EMI BLOOD TONIC	067	04-6219L	0.00086	0.01	0.01	0	0		
6	VENESTEN CLEANSER	068	04-6220L	0.00087	0.01	0.01	0	0		
7	ALIVE ULCERFAST	001	N/A	0.00081	0.01	0.01	0	0		
8	EROXIL 5000	241210	A7-0263L	0.00123	0.01	0.01	0	0		
9	BAKER CLEANSER	BWBLO5	A7-0273	0.00059	0.01	0.01	0	0		
10	RELIVA CAPLETS	SA046	A7-0285L	0.00095	0.01	0.01	0	0		
11	REJUVER HERBAL ANTI-OXIDANT	SA058	A7-0292L	0.0116	0.01	0.01	16	16		
12	SUPER CLEANER CAPSULE	001	04-9813L	0.0123	0.01	0.01	23	23		
13	SUPER 24/7 CAPSULE	068	A7-0213L	0.0178	0.01	0.01	78	78		
14	SUPER CLEAN CAPSULES	N/A	A7-0536L	0.0141	0.01	0.01	41	41		
15	SUPA – A1	110	A7-0374L	0.0156	0.01	0.01	56	56		
16	Me and you herbal formular capsules	012	04-9914L	0.0168	0.01	0.01	68	68		
17	UNIC CAPSULES	001	04-9782L	0.00973	0.01	0.01	0	0		
18	ELIMAX CAPSULES	0002	A7-0549L	0.0126	0.01	0.01	26	26		
19	ABABIO CAPSULES	001	04-9782L	0.0142	0.01	0.01	42	42		
20	VEROCIN CAPSULES	N/A	A7-0949L	0.0146	0.01	0.01	46	46		
21	ALPHAM CAPSULES	001	A7-0816L	0.0139	0.01	0.01	39	39		
22	AZOQ CAPSULES	AO4	A7-0408L	0.0167	0.01	0.01	67	67		
23	HP CAPSULES	001	04-9782	0.0125	0.01	0.01	25	25		
24	SMART HERBAL CAPSULES	002	A7-0860L	0.0206	0.01	0.01	106	106		

Table 6

NICKEL LEVEL IN NIGERIAN HERBAL REMEDIES (LIQUID (nos 1–9) AND SOLID (nos 10–24) DOSAGE FORMS).

S/NO	NIGERIAN HERBAL SUPPLEMENT (NHS)	BATCH NO.	NAFDAC NO.	LEAD LEVEL (mg/l)	WHO LIMIT (mg/l)	EU LIMIT (mg/l)	% VIOLATION WHO LIMIT	% VIOLATION EU LIMIT	USEPA LIMIT	% VIOLATION USEPA LIMIT
1	EVANS BITTERS	9108	A7-0249L	0.00174	0.02	0.02	0	0		
2	SUPER BITTERS	251210	A7-030L	0.00285	0.02	0.02	0	0		
3	JIMJAD BITTERS	L3	0384L	0.00325	0.02	0.02	0	0		
4	IJEBU HERBAL TONIC	010	04-9922L	0.00357	0.02	0.02	0	0		
5	EMI BLOOD TONIC	067	04-6219L	0.00144	0.02	0.02	0	0		
6	VENESTEN CLEANSER	068	04-6220L	0.00189	0.02	0.02	0	0		
7	ALIVE ULCERFAST	001	N/A	0.00344	0.02	0.02	0	0		
8	EROXIL 5000	241210	A7-0263L	0.00358	0.02	0.02	0	0		
9	BAKER CLEANSER	BWBLO5	A7-0273	0.000274	0.02	0.02	0	0		
10	RELIVA CAPLETS	SA046	A7-0285L	0.00068	0.02	0.02	0	0		
11	REJUVER HERBAL ANTI-OXIDANT	SA058	A7-0292L	0.0334	0.02	0.02	67	67		
12	SUPER CLEANER CAPSULE	001	04-9813L	0.0406	0.02	0.02	103	103		
13	SUPER 24/7 CAPSULE	068	A7-0213L	0.0306	0.02	0.02	53	53		
14	SUPER CLEAN CAPSULES	N/A	A7-0536L	0.0415	0.02	0.02	107	107		
15	SUPA – A1	110	A7-0374L	0.0308	0.02	0.02	90	90		
16	Me and you herbal formular capsules	012	04-9914L	0.0408	0.02	0.02	140	140		
17	UNIC CAPSULES	001	04-9782L	0.0338	0.02	0.02	69	69		
18	ELIMAX CAPSULES	0002	A7-0549L	0.0237	0.02	0.02	18.5	18.5		
19	ABABIO CAPSULES	001	04-9782L	0.0159	0.02	0.02	0	0		
20	VEROCIN CAPSULES	N/A	A7-0949L	0.0274	0.02	0.02	37	37		
21	ALPHAM CAPSULES	001	A7-0816L	0.0401	0.02	0.02	100.5	100.5		
22	AZOQ CAPSULES	AO4	A7-0408L	0.0376	0.02	0.02	88	88		
23	HP CAPSULES	001	04-9782	0.0337	0.02	0.02	68.5	68.5		
24	SMART HERBAL CAPSULES	002	A7-0860L	0.0338	0.02	0.02	69	69		

because of their presence in these preparations there is a probability of chronic toxicity and interactions with conventional medications, since these herbal supplements are perceived as “healthier” and safe [11]. Although only one sample violated the WHO and EU limits for chromium, we also observed that all the solid samples had between 51.4 – 81% of the permissible limits and also this calls for a closer look at chronic toxicity with chromium.

The three metals cadmium, lead and nickel which showed violation of the limits have always been categorized as reproductive toxicants [24]. The most common causes of adulteration of herbal products is with undeclared potent pharmaceutical substances, substitution or misidentification with toxic plant species, incorrect dosing, interaction with conventional medicine and use of products contaminated with potentially hazardous substances, such as microbial metabolites (eg mycotoxins) radioactive particles, heavy metals and agrochemicals [25]. Furthermore, metals are sometimes intentionally added to herbal preparations, because the traditional Indian (Ayurvedic) and Chinese medicine believe in their therapeutic efficacies [26]. Therefore such formulations usually have excessive toxic elements [15, 27]. In the case where the herbal remedy did not violate the limits, values for contamination were high. Although only one sample violated the limits for chromium, however most of the solid samples had 51.4 – 81% content of the permissible limits, raising fears about chronic toxicity.

Acute cadmium toxicity causes severe irritation of the gastrointestinal epithelium symptoms characterised by vomiting, nausea and abdominal pain [28]. The major long term toxic effects of low – level cadmium exposure are renal injury, obstructive pulmonary diseases, osteoporosis, and cardiovascular diseases [29]. Also human studies have shown evidence to support decreased semen quality and/or altered levels of reproductive hormones [30] with exposure to cadmium.

Lead was found to be a major contaminant of all the solid preparations. Soil and air pollution influence herb lead content [31,32]. Alternatively, uncontaminated herbs could acquire heavy metals during manufacturing due to contaminated water, equipment, pipes, or storage [33].

Lead serves no useful purpose in the human body; it exerts multi systemic toxic effects by inhibiting enzyme activity, interfering with the action of essential cations and by altering the structure of cell membranes and receptors [34]. High blood lead levels have been consistently been linked with reduced sperm count, poor semen motility and abnormal sperm morphology [35]. Lead is reported to accumulate in male reproductive tissues [36]. Both animal and in vitro studies have shown that lead causes testicular atrophy, changes in weight of accessory glands, alterations

in semen quality, and disruption of the hypothalamic – testicular Pituitary axis [37]. Also lead can interfere with heme production by enzyme interference and apoptosis [38]. After controlling for multiple factors, lead levels of women users of specific herbal supplements were 10% higher than women nonusers [39]. In Nigeria, the consumption of herbs either as supplements or remedies cuts across all ages and social groups and most often a combination of these products are consumed simultaneously. There is no documented implication of this practice and as such it has assumed an urgency to evaluate the acute and chronic toxicity profile of these herbal supplements.

Allergic dermatitis seems to be the main adverse effect of sensitized individuals ingesting nickel [40]. Nickel is also a respiratory tract carcinogen [41]. Cobalt is an essential nutrient in small amounts to animals including humans [42]. Cobalt can also be toxic when excessive amounts are ingested [43].

There is ample scope for health care workers such as doctors, nurses and pharmacists, ignorant of their patients’ self-medication with herbal medicines, to misinterpret an adverse reaction due to the herbal medicine and ascribe it to a conventional prescribed drug, or indeed to an OTC medicine. Stricter regulatory control would ensure that herbal products were adequately assessed for efficacy and safety particularly from the point of view of toxicity and drug interactions, which in turn would lead to the identification of contraindications and more adequate labeling and patient information. A more regulated environment would encourage greater awareness of the hazards and risks of herbal products by health professionals, and ensure that the more hazardous herbal products were not available through health food shops and other retail outlets. Indeed, the more dangerous materials could be removed entirely from the herbal product ranges. Better publicity and education are required to ensure that health care workers always bear in mind that their patients may be medicating themselves with herbal products and that patients be warned of possible dangers, including those arising from drug interactions.

According to WHO reports, the processing of herbal materials must observe Good Manufacturing Practice GMP with protocols that are similar to those applied in the manufacture of conventional medicines [44], in addition to published good practices and quality guidelines for herbal products [45]. As the World Health Organization has recognized, there is scope for further assessment and evaluation of herbal medicines for their efficacy and safety, as well as their potential uses in different parts of the world [46].

This study highlights the need for pharmaco-vigilance especially with respect to metallo-toxicity of Nigerian

herbal remedies and need for in–depth risk assessment to understand the extent of the problem.

Conflict of interest statement

We declare that we have no conflict of interest.

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