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Full Length Research Paper

Analysis of some selected toxic metals in registered herbal products manufactured in Nigeria

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The use of herbal medicine has been on the increase in many developing and industrialized countries and Nigerians in particular has been using herbal medicine for many centuries. The approval of these herbal remedies by regulatory bodies has further encouraged the use of herbal remedies. The safety of these herbal remedies is however poorly understood. This study investigated the concentration of arsenic, cadmium, lead and mercury in twenty registered ready to use herbal products. Twenty brands of herbal remedies were purchased randomly from the Pharmacy shops in Lagos, digested with aqua-regia (3:1 HCl: HNO_3) and were analysed using atomic absorption spectroscopy (Buck 205 Atomic Absorption Spectrophotometer). There was no detectable lead in any of the 20 herbal samples; however, all the samples contained a detectable amount of one or more of the other metals of interest. The Oral Component Limit (OCL) for arsenic, cadmium and mercury as stated by USP are 1.5, 0.5 and 1.5 µg/g, respectively. All the samples contained arsenic and mercury below the USP OCL, while sixty-five percent contained cadmium out of which fifty-five percent were above USP OCL. The results obtained from this study suggest a significant risk to consumers' health considering the toxicity of these heavy metals.

Key words: Herbal remedies, toxic heavy metals, atomic absorption spectrophotometry.

INTRODUCTION

The use of herbal medicine has been on the increase in many developing and industrialized countries (Barnes, 2003). It is known that between 65 and 80% of the world's population use herbal medicines as their primary form of health care (Barnes, 2003). In developing nations, most especially, regulation of sales, importation and manufacturing of herbal medicines are not subjected to rigorous scrutiny in terms of safety and efficacy as is the case for conventional western medicine, and heavy metals have been reported in some of these herbal products (Barnes, 2003; Zaleska, 2008).

Heavy metals have been defined differently by many authors depending on the angle from which each author looks at it, but toxicity, density as well as molecular weight are salient points that inevitably appear in all the definitions of heavy metals (Barnes, 2003; Philips and Balge, 2007). The term heavy metal refers to any metallic chemical element that has a relatively high density and is toxic or poisonous at low concentrations, and examples of heavy metals include mercury, cadmium, arsenic, chromium, thalium and lead (Philips and Balge, 2007; Zaleska, 2008). Heavy metals are also referred to as metals having atomic weight greater than sodium, a density greater than 5 g/cm^3 and possess some level of toxicity (WHO, 2000; Alqosouimi, 2006). Heavy metals are natural components of the Earth's crust. They cannot be degraded or destroyed and could enter human body via food, drinking water, soft drinks, hot drinks, cigarettes

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and air. These heavy metals constitute health risk to users because they bioaccumulate in the body when ingested via fluids, food or through other sources of contamination and are stored faster than they are broken down or excreted (Philips and Balge, 2007; Zaleska, 2008).

The term herb is applied by pharmacists to any plant or plant part that possess medicinal properties (John, 2004). Medical herbalism is the use of plant remedies in the prevention and treatment of illness. Currently, medical herbalism practiced by medical herbalists, draws on traditional knowledge, but increasingly, this is interpreted and applied in a modern context (Alqosouimi, 2006).

Traditional, medicinal or folk medicine practice is based on the use of plants and plant extracts. It is also known as botanical medicine, herbal medicine, herbology and phytotherapy. The scope of herbal medicine is extended to include fungal and bee products as well as minerals, shells and certain animal parts (Acharya and Shrivastava, 2008). The importance of herbal medicine cannot be over-emphasized as the World Health Organization (WHO) estimated that 80% of the world's population presently uses herbal medicine as part of primary health care (WHO, 2000).

The practice of herbal medicine includes a holistic approach which involves selecting herbs on an individual basis for each patient, identifying the underlying cause of a patient's illness and considering it in the treatment plan, stimulating the body's healing capacity to strengthen body systems and correcting abnormal body functions rather than treating observable symptoms directly (Alqosouimi, 2006).

The biological effectiveness of herbal products can be traced to the variety of chemical compounds produced in all plants. These are primary metabolites such as sugars and fats, found in all plants and secondary metabolites (Robert et al., 2008). In recent years, it has been discovered that some of these herbal products contain a considerable amount of toxic heavy metals such as arsenic, cadmium, lead and mercury (Martena et al., 2010). Some traditional herbal preparations used in Ayurveda, traditional Chinese medicine, traditional Tibetan medicine and other Asian traditional medicine systems were found to contain significant amounts of mercury, arsenic or lead (Martena et al., 2010). It has been shown that herbal remedies incorporated in Asian traditional herbal preparations for therapeutic purposes caused intoxications in users (Robert et al., 2008; Martena et al., 2010).

According to a report by Harvard Medical School (2004), it was observed that 14 of the 70 herbal medicine products (HMPs) tested contained lead, mercury and/or arsenic. Each of the 14 could result in heavy metal intakes above regulatory standards. Several of the HMPs could result in lead and arsenic intakes of 1,000 to 10,000 times greater than the regulatory standards. Fifty percent of the HMPs containing potentially toxic heavy metals were recommended by the manufacturers for use in infants and children. Eleven manufacturers produced at least one HMP containing heavy metals. Eighty percent of the stores sold one or more HMPs containing significant amounts of heavy metals (Harvard Medical School, 2004).

With the advent of this trend, there is an increasing need for investigative research to determine the concentration of the selected toxic metals in some commonly administered herbal medicinal products marketed in Lagos, Nigeria. High doses of arsenic can be deadly. Long-term exposure to low levels of arsenic can cause cancer of the skin, bladder, liver, lungs and kidneys (Delaware Health and Social Services, 2009). Cadmium has a primary effect on the lungs and kidneys and a secondary effect on the skeletal system. It competes with calcium for binding sites on regulatory proteins (Agency for Toxic Substances and Disease Registry, 2008). Lead and lead compounds are known human carcinogens and have been shown to cause serious damage to the nervous system and the brain of the unborn child (Agency for Toxic Substances and Disease Registry, 2007), while mercury has been reported to cause disruption of the nervous system, damage to brain functions, DNA damage, cancer, allergic reactions, negative reproductive effects, birth defects, miscarriages and memory loss (Agency for Toxic Substances and Disease Registry, 1999).

The objective of this study was to quantify some toxic metals such as arsenic, cadmium, lead and mercury in some commonly used herbal products manufactured locally in Lagos, Nigeria.

MATERIALS AND METHODS

The most frequently used analytical method for the analysis of heavy metal contamination in most matrices is atomic absorption spectroscopy (AAS) and this method was used in the analysis of lead and cadmium. However, for arsenic, hydride generator was attached to AAS for its estimation, while cold vapour technique attached to AAS was used to estimate mercury in this study (Poppiti and Charles, 1994). The samples were randomly purchased from pharmacy shops in Lagos, Nigeria. The manufacturer, brand name, manufactured date, expiry date, NAFDAC registration number and dosage form were recorded. All the reagents used were of analytical grade.

Preparation of standard solutions from 1000 part per million (ppm) standard stock solution GFS Fisher's AAS reference standard

A standard GFS Fisher's AAS reference standard stock solution of 1000 ppm of the metal ions was serially diluted using aqua-regia (1:3, HNO_3 : HCl) to 2, 4, 6 8 and 10 ppm.

Digestion of samples

All the samples were digested using aqua regia ((David, 2000). A 2.2 g of each sample was carefully weighed into a clean beaker, 15

Table 1. Regression data for the analysis of the standard solutions.

Metal	Arsenic	Cadmium	Lead	Mercury
Regression equation	y = 0.05x + 0.006	y = 0.031x - 0.009	y = 0.020x - 0.007	y = 0.05x + 0.006
Coefficient of determination (R^2)	R^2 = 0.998	R^2 = 0.996	R^2 = 0.994	R^2 = 0.998
Pearson's correlation coefficient	0.999	0.998	0.997	0.999

ml of the digesting acid (aqua-regia 1:3, HNO_3 : HCl) was added to the sample in the beaker. The beaker was heated on a hot plate in the fume cupboard until the observed brown fumes has disappeared. The beaker was carefully removed and allowed to cool. The solution was filtered with a filter paper, rinsed with 10 ml of aqua-regia to make up to 25 ml and stored in a sample bottle for analysis (David, 2000; Orisakwe et al., 2006).

Sample analysis

The analysis of the digested samples was carried out using a Buck 205 atomic absorption spectrophotometer for lead and cadmium. For arsenic, hydride generator was attached to AAS for its estimation, while cold vapour technique attached to AAS was used to estimate mercury. The calibration plot method was adopted for the analysis (De Stefano et al., 2010). The corresponding absorbance for the standard solutions was obtained and a graph of absorbance against concentration was plotted. The digested samples were analysed in triplicates. The concentrations of the digested samples were obtained from the regression equation obtained from the calibration plot using Microsoft Excel software and were converted to µg/g concentration of the corresponding sample.

RESULTS

The regression equations, Pearson's correlation coefficient and coefficient of determination, R^2, obtained from the calibration plot showed that the absorbance correlated with the concentrations (Table 1). Arsenic and mercury are present in all the samples at concentrations below the United States Pharmacopeia (USP) OCL (Table 2). Cadmium was present in sixty-five percent of the samples and fifty-five percent has concentration above the USP OCL (Tables 2 and 3). The numbers and percentages of the herbal samples containing the toxic metal ions, the minimum and maximum concentration of metal ions detected and the numbers of samples with metal ions above the United States Pharmacopeia (USP) oral component limits (OCL) are shown in Table 3.

DISCUSSION

For the safety of human health, various regulatory organisations such as USEPA, WHO, EPA, USP and BP, have set up parameters to limit the presence of heavy metals in herbal remedies. Parameters such as permissible daily exposure (PDE), rationale for reference doses (RFD's), oral component limit (OCL) and parenteral component limits (PCL) are guidelines set to regulate elemental contaminations in herbal remedies. Table 4 represents a summary of these parameters for the metals of interest in this study.

All the calibration plots were linear with Pearson's correlation coefficient ranging from 0.997 to 0.999. The concentrations obtained for each herbal sample in µg/g as contained in Tables 2 and 3 show the summary of the analysis. The concentration of arsenic in each sample ranged from 0.301 to 1.108 µg/g, cadmium ranged from 0.000 to 40.288 µg/g, mercury ranged from 0.163 to 0.869 µg/g while no detectable lead was found in any of the samples.

Arsenic and mercury were detected in all the 20 samples, while cadmium was detected in 14 of the samples analysed; however, concentration of cadmium in 11 samples exceeded the USP OCL. This is of great concern since cadmium and cadmium compounds are known human carcinogens (Agency for Toxic Substances and Disease Registry, 2007). Also, cadmium poisoning has been attributed to toxic effects such as renal and hepatic failures, damage to the CNS, infertility and damage to the immune system (Philips and Balge, 2007; Zaleska, 2008). In addition to its acute toxicity, cadmium has a long biological half life leading to chronic effects as a result of accumulation in the liver and the renal cortex (Hammer and Hammer, 2004; Adepoju-Bello et al., 2005; Agency for Toxic Substances and Disease Registry, 2007).

It can been shown that all the samples contained detectable amounts of one or more of the metals of interest (cadmium, arsenic and mercury) with all the samples containing arsenic and mercury, 13 of the 20 herbal samples contained cadmium. These explain the potential health risk that could be associated with the use of these herbal remedies which are contaminated with toxic metals. The salient question now is "how exposed is the populace to this menace?"

A large percentage of Nigerians do take herbal remedies as a ready therapy for all forms of diseases, however, they are unconsciously exposed to a high concentrations of toxic metals. These metal ions might have gained entrance into the herbs from plant uptakes, when the herbs are grown on polluted soils, atmospheric contamination from industries, packaging material and other mediums. There is a need for more regulatory measures to be taken in order to ensure the safety of users of herbal remedies.

Conclusion

There are detectable amounts of cadmium, arsenic and

Table 2. Concentrations of arsenic, cadmium, mercury and lead in the samples analysed.

Sample	Arsenic		Cadmium		Mercury		Lead
	Average concentration (ppm) ± SD	Concentration (µg/g)	Average concentration (ppm) ± SD	Concentration (µg/g)	Average concentration (ppm) ± SD	Concentrati on (µg/g)	
H1	0.055±0.009	0.624	1.545±0.047	17.561	0.024±0.003	0.270	ND
H2	0.070±0.010	0.792	0.000±0.000	0.000	0.024±0.005	0.270	ND
H3	0.037±0.010	0.415	0.062±0.001	0.705	0.019±0.004	0.216	ND
H4	0.062±0.006	0.704	0.000±0.000	0.000	0.024±0.004	0.277	ND
H5	0.076±0.007	0.859	0.422±0.012	4.795	0.028±0.003	0.324	ND
H6	0.044±0.008	0.496	0.000±0.000	0.000	0.036±0.005	0.404	ND
H7	0.078±0.006	0.886	0.000±0.000	0.000	0.023±0.004	0.257	ND
H8	0.036±0.006	0.408	0.263±0.017	2.989	0.020±0.004	0.230	ND
H9	0.032±0.010	0.368	0.023±0.001	0.261	0.028±0.005	0.317	ND
H10	0.098±0.006	1.108	0.711±0.033	8.076	0.036±0.004	0.411	ND
H11	0.061±0.007	0.691	0.000±0.000	0.000	0.021±0.003	0.243	ND
H12	0.071±0.006	0.812	0.000±0.000	0.000	0.025±0.003	0.283	ND
H13	0.087±0.007	0.994	0.031±0.014	0.348	0.021±0.004	0.243	ND
H14	0.038±0.005	0.435	0.428±0.014	4.860	0.014±0.005	0.163	ND
H15	0.037±0.010	0.415	0.205±0.001	2.333	0.017±0.004	0.196	ND
H16	0.026±0.008	0.301	1.248±0.001	14.178	0.020±0.005	0.223	ND
H17	0.043±0.006	0.489	1.080±0.007	12.273	0.024±0.004	0.270	ND
H18	0.071±0.008	0.805	0.000±0.000	0.000	0.026±0.004	0.290	ND
H19	0.037±0.007	0.415	3.545±0.0172	40.288	0.076±0.004	0.869	ND
H20	0.073±0.007	0.832	0.047±0.001	0.534	0.0150.004	0.169	ND

ND = Not detectable.

Table 3. Summary of the atomic absorption characteristics of arsenic, cadmium, lead and mercury metal ions.

Parameter	As	Cd	Pb	Hg
Number of Samples	20	20	20	20
Number of samples with detectable metal ions	20	13	0	20
Percentage of samples with detectable metal ions	100%	65%	0	100%
Minimum conc. of metal ion detected (µg/g)	0.301	0.261	0	0.163
Maximum conc. of metal ions detected (µg/g)	1.108	40.288	0	0.869
USP Oral Component Limits (OCL) (µg/g)	1.5	0.5	1.0	1.5
Number of samples above USP OCL	0	11	0	0
Percentage of above USP limits	0	55%	0	0

Table 4. Elemental impurities guidelines (De Stefano et al., 2010).

Parameter	Oral RFD (µg/kg/day)	Recommended daily oral dose* PDE (µg/day)	Oral component limit (OCL) (µg/g)	Parenteral component limit (PCL) (µg/g)
Arsenic	0.3	15	1.5	0.15
Cadmium	0.1	5	0.5	0.05
Mercury	0.3	15	1.5	0.5
Lead	0.2	10	1	0.1

*Recommended daily oral dose based on a 50 kg person.

mercury in most of the samples with that of cadmium significantly exceeding the USP Oral Component Level in 55% of the samples. This poses health risk to individuals who are using these herbal remedies.

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