Global Journal of Pharmacology 13 (2): 47-54, 2019
ISSN 1992-0075

DOI: 10.5829/idosi.gjp.2019.47.54

Assesment of Heavy Metals Concentration in Selected Abakaliki Herbal Preparations and Synthetic Drugs for Management of Disease Conditions

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Abstract: The use of herbal /synthetic medicines for treatment of different disease conditions has been as old as human existence. These drugs contain chemical substances which are considered as beneficial while others were not. Herbal products / synthetic drugs are consumed extensively in Ebonyi State for their medicinal properties. This study was undertaken to evaluate the concentration of heavy metals in selected traditional herbal preparation and synthetic drugs consumed in Abakaliki Ebonyi State. A total of 11 samples were used for the study: seven herbal preparations and 4 synthetic drugs. They include: Healing bitters, orak herbal formula, Goko cleanser, Clara ULC, Pro-life herbal remedy, golden seed, Deep root herbal mixtures, relcer gel, Reprofen suspension, ampiclox and P-alaxin. The drugs and herbal mixtures were purchased from the local Abakpa market in Abakaliki Ebonyi State Nigeria. They were analyzed for their, lead, copper, iron, manganese, potassium, chromium, Nikel, zinc calcium, mercury, manganese, contents. Microwave-assisted digestion were used for the dissolution of the samples and heavy metals concentration was determined using Atomic Absorption Spectrometry (AAS). Metals were found to be present in varied concentrations in the herb and synthetic drug samples. The concentration ranges were found as follows: 0.03-12.35 µg/g for essential metals and 0.12-3µg/g for toxic metals respectively for both herbal preparation and synthetic drugs. The gross level of contamination of lead, mercury and chromium metals could be attributed to poor adherence to good manufacturing practice and effective surveillance. Hence, this work suggest immediate action by relevant authorities in order to avert impeding health hazards from gradual accumulation of these toxic metals in the body system of consumers of these herbal preparations and synthetic drugs, to ensure safety of these medicines in Ebonyi State Nigeria.

Key words: Drugs · Heavy metals · Disease · Herb and hazards

INTRODUCTION

Drug is a vital substance required by all organisms for the sustenance of life and its support other functions, such as growth, development and maintenance of the body [1]. Most herbal materialsare mainly derived from plants. The use of medicinal plants or medicine in various forms has been popular for since man existence and despite significant developments in modern medicine [2]. Investigations of new drugs from natural sources are of great importance and assessment of safety in existing synthetic drugs is timely. Heavy metals are defined as elements with metallic properties and has an atomic number higher than 20. However, they are natural

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components of the earth's crust and ubiquitous in trace concentrations [3]. Research has shown that some herbal products contain heavy metals [4]. The presence of metal residues in the herbal plants is prevalent because they are absorbed during growth, development and processing [5]. After collection and transformation into drug form, heavy metals confined in plants finally enter the human body thus, leading to abnormal functions of different organ systems [6].

The presence of these heavy metals in herbal/synthetic drugs products may be attributed to several possibilities [7]. Some of the factors include: environmental, mining activities, fertilizes, lack of Good manufacturing practice, etc.

The intentional addition of heavy metals during the preparation as part of the ingredients for acurative purpose constitutes another source of herbal products contamination with heavy metals [8] Essential mineral element can also play major roles in biological activities either with organic molecules such as metallo-enzymes or independently like redox or catalytic reaction [9]. The knowledge of elemental contents of herbal preparations used for different medicinal purposes is of great importance and deserves more attention for screening than ever before [10] because of patients dependence on these herbal preparations and conventional drugs. The bio-toxic and poisoning effects of heavy metals occur due to bioaccumulation when consumed above the bio recommended limits [12]. This further interferes with the normal body biochemistry in the normal metabolic processes.

WHO has emphasized the importance of quality assurance of herbal products, whereas modern drugs also requires pre-market testing including heavy metals [13].

This study was undertaken to evaluate the safety of some herbal formulations and synthetic drugs prevalent in Abakpa market in Abakaliki Ebonyi State.

MATERIALS AND METHODS

Sample Collection and Preparation: The investigation was carried out on common herbal products /synthetic drugs used in Abakaliki Ebonyi State Nigeria for treatment of popular disease conditions such as sexually transmitted diseases, antimalarial, anti-ulcer, anti-hypertension, typhoid, asthma, stroke, infertility, anti-diabetes etc. The herbal preparations /synthetic drugs were sourced from Abakpa market at Abakaliki taken to laboratory for analysis.

Sample Digestion: One gram (1.0 g) of each sample was placed into beakers then added 20 cm^3 of concentrated nitric acid. It was kept for 24 hours thereafter were carefully heated on a powered electrically connected sand-bath in fume hood chamber with periodic addition of 10-20 cm^3 concentrated nitric acid before it produced red nitrous oxide (NO_2). The samples were cooled while 2-4 cm^3 of perchloric acid ($HClO_4$) was added then heated until the cleared sample solution was obtained. The samples were further diluted with deionized water, filtered into 100 cm^3 volumetric flasks and made up to mark, transferred into a capped labeled plastic bottle and stored in refrigerator before analysis. The ratio of the acids HNO3: HClO4 used for the digestion was 5:1 [14]. The same proportion of the reagents used in the sample digestion under the same experimental condition were used to prepare the Blank sample.

Preparation of Standard Solutions: Stock standards solution of the metals of interest was prepared by weighing out accurately 1.000g of the pure metal. It was further dissolved in concentrated nitric acid and made up to mark with 1 dm^3 of deionized water in volumetric flask. Furthermore, appropriate salt of the metal was weighed out as calculated in relation to the formula weight, then dissolved in 1 dm^3 volumetric flask and made up to mark with deionized water [15]. The working standards of appropriate concentrations were prepared from the stock solutions by diluting appropriate volume with deionized water. This was made up to mark in 100 cm^3 volumetric flask and used for calibrating the AAS equipment after optimization according to the standard conditions.

Pictures of Herbal/ Synthetic Drugs

Fig. 1: Clara ulc and Goko cleanser

Fig. 2: Healing biters, Prolife herbal remedy and Golden seed

Fig. 3: Orak herbal formula and deep root herbal mixture

Fig. 4: Synthetic drugs :P- alaxin, ampiclox, Relcer gel antacid and Reprofen suspension

Table 1: List of herbal mixtures/ synthetic drugs with indications used in the study

S/N	Name of Herbal Products/synthetic Drugs	Manufacturer	Manufactured Date	Indication	Batch Number
1	Goko cleanser Herbal mixture	Dr.Igudo Goko cleanser Herbal mixture	01/2019	Prevention of oedema, sugar, pile etc	0014
2	Golden seed	Joe Best natural health solution Enugu Nigeria	01/2019	sexual transmitted diseases	0049
3	Deep root Herbal mixture	Fesco Herbal mixture Nig.LTD	04/6/2018	malaria, thyphoid, weaknes of erection etc.	013
4	Clara ULC	Dr.F, C EzeAfrican healing herbs company	02/2018	Antiulcer mixture	002
5	Pro-life Herbal remedy	Pro-life Herbal remedy	9/2017	Malaria/thyphoid, hepatitis A and B	001
6	Orak Herbal formula	Orak herbal formula Lagos Nigeria	01/2018	Stroke, liver problems etc	Z012
7	Healing bitters	Healing bitters Research Outreach Ghana	01/2016	Rheumatism and waistpain	
8	P-Alaxin	Bliss GVS Pharma LTD India	03/2018	Malaria	H1AGX0017
9	Ampiclox 250mg/5ml	Medreich LTD INDIA	02/2017	Gram positive and negative diseases	170143
10	Relcer antacid	Glemark pharmaceutical LTD India	9/2018	Antiflatulent	10162235
11	Reprofen 100mg/ml suspension	Rajrab LTD Nigeria	11/2017	Reduction of fever	RD339

RESULTS AND DISCUSSION

Increasing numbers of people in the developed and developing countries use herbal medicinal products. This is based on the many misconception that herbal products are 'natural' implying that they are 'safe' [16]. New brands of herbal products are being introduced into the developing countries including Nigeria in the form of 'supplements'. Globally, there are warnings regarding the possible toxicity, adverse reaction and contamination. However, modern drugs on the other hand may pose danger to consumers depending on the composition [17]. Exposure to heavy metals for long time may cause adverse health effect and toxicity due to the capability of heavy metals to bioaccumulate and disrupt the functions of vital organs in the human body [18]. Some heavy metals are essential as trace amounts such as zinc and iron and they are dangerous if present in a higher concentration [19].

In present study the concentration of metals both herbal and synthetic drugs evaluated showed varying concentrations of heavy metals in both herbal mixtures and synthetic drugs.

Lead (Pb) showed 1.3-0.3, 0.3-0.8 ppm (Table 2 and 3). This was lower than the permissible limits WHO limits for lead is 10ppm.Lead is a heavy metals which have been recognized for its biological effects on different body organs. It has been reported that prolonged exposure to Pb decreases the performance of the nervous system and lowers renal clearance [20]. Its poisoning is considered one of the significant environmental health threats for children even at low levels of exposure [21]. It has the ability to inhibit or mimic the actions of calcium, which can

Table 2: Heavy metal composition of selected herbal and conventional drugs (ppm)

Drugs	Mn	Ni	Cu	Hg	Fe	Mg	Zn	K	Ca	Cr	Pb
Relcer antacid antiflatulent	0.0648	0.2051	0.000	0.000	0.4891	12.35	0.0606	0.6188	2.00	0.175	0.250
Reprofen 100mg/ml suspension	0.0324	0.7179	0.097	1.000	0.4891	0.8997	0.0519	0.6188	4.667	0.525	0.250
Ampiclox 250mg/5ml	0.1620	0.2051	0.0323	1.000	1.4672	0.9583	0.0433	2.475	4.667	0.117	0.750
P-Alaxin	0.1944	0.1026	0.0970	2.000	0.4891	0.7106	0.0433	1.779	4.00	0.117	0.250
Healing bitters	0.0648	0.4103	0.0647	0.000	0.3668	0.9453	0.0346	3.867	5.333	0.350	1.250
Orak Herbal formula	0.0324	0.3077	0.0647	2.000	0.3668	0.9779	0.0519	5.2597	4.666	0.117	0.250
Goko cleanser Herbal mixture	0.0972	1.2308	0.0647	3.000	0.6114	0.5998	0.0433	1.1602	8.667	0.233	0.750
Clara ULC Antiulcer mixture	0.0324	0.6154	0.0323	1.000	0.2445	0.8475	0.0346	6.8840	3.333	0.583	0.250
Pro-life Herbal remedy	0.0324	0.3077	0.0323	2.000	0.1223	0.8084	0.0346	3.3260	4.667	0.292	0.250
Golden seed for sexual transmitted diseases	0.0324	0.5128	0.0647	1.000	1.1004	0.9388	0.0260	3.3260	10.00	0.350	0.500
Deep root Herbal mixture	0.0648	0.6154	0.1293	2.000	0.7336	1.4538	0.0173	7.4254	2.667	0.058	0.250

Table 3: Level of metal concentrations in both herbal and synthetic drugs (ppm)

Metals	Herbal mixtures	Synthetic drugs
Manganes	0.032-0.09	0.2-0.03
Nickel	0.3-1.2	0.7-0.1
Copper	0.03-0.65	0.00-0.09
Mercury	0.00-3.00	0.00-2.0
Iron	0.12-1.1	1.5-0.49
Magnesium	0.6-1.5	12.35-0.71
Zinc	0.03-0.052	0.035-0.06
potassium	1.2-6.8	0.6-2.5
Calcium	3.3-10	2.-4.7
Chromium	0.058-0.58	0.12-0.5
Lead	0.3-1.3	0.3-0.8

affect calcium-dependent or related processes and to interact with proteins, including those with sulfhydryl, amine, phosphate and carboxyl groups [22]. Its high affinity for sulfhydryl groups makes it particularly toxic to multiple enzyme systems including heme biosynthesis [23]. A high lead level during pregnancy is directly related to several anomalies such as spontaneous abortion, low birth weight and impaired neurodevelopment [24]. Thus consumption of these drugs may lead to accumulation of the metal leading to toxicity. Many clinical cases had been reported regarding lead poisoning due to the consumption of different types of medicines [25]. In Bangalore a 45-years-old man case of lead poisoning had been reported, the patient's history revealed that he had been consuming 12 different Ayurvedic medicines for stress relief for the past 4 years. His blood lead level (BLL) was 1224 µg/L indicating lead poisoning [26]. Laboratory analysis of the 12 Ayurvedic products showed that 75% of the products contained high levels of lead, arsenic and mercury in concentration higher than the daily permissible limits [27].

Copper and zinc were determined in the test samples and concentration of copper showed 0.65-0.032, 0.00-0.09 ppm whereas zinc was 0.052-0.03, 0.035-0.06 ppm respectively (Table 2 and 3). Cu and zinc act as essential micronutrients up to certain concentration. Cu plays an important role in the oxidative defense system but at the high level leads to toxic condition. The present study showed similarities with the previous studies [28]. They are required for metabolic functions. Adequate amounts of copper are required for the growth of new blood vessels and wound healing [29], while zinc enhances immune systems. Zinc is an essential trace element and exists in all types of tissues of the body, perform vital roles for cell growth and other physiological activities [30]. Despite its important, it can be dangerous if exist in high concentration [31]. Excessive oral zinc exposure could lead to Zn accumulation in different organs leading to an adverse health effects in human. It affects serum cholesterol balance causing increase of the low density lipoprotein (LDL) cholesterol and a decrease in high-density lipoprotein (HDL) cholesterol [32]

A clinical case of gastrointestinal disturbances after the consumption of zinc sulfate was reported in England [33].

Nickel (Ni) was also detected 0.3-1.2, 0.1-0.7 ppm, exposure to Ni may cause a variety of pathological problems, oral exposure to large doses of nickel mainly targets the cardiovascular system [34]. The common adverse health effect of nickel in humans is allergic skin reaction in those who are sensitive to nickel this might be attributed to its interference with the physiological processes of zinc and calcium [35]. Carcinogenic nickel compounds have been shown to induce different types of tumours in experimental animal systems [36]. A clinical case of Ni toxicity had been reported [37]. Nickel poisoning cases were reported for a group of workers were exposed to nickel in an estimated dose of 7.1-35.7 mg /kg.

A number of studies had been reported for Ni detection in herbal mixtures and conventional drugs. In Furthermore, iron showed 1.10-0.1, 1.5- 0.4 ppm and is an essential micronutrient, it plays a critical role in major biochemical activities, such as oxygen transport and electron transfer [38]. Reports have shown that about 3-5 grams of iron (45-55 mg/kg) in human body, about 60-70% is utilized within hemoglobin in circulating red blood cells [39].Thus consumption these drugs may also boost the iron contents of an individual. This is in line with work of [40].

Iron is very important in metabolism and it can be hazardous when exist in high concentration [41]. Ingesting excessive doses of iron causes irritation of the gastrointestinal mucosa that increases the gastric discomfort symptoms like nausea, vomiting and diarrhea [42]. It may also cause severe damage to the mucosal cells which may lead to bleeding in the stomach and perforation of the gutwall [40]. Excess of iron disrupts the redox balance of the cell resulting in generation of chronic oxidative stress, which organized the signaling networks related to malignant transformation [41]. In humans, high concentration of iron storage has been shown by scientist to increase the risk of cancers, including breast cancer [42]. Other metals evaluated showed varying concentrations; chromium 0.058-0.06, 0.53-0.12 ppm, while calcium, magnesium potassium were 3.3-10, 2-4.7 ppm 0.6-1.5, 0.7-12.4, 1.2-6.8 ppm and 0.6 -2.5 ppm respectively (Table 2 and 3). The result of this study reveals that the concentration of the metal analyzed were within the permissible level for each of the metals, example 0.5 ppm for lead, 30 ppm for chromium, even though ATSDR says; there is no save limit for lead.

CONCLUSSION

Herbal medicines and conventional drugs are consumed by a wide range of the world population. The presence of heavy metals in these medications could expose the consumers to different adverse health effects. These toxic heavy metals might result in serious safety issues due to the increasing popularity of herbal /modern drugs remedies in the world. This work demonstrated that in some herbal / modern medicines prevalent in Abakaliki have heavy metal content within permissible limits. Based on the results, it is strongly recommend that authorities should enforce regulations for pre-marketing safety studies on herbal products and conventional drugs in order to protect the health of the public.

ACKNOWLEDGEMENT

The authors are grateful to the technical staff of Atomic Energy Laboratory, Nsuka, Enugu Nigeria for their assistance in this work.

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