Article

Trace metals quality of some herbal medicines sold in Accra, Ghana

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Abstract

Ten brands of herbal medicines were selected on the market for the analysis of trace metals quality using the Atomic Absorption Spectrometer. The results were reported as the mean concentration of three representative samples for each of the ten brands. The respective percentage incidence of the trace metals analyzed were; Fe (20%), Zn (80%), Cu (20%), Cd (40%); Al (100%) and Pb (100%). The range of the mean concentrations measured for all the brands were; Fe (<0.006-3.298 mg/L), Zn (<0.001-0.091 mg/L), Cu (<0.003-0.009 mg/L), Cd (<0.002-0.003), Al (0.278-0.533 mg/L) and Pb (0.0056-0.085 mg/L). The mean concentrations of the trace metals measured were generally low and below stipulated national limits as per WHO (2007). A hierarchical cluster analysis indicated two clusters; cluster 1 (CA1) loading Zn, Al and Fe whilst Cluster 2 (CA2) loaded Cd and Pb. The presence of these trace metals may be the result of accidental contamination during manufacture, for instance, from grinding weights or lead-releasing containers or other manufacturing utensils and contamination from polluted soils on which the herbs were harvested. Some brands of the herbal medicines sampled do not have the code in Food and Drugs Board of Ghana. Hence a routine analysis of these herbal medicines must be carried out to ensure the safety of the consuming populace.

Keywords trace metal; concentration; contamination; herbal medicine; cluster analysis; limits; safety.

1 Introduction

About 70–80% of the world's population particularly in developing countries relies on non-conventional medicine in their primary healthcare as reported by the World Health Organisation (Akerele, 1993). Herbal medicine in recent years are used to treat many conditions, such as asthma, eczema, premenstrual syndrome, rheumatoid arthritis, migraine, menopausal symptoms, chronic fatigue, and irritable bowel syndrome, among others. The popularity of herbal medicines notably increased in the past years due to rapid increase in allopathic drugs price and reports on their safety. People are often using herbal products especially in rural areas because of availability and affordability. There is also a general public perception that herbal products are safer and harmless because of their natural plant based origin/material.

In some countries in Europe unlike the U.S. herbs are classified as drugs and are regulated. The German Commission E, an expert medical panel, actively researches their safety and effectiveness. Unlike in most developing countries, in Ghana, the food and drugs board is responsible for drug administration and control of the quality of medicinal products generally available in the market.

Contamination or adulteration of herbal products with heavy metals such as lead, mercury, cadmium, arsenic, etc., is of major concern. However some herbal products do contain heavy metals as essential ingredients. The poor quality control of these products causes health hazard as some products may present unusually high concentrations of toxic metals that could lead to fatality if consumed. A number of case reports have been published in the media and the problem has been discussed among various stakeholders. For instance, the Asian and Indian traditional remedies have been reported to contain high levels of arsenic, lead and mercury (Garvey et al, 2001) and high level of lead (Ernst, 2002) respectively. In a research report (Liang et al., 1998), the authors measured various metallic elements (K, Na, Mg, Ca, Fe, Cu, Zn, Mn, Co, Cr, Ni, Mo and heavy metals As, Pb, and Cd) by atomic absorption spectrophotometer in some Chinese herbal medicines. The heavy metals contamination in traditional medicines may occur due to polluted environment in which the medicinal plants grow (Sayyed and Sayadi, 2011), the polluted conditions in which the plants are dried and processed, the storage conditions and/or manufacture of the products in the final dosage form (Chan, 2003).

The emerging importance of herbal products cannot be ignored. Increasing concern and fear have also been expressed to their unsupervised use, efficacy, toxicity and quality of these natural products as well as the legal responsibilities of their practitioners as well. The purpose of this research was to determine the levels of toxic heavy metals in order to ensure the safety of the locally manufactured traditional medicines.

2 Material and Methods

2.1 Sample collection

A total of thirty (30) herbal medicinal products that were made for *in-vitro* administration were randomly sampled from traditional medicine distributors and retail pharmacy outlets in the Greater Accra region of Ghana. Ten (10) different brands were sampled in all. Three replicates of each of the ten brands were selected for the analysis. These samples were all in the liquid state and were intended to be administered orally. Products sampled included those that have been registered with the Ghana's Food and Drugs Board, (the country's drug regulatory body) as well as those not registered with the board. The details of samples collected together with their therapeutic indications are presented in Table 1.

2.2 Sample preparation and analysis

The herbal product samples were subjected to acid digestion prior to the atomic absorption spectrometry analysis of Fe, Zn, Cu, Cd, Al, and Pb. 0.5 g of each sample was weighed and mixed with 6 ml of 65% nitric acid (Sigma-Aldrich, Germany) Teflon beaker. The mixture in the Teflon beaker was heated in an ETHOS 900 microwave for 25 min to allow for complete digestion of the ingredients. The digested extracts were allowed to cool at room temperature and the volumes made up to 20 ml with de-ionized distilled water. Blanks and reference standards were digested similarly. The digested extracts were then analyzed using atomic absorption spectrophotometer (VARIAN AA240 FS). Calibration standards were used to generate a calibration curve prior to the analysis of sample, blank and reference materials. Standard solutions of the trace elements analyzed were prepared by diluting stock solutions obtained from Fluka, Sigma-Aldrich Chemie GMBH, Switzerland. Quantifications were achieved using calibration curves obtained from standard solutions. Each sample was analysed in triplicate to confirm the precision and accuracy of the AAS.

Table 1 Label data of the herbal products sampled

Brand code	Dosage form	Date of manufacture	Expiry date	FDB number	Content	Therapeutic indication
A_1,A_2,A_3	liquid	2008	2015	58732	Karika papaya, Khaya senegalensis & ginger	Piles, waist pains, sexual weakness, constipation, removal of excess phlegm, stomach pains, improves eyesight, menstrual pains, headache, infertility, body pains, high fever and white, toothache
B_1,B_2,B_3	liquid	2010	2013	FDB/HD. 05/4020	Raufwolfia vomitoria, Xylopia aethiopica, Trichilia monadelph, Triplotaxis, stellulifera, Grosseria vignei, Anthocleisa nobilis Garcinia Kola, Spathodea companula, Honey	Piles, menstrual pains, anaemia, abdominal pain, lumbago, dyspepsia, purifies blood, enhances circulation
C_1,C_2,C_3	liquid	2008	2012	none	Aloe -ferove, cassava slebeneena, panllina painnata, Piper guineese, Khaya	Relief of piles, constipation, waist pains, headache, fever, sexual weakness, fibroid, hernia
D_1,D_2,D_3	liquid	2010	2013	FDB/HD. 05-12102	Vernonia amygdalina, Kigelia africana, Anthocleisa nobilis, Combretodendron macrocarpum	Ordinary piles, bleeding piles, eyes itching, sexual weaknesses, menstrual pains, constipation, rheumatism
E_1,E_2,E_3	liquid	2010	2013	AT/F92A*	Anthocleista nobilis, Combretodendron Macrocarpum, Khaya senegalensis, Ricinodendron heudelotii, Sorgumbicolor	Rheumatism, anaemia, menstrual disorder, loss of appetite, tiredness, general disability, piles, fevers
F_1,F_2,F_3	liquid	2009	2012	BN-50, 836*	Anthocleista nobilis, Combretodendron Macrocarpum, Khaya senegalensis, Ricinodendron heudelotii, Sorgumbicolor	Rheumatism, anaemia, menstrual disorder, loss of appetite, tiredness, general disability, piles, fevers
G_1,G_2,G_3	liquid	2010	2013	none	African aloe, Cassle sleberlana	Constipation, kidney related problems, asthma, sexual weakness, menstrual imbalances, removes phlegm, appetizer
H_1,H_2,H_3	liquid	2009	2015	none	none	None
I_1,I_2,I_3	liquid	2009	2012	none	none	None
J_1,J_2,J_3	liquid	2010	2013	none	none	Loss of appetite, anaemia, general body weakness, rheumatism,

*= not available/stated

3 Results and Discussion

The safety and quality of medicinal herbal products have become a major concern for health authorities, pharmaceutical industries and the general public (WHO, 2007). The use of agrochemical products on

agricultural lands and some organic solvents used during the extraction and preparation of these herbal medicines can be a great source of physico-chemical contaminants. About 50 % of the herbal medicines that were analysed had food and drugs board's codes written on their labels while 50 % did not have any of such codes from the Food and Drugs Board of Ghana (Table 1). Trace metals are well noted for their wide environmental dispersion, their tendency to accumulate in selected tissues of the human body and their potential to be toxic at relatively lower levels of exposure. The results of the analysis are shown in Table 2 below. Concentrations of Al and Pb were measured in 100 % of the herbal samples that were analyzed. The mean concentrations of Al were relatively high in all the medicinal herbal products that were analyzed. The highest mean concentration of 0.533 mg/L was measured in sample C whilst the least; 0.278 mg/L was measured in sample I. This may be contributed partly by the use of aluminium boilers during the extraction stages of most of these Ghanaian herbal medicines. Aluminium has no known biological benefit to humans. When levels of Al are high in the body, the bones act as a sink and subsequently releasing it slowly through the digestive system over a long period. Patients with kidney failure, however, face a multitude of problems, including the inability to excrete absorbed aluminium (European Aluminium Association, 2008). Pb is a well known toxic element to the human body. Lead occurs naturally in the environment; however, most lead concentrations that are found in the environment are a result of human activities (Dhote and Dixit, 2011). The mean concentrations of lead in the herbal medicines analyzed were below the Canadian National limit in herbal medicines and products of 10 ppm. The Food and Agricultural Organization/World Health Organization (FAO/WHO, 1993) has established a "provisional tolerable weekly intake" (PTWI) of 25 μg lead/kg body weight for humans. The mean blood lead level intake of adults is in the range of 20–514 μg/day (NRC, 1980).

Fe was measured only in samples A and C with sample A measuring an extremely high mean concentration of 3.298 mg/L. Fe forms part of hemoglobin, which allows oxygen to be carried from the lungs to the tissues (Anim et al., 2011). Severe Fe deficiency causes anaemia in humans. The maximum permissible level (MPL) of iron is 1000 μg/day (NRC, 1980). Iron salts have an astringent action resulting in irritation of the gastrointestinal mucosa which gives rise to gastric discomfort, nausea, vomiting and diarrhea or constipation (Bourman and Rand, 1980). With large oral doses of iron, the astringent action of iron salts damages the mucosal cells. Severe damage causes bleeding in the stomach or haematemesis. Necrosis of mucosal cells may also lead to perforation of the gutwall (Bourman and Rand, 1980). Similarly, Cu was measured in only two of the samples; F (0.003 mg/L) and I (0.009 mg/L). Cu also forms an integral part of several enzymes and it is necessary for the synthesis of haemoglobin. Cu, which is an essential element to humans measured concentrations below the Singapore National limit of 150 ppm (WHO, 2007). In humans, acute copper poisoning is rare and usually results from contamination of foodstuffs or beverages by copper containers or from the accidental or deliberate ingestion of large quantities of copper salt (Williams, 1982). Symptoms of acute copper poisoning include salivation, epigastric pain, nausea, vomiting and diarrhoea, all of which are probably due to the irritant effect of copper on the gastrointestinal mucosa (Williams, 1982). 80 % incidence was however measured for Zn in all the samples analyzed. Zn is also an essential trace metal for both animals and humans. A deficiency of zinc is marked by retarded growth, loss of taste and hypogonadism, leading to decreased fertility (Sivapermal et al., 2007). The levels of copper and zinc in the samples, apart from natural sources might also have emanated from the input of fertilizers. Cd was also measured in 40 % of the samples with relatively low concentrations. The source of Cd in humans is through food consumption. Severe toxic symptoms resulting from Cd ingestion are reported between 10 to 326 mg (Sivapermal et al., 2007). Fatal ingestions of Cd, producing shock and acute renal failure, occur from ingestions exceeding 350 mg (NAS-NRC, 1982). The manifestations of cadmium nephrotoxicity, aminoaciduria, glycosuria and tubular necrosis have been detected at renal cadmium concentration of less than 50 μg/g tissue (Obi et al., 2006). The effect of

cadmium on the kidney takes the form of renal tubular dysfunction and subsequent pathological changes (Obi et al., 2006). The concentrations of Cd were however below the Canadian National limit of 0.3 ppm in herbal medicines. The presence of heavy metal may be the result of accidental contamination during manufacture, for instance, from grinding weights or lead-releasing containers or other manufacturing utensils (Koh and Woo, 2000). According to Schicher (1983), medicinal herbs may contain heavy metals when grown in seriously polluted soil.

Table 2 Statistical summary of mean concentration, mg/L (range) of trace elements

ID	Fe	Zn	Cu	Cd	Al	Pb
A	3.298±0.004 (<0.006-6.794)	0.086±0.010 (0.081-0.090)	<0.003	<0.002	0.345±0.003 (0.203-0.544)	0.009±0.002 (<0.010-0.027)
B	<0.006	0.0747±0.005 (0.061-0.086)	<0.003	<0.002	0.389±0.002 (0.266-0.464)	0.0056± 0.003 (<0.010-0.017)
C	0.166±0.004 (<0.006-0.498)	0.069±0.014 (0.066-0.071)	<0.003	0.003±0.001 (<0.002-0.009)	0.533±0.017 (0.441-0.653)	0.0066±0.002 (<0.010-0.02)
D	<0.006	0.0453± 0.001 (<0.001-0.068)	<0.003	0.003±0.002 (<0.002-0.007)	0.289 ±0.023 (0.270-0.303	0.022±0.001 (0.013-0.039)
E	<0.006	0.078±0.011 (0.067-0.087)	<0.003	<0.002	0.423±0.006 (0.355-0.520)	0.036±0.001 (<0.010-0.032)
F	<0.006	0.091±0.001 (0.083-0.095)	0.003±0.002 (<0.003-0.010)	<0.002	0.357±0.012 (0.295-0.421)	0.020±0.003 (<0.010-0.033)
G	<0.006	0.097±0.004 (0.087-0.116)	<0.003	<0.002	0.437±0.002 (0.415-0.468)	0.012±0.002 (0.010-0.036)
H	<0.006	<0.001	<0.003	0.003± 0.002 (<0.002-0.004)	0.317±0.015 (0.268-0.335)	0.045±0.003 (0.016-0.064)
I	<0.006	0.0056± 0.011 (<0.001-0.017)	0.009± 0.002 (<0.003-0.027)	0.0027±0.001 (<0.006-0.008)	0.278 ±0.022 (0.247-0.327)	0.085±0.005 (0.066-0.109)
J	<0.006	<0.001	<0.003	<0.002	0.301±0.010 (0.169-0.401)	0.033±0.002 (0.018-0.054)

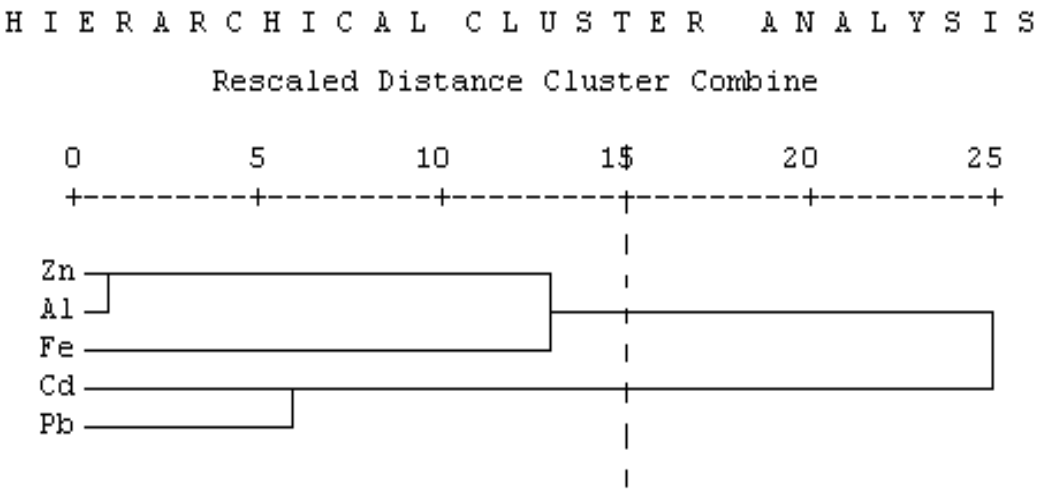

Fig. 1 A dendogram of cluster analysis showing clusters of the trace metals

A dendogram in Fig. 1 shows the relationship between the trace elements that were analysed from a cluster analysis using SPSS 16.0 package. Cluster analysis (CA) gives a diagrammatic representation by way of grouping herbal medicinal products into particular clusters characterized by high mutual similarity. The dendogram with the phenon line set at a rescaled distance of 15 indicates two clusters. Cluster 1 (CA1) is loaded with Zn, Al, and Fe while cluster 2 (CA2) is loaded with Cd and Pb. CA1 is a cluster containing two essential elements; Zn and Fe and may be introduced into the herbal medicinal products from similar sources. Even though, Aluminium has no known biological importance to humans, it is noted to be a geological component together with Zn and Fe. Cd and Pb are both toxic trace elements and may have been introduced into the plants/herbs at source through soil contamination. Chemical and microbiological contaminants can also result from the use of human excreta, animal manures and sewage as well as fertilizers.

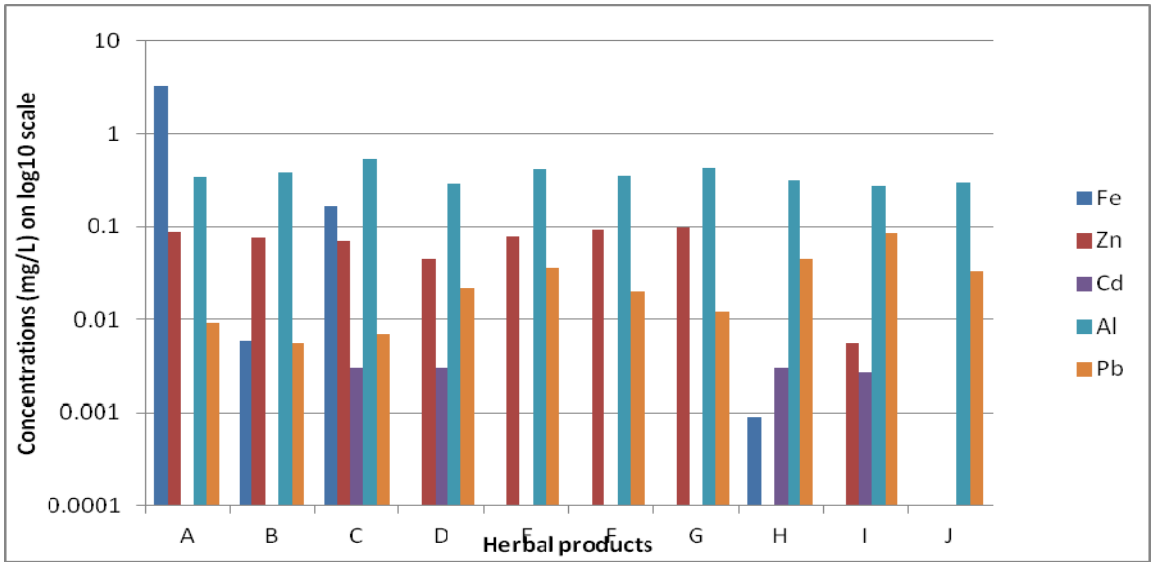

Fig. 2 Mean concentration of trace metals in the herbal products

Fig. 2 is a graphical presentation of the mean concentrations of trace metals in the herbal medicines analysed. The concentration of Al is the highest in all the brands except for brand A where the concentration of Fe was the highest. The highest concentration of Fe, 3.298 mg/L was measured in only brand A, of the herbal medicines. Interestingly, sample J did not record any conentrations of Fe, Zn and Cd above the respective detection limits. Only Pb and Al which are not essential elements were measured in J. This trend may be due to the fact that, the medicinal brands have different plant compositions and they might also have been harvested from different geographical locations. Vijayakumar et al. (2011) noted that micronutrients such as Cu, Zn, Mn and Fe plays a vital role in maintaining soil health and also productivity of crops (Vijayakumar et al., 2011). Handling and processing may also be a contributing factor to the introduction of some of these trace metals. The concentrations of Pb and Al are more likely to be introduced into the plant materials through the soil.

4 Conclusion

It is evident from the analysis that all the samples analysed measured concentrations of trace metals below recommended National limits. The herbal medicines analyzed are therefore safe for human consumption. Some of the samples also did not contain detectable levels of essential trace metals, notably Fe and Cu. Since medicinal plants have been used and continue to be used therapeutically all around the world, and being an

important aspect of various traditional medicine systems, it is imperative to monitor the quality of these preparations. The fact that some herbal medicines are not registered with the Food and Drugs Board of Ghana is very discouraging. This research is a preliminary work and therefore needs to be continued periodically to establish whether all herbal medicines, prepared and sold on the Ghanaian market are wholesome and safe for human consumption.

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