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Heavy Metal Content of Selected Raw Medicinal Plant Materials: Implication for Patient Health

P. Dzomba*, T. Chayamiti, E. Togarepi

Chemistry Department, Faculty of Science, Bindura University of science education, P. Bag 1020, Bindura, Zimbabwe

Email pdzomba@gmail.com or pdzomba@buse.ac.zw

ABSTRACT

The safety and quality of herbal medicines has become increasingly important for health authorities, scientific community and the public alike. Thus this study was aimed at determining the amount of heavy metals in selected raw traditional medicines. Heavy metal concentrations in these raw herbal drugs were found to be in the range of, 0.23-19.01 for Pb, 0.12-0.39 for Cu, 0.25-1.30 for Zn, 0.01-0.14 for Ni,1.41-30.84 for Fe and 0.01-0.46 mg kg^{-1}for As. Heavy metal content that were found above permissible limits were: 19.01 for U. kirkiana bark and roots (Pb), U. kirkiana bark (12. 25 ± 0,01), roots (12.11 ± 0. 00) and O. americanum leaves (33.61.±0.07) and roots (30.84 ± 0.02) for iron. Significant difference was only noticed for each heavy metal among raw herbal drugs sampled from twenty one places for C. imberbe leaves and L. discolor roots (Pb) (ANOVA followed by least significant test at p = 0.05). Generally most of the drugs that are being used by people in Mashonaland central province were found to be toxic and unsafe for human consumption due to elevated levels of heavy metals especially Cu, Fe, As and Pb. It is suggested that pharmacovigilance must always be done to improve the quality, safety, and efficacy of herbal drugs. Every person dealing with plant medicine should be sensitized on how to maintain efficacy, quality and safety of such medicines.
Keywords: *raw herbal medicine, heavy metal content, patient health, safety.*

INTRODUCTION

Traditional medicine use is increasing steadily due to increased cases of bacterial resistance to current pharmaceuticals, affordability and readily availability [1; 2]. About 70 – 80% of the world population continues to rely on non-conventional medicines which predominately consist of herbal sources in their primary health care [3]. Herbal medicines are likely to be contaminated with heavy metals [4; 5]. In trace amounts some heavy metals are essential for the human body however they maybe be toxic if present in a higher concentration [6; 7]. They have the ability to bioaccumulate and disrupt functions of vital organs and glands in the human body such as brain, kidney and liver [8]. Medicinal plants can be contaminated by heavy metals via roots uptake or by direct deposition of contaminants from the atmosphere onto plant surfaces. Lead is considered a potential carcinogen and is associated with pathology of many diseases which includes cardiovascular, kidney, blood, nervous, and bone diseases [9]. Lead is a protoplasmic poison with affinity for the grey matter of brains. It invades neurons, damages cells, nerve synapse and dendrites, and reduces the number of oxygen carrying red blood cells [10; 11]. It combines with phosphorous and enters the blood stream where it goes to the spleen, liver, and kidneys [10]. Excessive concentration of Zn and Cu in the body is of great concern because of their toxicity to humans and animals [12]. Arsenic and many of its compounds are potent poisons. It disrupts ATP product. Excess iron is stored in the liver, pancreas, pituitary, adrenals, heart, and skeletal muscles. When the body gets too much iron it leaches out of its storage sites and moves into the blood stream where it is taken to the brain [13]. Too much iron in the brain destroys neurons, leading to neurodegenerative diseases and neurological dysfunction, with Alzheimer‘s like symptoms [13]. Increasing use of traditional medicines is of special concern because they are not rigorously regulated thus the focus of this study was to determine the amount of toxic heavy metals in selected raw medicinal plant materials. The plants studded in this research include, *Combretum imberbe*, *Lannea discolor, Ocimum americanum, Uapaca kirkiana, and Pseudolachnostylis maprouneifolia.* These plants are widely used in many Southern African countries such as Zimbabwe, Zambia, Mozambique, South Africa, Namibia, Tanzania and Botswana as traditional medicines. Unfortunately there is limited knowledge about heavy metal safety of these herbs.

MATERIALS AND METHODS

All chemicals and reagents used were of analytical grade. HCL, HNO_3 and H_2O_2 were obtained from Merck, New Jersey, USA. Calibration and certified reference materials were obtained from Aldrich, Steinheim, Germany. Double deionized water was used for all analysis. Analysis of arsenic was done using ICP-AES, Perkin Elmer 5300 / 7300 Dual view while for the other heavy metals AAS, Varian Spectra AA 600 flame Atomic Absorption spectrophotometer was used.

SAMPLE COLLECTION AND PREPARATION

All samples (Table 1) were collected from twenty one places in Mashonaland central Zimbabwe from traditional healers.

Table 1: Raw medicinal plant materials, their uses and dosage

Sample ID	Family	Local names	Part used	Medicinal use (Quote frequency = ≥ 60%
C. imberbe	Combretaceae	Muchenarota, mutsviri, ubimba,	Leaves, Bark, roots	boiled in water to produce a decoction to treat stomach ache and malaria, Green leaves placed on hot coals produces a smoke that can be inhaled to relieve coughs, colds and chest complaints. infusion from bark is used for the treatment of bilharzia, Ashes are used as tooth paste, roots make a decoction taken orally to treat diarrhea and stomach disorders
O. americanum	Lamiaceae	Kamangi	Leaves, flowers, stems	Useful for intestinal worms, infusion used to treat Ingestion, dysentery, coughs, hiccups, vomiting and nausea, gas pains, earache, snakebites, ulcers, gonorrhea, rheumatic pains
U. kirkiana			Bark, root	infusion used to treat Ingestion, dysentery
P.maprouneifolia	Euphorbiaceae	Mutsonzowa, Mudyamhembwe mukuvazviyo	bark	Cancer, eyes, stomach ache coughs, hiccups, vomiting and nausea, gas pains,
L. discolor	Anacardiaceae	musamba , musinga, mushama, Chizhenje, Mugan'acha, Muhumbukumbu	Leaves, Roots, bark	Malaria, stomach ache, fevers and constipation. Bark & roots used for childrens ailments, convulsions, dizziness, bladder & bowel ailments and for vomiting and female sterililty Roots also for diarrhoea

Percentage frequency of quote was calculated as number of responses agreeing to a usage/ number of total respondents.

Sample names were validated by taxonomists at Harare national herbarium gardens and voucher specimens were deposited in the chemistry department (natural product section) for future reference. Frequency of quote as an indicator of the usage of the plants by the community was determined using interviews. Twenty people were interviewed from each area and participation was voluntary. Only uses that had a frequency of quote that was equal or greater than 60% were recorded. In all cases, samples were collected in clean polythene bags and transported straight to the laboratory. Samples were then dried at room temperature, crushed using a wooden mortar and pestle and passed through a laboratory king test sieve of 0.75 m. For analysis of Pb, Zn, Cu, Fe, and Ni the resulting powder was digested by weighing 0.5 g into an acid-washed porcelain crucible and placed in a muffle furnace for four hours at 500°C. The crucibles were removed from the furnace and cooled. 10 ml of 6 M HCl were added covered and heated on a steam bath for 15 min. Another 1 ml of HNO_3 was added and evaporated to dryness by continuous heating for one hour to dehydrate silica and completely digest organic compounds. Five milliliters of 6 M HCl and 10 ml of Milli-Q water were then added and the mixture heated on a steam bath to complete dissolution. The mixture was cooled and filtered through a Whatman no. 1 filter paper into 50 ml volumetric flasks and made up to the mark with Milli-Q water. For analysis of arsenic 0,5 g (dry mass) of plant sample was weighed into the digestion vessel. Then 5,0 ml of concentrated HNO_3 and 1,0 ml of 30% H_2O_2 were added to each sample. Samples were pre-digested overnight (16 h) in a fume hood at room temperature. After cooling the entire digest was filtered through a Whatman no. 1 filter paper into 50 ml volumetric flasks and made up to the mark with Milli-Q water.

ELEMENTAL ANALYSIS OF SAMPLES

Determination of Cu, Zn, Fe, Ni and Pb in samples was made directly on each of the final solution under atomic absorption spectroscopy (AAS). Determination of As was performed on an ICP-AES.

STATISTICAL ANALYSIS

Heavy metals content of the raw herbal drugs are presented as mean ± standard deviation (SD) of five determinations. Differences among sampling areas were analyzed by ANOVA using a probability factor of $p = 0.05$, software (SPSS 17 Inc., Chicago, IL, USA).followed by multiple comparison of mean using least significant difference (LSD) test to locate the significantly different pairs of mean.

RESULTS AND DISCUSSION

Quality assurance and quality control protocol

Quality control and assurance protocols were carried out to ensure accuracy and reliability of the results. Milli-Q water was used throughout the study. Glassware was properly cleaned, and the reagents used were of analytical grade. Reagents blank determinations were used to correct the instrument readings. All analyses were performed five times. Certified reference materials (CRM) for plant samples were used for validation of the analytical procedure. The results of measurements of CRMs are summarized in Table 2.

Table 2. Certified reference material concentrations (mg Kg^{-1}) mean ± SD, n = 5

	CRM 1			CRM 2		
Metal	Certified value	Measured value	Recovery (%)	Certified value	Measured value	Recovery (%)
Cu	120 ± 0,4	120 ± 0,5	100	2,5 ± 0,03	2,5 ± 0,01	100
Zn	260 ± 0,5	260 ± 0,5	100	13,1 ± 0,5	12,8 ± 0,5	98
Ni	1,2 ± 0,01	1,1 ± 0,05	92	0,10 ± 0,00	0,10 ± 0,00	100
Pb	73 ± 0,5	73 ± 0,5	100	0,11 ± 0,01	0,12 ± 0,00	109
As	1,6 ± 0,5	1,5 ± 0,01	94	0,05 ± 0,00	0,05 ± 0,00	100

% recovery = mean measured value/mean certified value X 100%

The average concentrations of heavy metals (mg kg^{-1}, on dry weight basis) in selected raw medicinal plant material are listed in Table 3. The concentrations of heavy metals were highest for Fe, followed by Pb. Ni and As recorded the lowest concentrations. Among the raw medicinal plant material, the average concentration of Pb was highest in *U. kirkiana bark* (19,01 ±0,01) followed by *L. discolor* leaves (0,60 ± 0,05) and then *C. imberbe* leaves (0,56 ± 0,05). *O. americanum* leaves recorded the lowest Pb concentration (0,37 ± 0,07). *O. americanum* showed the highest concentration of Zn (1,30 ± 0,00) while the lowest concentration was recorded in *C. imberbe* (0,30 ± 0,01). For Fe, *O. americanum leaves* recorded the highest (33,61±0,07) and *C. imberbe* leaves recorded the lowest (1.42± 0,09). Ni concentration ranged in the following order *O. americanum* leaves > *D. mespilifemis* leaves > *P.maprouneifolia* bark bark > *C. imberbe* roots > *L. discolor* roots. *U. kirkiana bark* showed the highest concentration of Cu (0,39± 0,00) while *L. discolor* roots concentration was the lowest (0,12± 0,01). Arsenic concentration was highest in *P.maprouneifolia* bark (0,46± 0,02) and lowest in *C. imberbe* leaves. Significant differences among the twenty one areas p > 0,05, ANOVA and multiple range (LSD) were observed only for heavy metal content of *C. imberbe* leaves and *L. discolor* roots for lead.

Table 3. Mean heavy metal concentration (mg kg^{-1}) DW of raw medicinal plant material, (n = 5, ± SD)

Sample ID	Pb ± SD	Zn ± SD	Fe ± SD	Ni ± SD	Cu ± SD	As ± SD
C. imberbe leaves	0,56 ±0,05*	0,30 ± 0,01	1.42± 0,09	0,01 ± 0,00	0,24± 0,00	0,04± 0,00
C. imberbe stems	0,45 ± 0,02	0,30 ± 0,00	1,41± 0,02	0,01 ± 0,00	0,20± 0,00	0,01± 0,00
C. imberbe roots	0,23± 0,01	0,25 ± 0,01	1,42± 0,01	0,02 ± 0,00	0,20± 0,03	0,02± 0,00
O. americanum leaves	0,37 ± 0,07	1,30 ± 0,00	33,61±0,07	0.14 ± 0,03	0,17± 0,06	0,06± 0,00
O. americanum stems	0,32 ± 0,09	1,30 ± 0,02	30,84±0,02	0,10 ± 0,03	0,16± 0,04	0,03± 0,00
U. kirkiana bark	19,01 ±0,01	0,61 ± 0,08	12,25±0,01	0,12 ± 0,03	0,39± 0,00	0,32± 0,00
U. kirkiana roots	19.01 ±0,05	0,46± 0,00	12,11±0,00	0,09± 0,01	0,32± 0,00	0,32± 0,02
P.maprouneifolia bark	0,43 ± 0,00	0,33 ± 0,01	2,10 ± 0,03	0,06 ± 0,00	0,22± 0,05	0,46± 0,02
L. discolor leaves	0,60 ± 0,05	0,83 ± 0,09	4,65 ± 0,06	0,05 ± 0,00	0,19± 0,00	0,12± 0,01
L. discolor roots	0,55± 0,00*	0,73 ± 0,01	3,44± 0,01	0,01 ± 0,00	0,12± 0,01	0,11± 0,00

DW- Dry weight bases, * represent a significant difference using ANOVA (p > 0.05) followed by multiple comparison of mean by least significant difference (LSD) test Statistical comparisons were performed for different collection areas of raw herbal drugs for each heavy metal.

Contamination of traditional medicines by heavy metals is of major concern because of the toxicity, persistence and bioaccumulative nature of such metals [14]. Even though WHO has formulated guidelines for quality assurance and control of herbal medicine, traditional practitioners lack enough knowledge which may results in medication with various types of heavy metal contamination. The heavy metal concentrations assessment in this study was done for certain metals (Pb, Cu, Zn, Fe, As and Ni). Lead is one of the most toxic metals. It is well known for its adverse effects on many parts of the body. Progressive exposure to lead results in a decrease in the performance of the nervous system and affects renal clearance [15]. Inorganic lead is carcinogenic and cause miscarriages in pregnant women. The results of the five selected raw medicinal plant material show that all of them consist of lead in a concentration range of 0,23-19,01mg Kg^{-1}. Most of the samples are within permissible limits as laid down by guidelines for quality standardized herbal formulations [16] except that for *U. kirkiana* bark and roots 19, 01mgKg^{-1}. Heavy metals that are essential for the health of the body include Cu, Zn and Fe and are required in negligible quantities for the proper functioning of enzymes, hemoglobin formation and vitamin synthesis in men [17]. In case of both deficiency and excess of these essential metals metabolic disturbances are encountered. Toxic metal As is not required by the body and cause serious effects upon exposure even at very low concentrations [18, 19, 20]. Heavy metal content of Pb and Cu in the selected raw herbal medicines pose serious health risks to patients because of Pb and Cu contamination, crossing the safety limit of 10 mg/kg Pb [21, 22], 4-20 g/kg Cu[23]. *U. kirkiana can* give rise to damage of respiratory organs, nerve cells, and hemoglobin due to Pb poisoning [24, 25, 26]. Concentrations of essential metals Fe, Zn and Ni for most samples except for *U. kirkiana* and *O. americanum* (Fe content) are below their average daily intake of 0.3 mg / day Ni, given by WHO [24], Fe 7 -10 mg/day, Zn 60mg/day [22] making these drugs good sources of essential metals. Fe content for *U. kirkiana* (12,25±0,01 bark and 12,11±0,00 roots and *O. americanum (*33,61±0,07 leaves and 30,84±0,02 roots) are above safety limits. Even though As levels are in low quantities as compared to WHO standards their presence is worrisome as continuous exposure can be toxic since it is a non essential element. Differences among the sampling areas can be rationalized as due to anthropogenic contamination [27]. The greater the amount of heavy metals in the soil the increased chance of the metal to accumulate in plant tissues [28]. Contamination due to improper sampling and storage might have played significant role as traditional healers are less educated in such areas.

CONCLUSION

Most of the raw herbal drugs that are being used by people in Mashonaland central province were found to be toxic and unsafe for human consumption due to elevated levels of heavy metals especially Cu, Fe, As and lead. Generally studies on the heavy metal contents of the raw herbal drugs obtained from twenty one different sampling areas revealed no wide variation in the results. Cu, Fe, Pb and As were found to be major pollutants. It is suggested that pharmacovigilance must be done to improve the quality, safety, and efficacy of herbal drugs not only during their growth, but also during their sampling, processing and storage by traditional healers in order to avoid heavy metal contamination. Everyone involved in traditional herbal medicine should be sensitized to heavy metal contamination risk to improve the quality, safety, and efficacy of herbal drugs.

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