INVESTIGATION OF SELECTED METALLIC IMPURITIES IN ANTIMALARIAL HERBAL DECOCTIONS '*AGBO IBA*' COLLECTED FROM FOUR LOCATIONS IN LAGOS STATE, NIGERIA.

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ABSTRACT

Herbs constitute a common medicinal alternative for disease treatment in many cultures around the world. In Nigeria, these medicinal herbs are widely used in the treatment and prevention of various ailments including malaria, a global disease endemic to the tropics. In spite of their cultural trust and claimed medicinal properties, lack of standardization and poor-quality presentation make medicinal scientists to be wary of herbal medicinal preparations. However, due to their increasing patronage, the safety and quality of these herbal medicines have become increasingly important for health authorities, scientific community and the public alike. Thus this study was aimed at determining the amount of selected heavy metals in a herbal antimalarial decoction popularly known as 'Agbo iba' consumed in selected areas of Lagos.

The investigated heavy metals: Pb, Ni, Hg and Cd were detected using Atomic Absorption Spectroscopy (AAS) after sample pretreatment with wet digestion using HNO_3. Heavy metal concentrations in the decoctions were found to be in the range of 0.331 - 0.896 mg/L for Pb, 0.185 - 0.338 mg/L for Ni, 1.612 - 17.894 mg/L for Hg, while cadmium was not detected in the samples. These concentrations exceeded the World Health Organization (WHO) Permissible Limits (PL) and sources of contamination could be from sources of plants, harvest and transport conditions, method of preparations, to mention but a few. These products should be governed by standards of safety, quality, and efficacy that are equivalent to those required for other medicinal products of international standard.

***Keywords**: Antimalarial, herbal, Heavy metals, WHO, Safety, AAS, Agbo iba*

INTRODUCTION

Herbs have been used for medicinal purposes in many cultures since time immemorial. In recent decades, interest in herbs and other natural remedies has greatly increased due to heightened concerns of side effects and development of resistance to many conventional drugs. According to World Health Organization (WHO) estimates, nearly 70 – 80 % of the world population relies on nonconventional medications, mostly derived from herbal plants (WHO, Traditional Medicine Strategy, 2002), often because of their affordability and readily availability. In a further attempt to explore and regulate the use of alternative medicine, WHO set up a strategy committee with a mandate to achieve

integration of traditional medicine into National health systems between 2014 and 2023 (WHO, Traditional Medicine Strategy, 2013).

One out of the many herbal remedies used in Nigeria is an antimalarial decoction popularly called *Agbo iba*, which receives great patronage, majorly in the South Western region of the country. Malaria remains one of the most deadly global diseases, having high morbidity and mortality than any other infectious disease of the world. In 2017, the global malaria cases and deaths were estimated to be 219 million and 435,000 respectively (WHO, World Malaria Report, 2018). This report further revealed that malaria still kills a child every two minutes and indicates that no significant progress has been made in global malaria control in recent years. Malaria burden is predominant in Africa, where 92% of all cases and 93% of deaths occurred in 2017 (WHO, World Malaria Report, 2018). These are disturbing indices and particularly worrying is that Nigeria accounted for the highest malaria cases (25%) and deaths (19%) worldwide.

Herbal preparations have been used by poor masses for the treatment and prevention of malaria in the endemic regions of the world due to the emergence of resistance and ineffectiveness of the relatively cheap chloroquine and unaffordability of the WHO recommended artemisinin and artemisinin-based combination therapies (ACTs). These herbal remedies are often prepared in form of infusions, macerations or decoctions, tinctures, poultices, compresses and baths.

Despite the increasing interest in the therapeutic benefits of these herbal products and their use as alternatives to or to complement conventional drugs, there has been parallel increasing concern and reports on incidences of toxicity and adverse effects linked to the use of herbs and their formulations in different parts of the world (Ernst, 2012). Herbal decoctions are peddled on the streets, and sold in markets and garages in rural and urban centers across Nigeria. Their sources of toxicity and contamination vary and encompass the inherent chemical toxins, environmental contaminants such as pesticides, microbes, heavy metals, and other adulterants. In other words, the geochemical soil characteristics, contaminants in the soil; water; and air, and transportation and storage conditions can significantly affect the properties and the quality of herbs and their formulations (Saad *et al*., 2006).

Heavy metals are elements having specific gravity greater than 4 g/cm^3, that is, at least 5 times that of water. The toxicity of heavy metals to human health and the

environment has attracted considerable attention in recent years. Although they are often detected in consumables in trace quantity, heavy metals possess tendency to accumulate in human system, having low excretion rates through the kidney. Metals can cause serious health effects depending on the quantity as well as the nature of the metal ingested (Adepoju-Bello and Alabi, 2005). Metals such as zinc, copper, iron, manganese, and chromium are essential nutrients. They are important for the physiological and biological functions of the human body. However, an increase in their intake above permissible limits can lead to toxic effects. The most important heavy metals that humans are exposed to include arsenic, aluminium, cadmium, chromium, cobalt, copper, lead, nickel, zinc and mercury (Okewole and Omin, 2013).

Nickel occurs in the environment at very low levels; however it has some important human applications, such as in jewellery, steel and other metal products (Wilson, 2009). Nickel toxicity is associated with the following health risks: high chances of development of nose cancer, lung cancer, larynx cancer and prostate cancer, lung embolism, respiratory failure, asthma, chronic bronchitis, birth defects, and allergic reactions (Kasprzak *et al*., 2003). Cadmium may accumulate in the kidney on chronic exposure, due to its long biological half-life, and may lead to kidney damage and hypertension (Maduabuchi *et al*., 2006; Akan *et al*. 2010). Lead and mercury are highly harmful metals; high levels of exposure to these metals may result in acute or chronic toxic effects on the nervous system. Lead toxicity is also associated with impairment of brain functions in children and reproductive system in adults (Horowitz *et al*., 2002; Okewole and Omin, 2013). Mercury is linked to abnormalities in foetus during development, as well as reproductive, immune and respiratory toxicity (Adepoju-Bello *et al*., 2012a).

While nickel is essential in very small amounts, cadmium, lead and mercury are toxic to the body, even at low concentration with no health advantage to human body. It has been reported that nearly half of the means of ingestion of cadmium, lead and mercury through food is due to plant origin (Adepoju-Bello *et al*., 2013). Plants are contaminated by these metals through residues in the air, excessive use of fertilizers and pesticides and sewage sludge or irrigation with contaminated water. The World Health Organization (WHO) recommends that medicinal plants which form the raw materials for the finished products be checked for the presence of heavy metals.

Due to the high consumption of antimalarial decoctions in our communities, there is a need to analyse the concentrations of heavy metals in these samples.

Particularly, in Nigeria, many herbal preparations are yet to be enlisted and consequently neither controlled nor regulated. These concerns drive the focus of this research study, which is to determine the amount of lead, nickel, cadmium and mercury in antimalarial decoctions '*Agbo iba*' obtained from selected areas of Lagos in Nigeria.

METHODS

Collection and Pretreatment of Samples:

Four antimalarial decoctions '*Agbo iba*' were purchased within the period of June – September, 2016 from different vendors from four markets: Agege, Berger, Ketu, and Onipanu, in Lagos, Nigeria. The study was verbally explained in detail to the vendors, and informed consents were obtained from them prior to their participation. The vendors provided information about the herbs and other constituents used in the preparations, method of preparations and dosage of the decoctions. The decoctions were filtered twice with cotton wool through a glass funnel into glass beakers. The filtrates were concentrated in an oven at 55ºC and the concentrates were transferred into sample bottles, weighed and stored prior to digestion.

Preparation of the Samples and Standard Solutions of the Metals:

Preparation of the samples was carried out according to the method described by Bakar, *et al.*, (2011) with some modifications. Each decoction concentrate, 1 g, was weighed into a porcelain crucible and heated for 15 min on a hotplate at 55ºC in a muffle. Each crucible was then put in a Carbolite furnace at 500ºC for 2 h for ashing. Concentrated nitric acid, 10 ml, was added to the resultant ash and heated gently on a hot plate until the fumes disappeared for digestion. Then, 5 ml of distilled deionized water was added and heated until a colourless solution was obtained. The mineral solution in each crucible was filtered into a 100 ml volumetric flask and the filtrate volume made to the mark with distilled deionized water. Standard solutions (100 mg/L) of lead (Pb), nickel (Ni), cadmium (Cd) and mercury (Hg) were prepared from their stock solutions (1000 mg/L) and working solutions (0 - 10 mg/L) were prepared by serial dilutions from the standard solutions.

Heavy Metal Analysis:

Determination of Pb, Ni, Cd, and Hg in the samples was made directly on each of the final solution under atomic absorption spectroscopy (AAS), Model – S Series 711438v1:23. The atomic absorption instrument was set up and flame condition and absorbance were optimized for the analyte. For each metal, the instrument

was zeroed with the blank (distilled deionized water), then the standard solutions and sample were aspirated into the flame. The absorbance were obtained and recorded. The calibration curve of the standard solutions of each metal was prepared and used to extrapolate the concentrations of the metal in the samples. The analysis was carried out in duplicates and the concentrations of the metals are presented as mean ± S.D (standard deviation).

RESULTS

Herbs used for the Antimalarial Decoctions

The constituents of the different antimalarial decoctions '*Agbo iba*' are as presented in Table 1. The vendors provided the local names of the different constituent and these were used for their identification with the aid of Odugbemi and Akinsulire (2008).

Table 1: Some constituents of antimalarial decoctions from four locations in Lagos

Common name	Local name	Botanical name	Family	A	B	K	O
Maize mash	*Omi Idun*	*Zea mays*	Poaceae	+	-	+	+
Lemon grass	*Ewe Tea*	*Cymbopogon citratus*	Poaceae	+	-	+	+
Key lime	*Osan wewe*	*Citrus aurantifolia*	Rutaceae	-	-	-	+
Guinea henweed	*Epo Awogba*	*Petiveria alliacea*	Petiveriaceae	+	-	+	+
African peach tree	*Egbo Egbesi*	*Nauclea latifolia*	Rubiaceae	+	+	+	+
Bambara	*Egbo Idii*	*Terminalia avicennioides*	Combretaceae	+	-	-	+
Axle wood	*Epo Ayin*	*Anogeissus leiocarpus*	Combretaceae	+	-	-	-
Serpent wood	*Asofeyeje*	*Rauvolfia vomitoria*	Apocynaceae	+	+	-	-
Henna plant	*Ewe Laali*	*Lawsonia inermis*	Lythraceae	+	-	+	-
Stool wood	*Epo Ahun*	*Alstonia boonei*	Apocynaceae	+	-	+	-
Ginger	*Ata Ile*	*Zingiber officinale*	Zingiberaceae	-	-	+	-
—	*Egbo Ata*	*Zanthoxylum zanthoxyloides*	Rutaceae	-	-	+	-
Tumeric	*Ata ile pupa*	*Curcuma longa*	Zingiberaceae	-	-	+	-
Extra-long staple cotton	*Owu*	*Gossypium barbadense*	Malvaceae	-	-	-	+
Brimstone tree	*Egbo Oruwo*	*Morinda lucida*	Rubiacea	+	+	+	+
Onion leaves	*Ewe Alubosa*	*Allium cepa*	Amaryllidaceae	-	-	+	-
Neem tree	*Dongoyaro*	*Azadirachta indica*	Meliaceae	+	+	-	+
Mango tree	*Epo mangoro*	*Magnifera indica*	Anacardiaceae	-	-	+	-
Bitter gourd	*Tagiri*	*Lagenaria breviflora*	Cucurbitaceae	-	+	+	+
African Mahogany	*Epo Oganwo*	*Khaya grandifoliola*	Meliaceae	-	-	-	+
Bush buck	*Egbo* Madunmarun	*Gongronemia latifolium*	Asclepiadaceae	-	-	-	+
African pepper	*Eru Alamo*	*Xylopia aethiopica*	Annonaceae	+	-	-	-
Tick weed	*Epo Ekundan*	*Cleome viscosa*	Capparidaceae	-	-	-	+
Sapele	Epo Ijebo	*Entandrophragma cylindricum*	Meliaceae	-	-	-	+

Key: + : *Herb was included in the decoction preparation* **− :** *Herb was not included in the decoction preparation*
A*: AGEGE;* ***B****: BERGER;* ***K****: KETU;* ***O****: ONIPANU*

Results of the Atomic Absorption Spectroscopy (AAS) Analysis
The results of the analysis of concentrations of metals in the antimalarial decoctions '*Agbo iba*' from the four locations are as presented in Table 2. Nickel showed the lowest levels (0.185 – 0.338 mg/L) among the metals analyzed, mercury showed the highest levels (1.612 – 17.895 mg/L) and cadmium showed non-detectable level in all the samples.

Table 2: Concentrations of metals in antimalarial decoctions from four locations in Lagos

Sample	**Lead (Pb)** Conc. (mg/L)	**Cadmium (Cd)** Conc. (mg/L)	**Nickel (Ni)** Conc. (mg/L)	**Mercury (Hg)** Conc. (mg/L)
AGEGE	0.896 ± 0.013	ND	0.185 ± 0.005	5.378 ± 0.011
BERGER	0.472 ± 0.002	ND	0.292 ± 0.003	17.895 ± 0.007
KETU	0.331 ± 0.043	ND	0.338 ± 0.011	1.612 ± 0.002
ONIPANU	0.666 ± 0.008	ND	0.331 ± 0.002	9.149 ± 0.020

Values are mean ± S.D. (n=2). ND**:** not detected

DISCUSSION
The historic role of medicinal plants in the treatment and prevention of diseases and their importance as sources of lead molecules in drug discovery and development cannot be challenged. However their benefits, poor standardization and inadequate safety measures have led to their limited value as well as hindrances to their full acceptance in the international health market especially those herbal preparations from developing countries like Nigeria. Studies have also reported that plants and herbs can accumulate heavy metals and other environmental pollutants like pesticide residues (Saad *et al*., 2006). Therefore, determination of heavy metals contents in herbs is regarded as an important measure for assessing their safety and toxicity. To this effect, the concentration of four heavy metals with health implication; lead (Pb), nickel (Ni), cadmium (Cd), and mercury (Hg) were investigated in antimalarial decoctions popularly known as *Agbo iba* purchased from four different market locations in Lagos State, Nigeria; Agege, Berger, Ketu, and Onipanu using Atomic Absorption Spectroscopy (AAS).

Information regarding the herbs used, their sources, methods of preparation and dosages was gathered from the vendors of the antimalarial decoctions. The

constituents of the different decoctions are as presented in Table 1, which show that certain herbs are commonly used. These include *Nauclea latifolia*, *Petiveria alliacea*, *Cymbopogon citratus*, *Morinda lucida*, *Azadirachta indica*, *Lagenaria breviflora*, which have been reported to have antimalarial properties. Another important constituent present in *Agbo iba* is *Omi idun*: aqueous extract of fermented maize (*Zea mays*) which is believed to enhance the efficacy of the decoction. The consumers were advised to take one cup 2-3 times daily for 3-5 days. Among these consumers are market sellers, bus drivers and conductors in public garages and their family members who rely solely on these alternative medicines for treatment of ailments due to their affordability and availability compared to the conventional medicines.

The results of heavy metals concentrations in the antimalarial decoctions showed lead (Pb) concentration as 0.896 ± 0.013 mg/L, 0.472 ± 0.002 mg/L, 0.331 ± 0.043 mg/L and 0.666 ± 0.008 mg/L for samples from Agege, Berger, Ketu, and Onipanu respectively as presented in Table 2. These values exceeded the permissible limit, 0.01 mg/L, according to WHO and Nigerian Industrial Standard (NIS). Lead has been reported in herbal products around the world. Sarpong and Boateng (2013) reported lead levels between non-detectable amount (ND) and 0.830 mg/L in some traditionally used unregistered herbal drugs sold in Kumasi, Ghana. Lead concentrations were found in the ranges of 3.26 – 30.46 ppm and 0.125 – 4.79 ppm in herbal medicine samples studied in Pakistan and China respectively (Hina *et al*., 2011; Qi and Huirong, 1998). Lead has been reported to be one of the highly toxic environmental pollutants. It is a non-essential trace element; having functions neither in human's body nor in plants. In human, lead is mainly accumulated in the nervous system and can complex with various biomolecules; exerting multi-systemic toxic effects by inhibiting enzyme activities, interfering with the action of essential cations and altering the structure of cell membranes and receptors (Kosnett, 2014; Johnson, 1998; ATSDR, 2007; Eibenstenei *et al*., 2005).

Results of concentration of nickel in the samples from Agege, Berger, Ketu, and Onipanu are reported thus; 0.185 ± 0.005 mg/L, 0.292 ± 0.003 mg/L, 0.338 ± 0.011 mg/L and 0.331 ± 0.002 mg/L respectively as given in Table 2. These values obtained from the samples are above the permissible limit, 0.02 mg/L, by WHO and NIS. Nickel has been reported in different herbal products. Yap *et al*. (2018) reported nickel levels between below detection limit (BDL) and 54.5 ppm in 20 Traditional Chinese Herbal Medicines bought from shops in Malaysia. Nickel was found in concentration ranges of 0.2 – 56.3 ppm and 0.48 – 76.97 ppm

in two different studies on selected herbal products in Pakistan (Saeed, 2010; Hina *et al*., 2011). Generally, nickel toxicity in human is not a very common occurrence. However, the most common ailment reported of nickel is an allergic dermatitis known as nickel itch, which usually occurs when skin is moist (ATSDR, 2005). Nickel has also been identified as a suspected respiratory tract carcinogen and adversely affects lungs and nasal cavities (IARC, 1990). On the other hand, in plants, it has been reported that nickel regulates mineral metabolism, enzyme activity and several other metabolic processes. In a controlled concentration, nickel can be used as a fungicide but at high concentrations, it has a well-known toxic effect to the germination of some seeds, causes mitotic disturbances in root tips of some plants, severe chlorosis and necrosis and a host of other growth abnormalities and anatomical changes (Abu Bakar and Bhattacherjy, 2012).

Results of mercury concentration were; 5.378 ± 0.011 mg/L, 17.895 ± 0.007 mg/L, 1.612 ± 0.002 mg/L and 9.149 ± 0.020 mg/L for the samples from Agege, Berger, Ketu, and Onipanu respectively as presented in Table 2. These values exceeded 0.001 mg/L, the permissible limit by WHO and NIS for mercury. Adepoju-Bello *et al*. (2012b) reported mercury levels in the range of 0.014±0.005 – 0.076±0.004 ppm in 20 herbal products manufactured in Nigeria. In a similar study, Yu *et al*. (2017) found no detectable mercury in 155 different traditional herbal decoctions marketed in Korea. It has been reported that accumulation and exposure to high levels of mercury can permanently damage the brain, heart, kidneys, lungs, and developing foetus (Maobe *et al*., 2012).

Nevertheless, cadmium was not detected in any of the four samples. The WHO and NIS maximum permissible cadmium concentration for Standard Drinking Water is 0.003 mg/L. Cadmium concentration was found to be between non-detectable amount (ND) and 1.012 mg/L in a study by Sarpong and Boateng (2013) on some unregistered herbal drugs in Ghana. Similarly, cadmium concentration was reported to be between non-detectable amount (ND) and 219.0 µg/kg by Yu *et al*. (2017) in different herbal decoctions in Korea. Musa and Hamza, (2009) reported cadmium concentration in the range of 16.438 – 29.796 mg/g in herbal drugs used in Zaria, Nigeria. In Pakistan, cadmium was detected in 25 branded herbal products in a concentration range of 1.9 – 45.2 ppm (Saeed, 2010). Cadmium has been known to cause acute poisoning typical of severe irritation of the gastrointestinal epithelium symptoms characterized by vomiting, nausea and abdominal pain (ATSDR, 2012), while chronic exposure may lead to

renal injury, obstructive pulmonary diseases, osteoporosis, altered levels of reproductive hormones and cardiovascular diseases (Akinloye *et al*., 2006).

Efforts and resources to improve the malaria control programs have increased in Nigeria, where the burden of malaria is greatest in Africa mainly due to the large population. This same reason, inadequate supply of aids and reliefs by local, national and international governmental and non-governmental organizations, and the country's economic predicaments have resulted in many people increasingly resorting to the alternative herbal system for primary health care.

Nonetheless, contamination of herbal medicines by heavy metals is of major concern because of the toxicity and bioaccumulative nature of such metals. Even though WHO has formulated guidelines for quality assurance and controls of herbal medicines, traditional practitioners lack enough knowledge, guidance and expertise to handle such health contaminants. Four heavy metals; Pb, Cd, Ni, and Hg concentrations were investigated in samples collected from four locations in suburban area of Lagos State and results showed that Pb, Ni and Hg levels exceeded the permissible limits in the antimalarial decoctions. This contamination may be from plant/herb growing site, soil, harvesting, during preparations such as sources of water, storage and transportation. It is imperative that everyone involved in alternative herbal medicine should be concerned not just in the efficacy of these herbs but much importantly to be more sensitive to heavy metals contamination among other risk contaminants in order to improve the general quality and safety of these herbal medicines.

CONCLUSION

This research study was carried out to investigate the presence of some heavy metals, Pb; Ni; Hg; and Cd, of health risk in antimalarial decoction popularly known as *Agbo iba*. Findings showed that three heavy metals concentrations, Pb; Ni; and Hg, were not within the permissible limits recommended by WHO and NIS while Cd was not detected in any of the four samples. This study recommends safety, standardization, hygiene and good production practices (HGPP) during the cultivation, collection, transportation, preparation, consumption and storage of herbal products. It is evident also, that there is a need to enforce a regular monitoring scheme by health regulatory bodies to ascertain the quality of the local herbs and herbal preparations sold across Lagos and entire country, Nigeria.

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