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# Investigating some Selected Heavy Metals and Micronutrients Levels in Herbal Preparation Marketed in Nigeria: A Pilot Study

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***Authors' contributions***

*This work was carried out in collaboration between all authors. Author AAO conceptualized and designed the study, developed the protocol, managed literature search, drafted and managed manuscript revision. Authors IOO and ARS finalized study concept reviewed the manuscript and contributed to the final draft. All authors read and approved the final manuscript.*

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## ABSTRACT

**Background:** The use of herbal remedies has become a global practice. The role of several inorganic elements in the maintenance of normal body metabolism has been documented. Previous studies examining trace metals content of approved herbal preparations have focused mostly on heavy metals with little or no attention given to micronutrients. A pilot study on selected trace metal and micronutrient constituents of one of the herbal products regularly consumed by the populace was conducted to bridge this gap.
**Methods:** A well known herbal product Yoyo bitters (YYB) was purchased from one of the pharmaceutical shops within the Metropolis. As an inclusion criterion, the product was ascertained to have been registered with the National Agency for Food, Drug Administration and Control (NAFDAC). The manufactured and expiry dates of the products were inspected and all were

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confirmed to be within the acceptable time frame. In all, fifteen (15) bottles of the product, each containing a 100 ml of syrup were purchased and levels of Iron, Copper, Zinc, Lead and Iodine were determined using standard method. Data obtained were compared with United States Environmental Protection Agency (USEPA) and the World Health Organization (WHO) recommended allowable intake for these metals.

**Results:** Showed that the selected herbal remedy contained mean (±SD) levels of: Iron 12600 (350) µg/L); Copper 200 (0) µg/L); Zinc 300 (0) µg/L); Lead 400 (10) µg/L) and Iodine 145500 (3560) µg/L respectively.

**Conclusion:** While the herbal product investigated contained allowable levels of copper and lead, high levels of iodine and iron were detected. This might imply that iodine and iron toxicities could be a likely adverse effect associated with the use of this product. The need to exercise caution to avoid possible Iodine and Iron overload due to excessive consumption of this herbal product was highlighted in this work.

*Keywords: Herbal Medicine; microelements; heavy metals; yoyo bitters; toxicity.*

## 1. INTRODUCTION

Medicinal plants constitute a source of raw materials for both traditional and modern medicine [1]. Globally, traditional medicine has been accepted as one of the ways that individuals seek remedies to all kinds of medical problems ranging from simple headache to severe and terminal disease such as cancer. As a result of the wide usage of herbal medicine, it has contributed greatly to the growth of the global pharmaceutical market [1]. Herbal remedies consist of portions of plants or unpurified plant extracts containing several constituents, which often work synergistically to produce a desired effect. As a result of poverty, high cost of modern medicine, inaccessible medical facilities, inequalities in health distribution and limited access to modern medicine, about 80% of the world's population living in developing countries use herbal medicine as their source of primary health care [1,2]. In spite of the benefits associated with herbal remedies, their use has been associated with some concerns. One of such is that most remedies contain more than one plant constituents. The presence of more than one constituent in most herbal remedies could demonstrate a synergistic effect or elicit a deleterious effect when drugs interact between each other (pharmacokinetics) and between the body systems (pharmacodynamics).

Heavy metals such as lead (Pb) and mercury (Hg) are natural constituents of the environment-like air, water and soil. They are produced by human and industrial processes and thus have gained importance as contaminants within the environment [3]. Medicinal plants growing in nature can accumulate heavy metals to a certain extent depending on their individual properties, the concentration of heavy metals within the environment, the nature of air and water where they are grown. As heavy metals and other micro elements could pose a hazard to human and animal health, the level of heavy metals in medicinal plants used for the formulation of herbal medicine should be limited. For this reason limits for heavy metals and several other micro elements have been set for foodstuffs and medicinal products by different regulatory authorities and agencies [3].

The roles played by heavy metals and micro elements in the physiological functions and metabolism within the body cannot be overemphasized. Zinc for instance is highly essential in membrane function, while iodine is indispensible in the maintenance of the physiological function of the thyroid gland. In spite of the physiological benefits associated with some heavy metals and micro elements, excessive heavy metals contamination of herbal medicines has been widely reported. Adepoju et al. [4] investigated the concentration of heavy metals in some registered herbal remedies purchased from some pharmaceutical shops. The study showed that of all the samples analyzed, lead was not detected in any of the samples, but there were significant levels of cadmium, mercury and arsenic which were well above the recommended oral component limit (OCL). Acceptable report by the Harvard Medical School [5], revealed that 14, out of 70 herbal products (HPs) approved for public use contained lead, mercury and /or arsenic. Each of the 14 HMPs could result in heavy metal intake above the acceptable limits. The authors also observed that several of the herbal medicine products studied were recommended for use in

children and that 80% of the stores sold one or more HMPs containing significant amounts of heavy metals. In all, several studies performed on the metal contamination of registered herbal products have focused majorly on heavy metals with little or no attention to other micronutrients which could also be able to precipitate some health challenges when consumed in excess. This study was therefore designed to increase the level of information in this specialty.

## 2. MATERIALS AND METHODS

### 2.1 Selection of Herbal Products

The herbal product, YYB was purchased from a registered pharmaceutical shop. The product was a combination of several medicinal plants. As an inclusion criterion, the product was ascertained to have been registered with the National Agency for Food, Drug Administration and Control (NAFDAC). The manufactured and expiry dates of the products were inspected and all were confirmed to be within the acceptable time frame. The manufacturer's seal was also confirmed in the products purchased as a confirmation for the authenticity of the product. In all, we purchased fifteen bottles of the product, each containing a 200 ml of syrup. These were used for the required laboratory analysis.

### 2.2 Analysis of Trace Elements and Micro Nutrients

#### 2.2.1 Digestion process and analysis

10 ml of sample was pipetted into a conical flask. This was followed by the addition of 10 ml mixture of Nitric ($HNO_3$) and Hypochloric ($HOCL_3$) acids in the ratio of 2:1 into each of the pipetted samples. This mixture was allowed to digest until a clear fume was attained. The digested samples were allowed to cool, washed into a 25 ml standard volumetric flask and the volume made up to the mark (25 ml) with distilled water. A blank sample was treated the same way, but without any samples. The concentration of elements (Pb, Cu, Zn, Fe and I) present in the digested samples were analyzed using Atomic Absorption Spectrophotometry (AAS, Bulk Scientific, Model Buck 201VGP). The instrument was calibrated using the appropriate standard and the hallow cathode lamp (HCL) of respective element. In order to ensure analytical precision, the measurement of micro and macro elements were made five (5) times. The Mean ± Standard Deviation (±SD) of the values obtained were expressed first in mg/dl, then in µg/L of drug sample.

## 3. RESULTS AND DISCUSSION

The Mean (±SD) µg/L values of Fe, Cu, Zn, Pb and I obtained after the analysis are presented in Table 1.

Trace elements and micronutrients though found in very small concentrations in tissues and body fluids, yet they do play very crucial roles in normal body metabolism. Their deficiency or excess in body concentration could precipitate numerous medical abnormalities. Based on the importance associated with different micronutrients, recommended daily amounts (RDAs) of all micronutrients have been adopted. Recommended Daily Allowances are the lowest levels required in order to prevent obvious pathology.

Zinc is versatile in all living organisms. It has been known to play an important metabolic role in all human metabolic activities; and is a well known cofactor to numerous body enzymes including insulin. Abnormal levels of zinc have been implicated in infertility, diabetes mellitus, poor wound healing, decreased immune response and other metabolic disorders. Findings from this study showed that the herbal product contained a higher level of Zinc (300 µg/L) more than the EPA/WHO recommended level (100 µg/L). One of the medicinal plants used for the formulation of this herbal product was Aloe vera. This plant is very rich in zinc, copper, iron and selenium. It is possible that the elevated levels of zinc observed from this study could be attributed to the Aloe vera contained in the herbal product. In spite of the beneficial functions attributable to zinc, high intake of zinc inhibits absorption of copper by inducing production of metallothionein [8]. Metallothionein has been known to protect the body against metal toxicity, regulates the physiological levels of copper and zinc; and protects the body against oxidative stress [8]. Although zinc has been shown to play important physiological roles in the general metabolism such as boosting immune response and wound healing, yet excessive intake of zinc higher than the RDA could interact with the physiological metabolism of other trace elements thereby precipitating adverse metabolic consequences.

**Table 1. Mean Values of micronutrient contents of herbal products as compared with the USA Environmental Protection Agency / WHO Recommended Allowable Intake [6,7]**

| | Fe | **Cu** | Zn | Pb | I |
|---|---|---|---|---|---|
| Mean (±SD) in µg/L | 12600 (350) | 200 (0) | 300(0) | 400(10) | 145500(3560) |
| EPA/WHO Level (µg/L) | 300 | 500 | 100 | 2000 | 150 |

Aloe vera is a rich source of many enzymes such as catalase, alkaline phosphatase, bradykinase among others [9]. Copper and Zinc are cofactors for these enzymes. It could be postulated that increased consumption of this herbal product, could result in more supply of these micronutrients. Increased supply of these micronutrients could result in increased catalytic activities of these enzymes thus culminating in producing the desired effects. One of the medical benefits attributed to this herbal product is its strong ability to scavenge for free radicals via its antioxidant property [10]. High concentration of zinc in the herbal product might elevate the antioxidant properties of zinc on metabolic processes. Zinc is a known cofactor for glutathione reductase and superoxide dismutase thus enhancing their antioxidant capabilities.

Iodine is an essential micronutrient for all species of animals including humans. It is a chemical element like oxygen, hydrogen and iron. It occurs in a variety of chemical forms, the most important being iodide ($I^-$), Iodate ($IO_3^-$) and elemental iodine ($I_2$) [11]. Iodine is generally distributed in major food items including dietary products. Iodine is an essential micronutrient required by the body. It is a component of thyroid hormones: thyroxine ($T_4$) and tri-iodothyronine ($T_3$), which in turn regulates general body metabolism. From the data obtained from this study, it showed that the herbal product contained excessive iodine (145500 µg/L) more than the allowable recommended consumption of 150 µg/L [11]. This amount, in addition to that consumed from other sources could predispose the users of this product to serious metabolic consequences such as iodine induced hyperthyroidism (IIH). Iodine-induced hyperthyroidism (IIH) has been reported as the main complication of iodine prophylaxis and excessive consumption of iodine [12]. In iodine deficiency, the proliferation and mutation rate of thyrocytes are increased. This in turn makes the cell to secrete auto antibodies and TSH- secreting cells. Excessive supply of iodine to the thyrocytes enhances auto production of thyroid hormones causing Iodine Induced Hyperthyroidism. In countries where iodine deficiency disorders have existed, supplementation with iodine had been reported to accelerate IIH [12].

Furthermore, recent studies [13] have shown that iodine although essential for the synthesis of thyroid hormones and maintenance of hormonal balance, yet it has been reported that breast tissues require as much iodine for their normal function as deficiency results in fibrocystic disease of the breast which could ultimately result in breast cancer. It has been reported that countries with highest consumption of iodine had the lowest risk of breast cancer [14]. It could be possible that the high content of iodine in the investigated herbal product might be responsible partly for the cancer curing claims ascribed to the product. Nevertheless, further studies are required to elucidate the relationship between the use of this herbal product, its high iodine content and the pathology of breast cancer.

Iron is essential for virtually every living thing, including humans. It is a key part of various proteins and enzymes involved in the transport of oxygen and the regulation of cell growth and differentiation. It is a major constituent of heme, an essential component of hemoglobin, a blood transport protein through which oxygen is carried throughout the body system. The findings from this study showed that the herbal product contained a higher amount of iron (12600 µg/L) much higher than the EPA recommended levels (300 µg/L) [15].

Aloe vera is an essential component of this herbal product. One of the major chemicals contained in Aloe vera is iron. This could be responsible for the increased level of iron observed in the study.

Iron is an extremely reactive metal and it does facilitate oxidative changes in lipids, proteins and other cellular components. The ferrous ($Fe^{2+}$) state of iron has been known to accelerate lipid oxidation by breaking down hydrogen and lipid peroxides to reactive free radicals via the Fenton reaction pathway ($Fe^{2+} + H_2O_2 \longrightarrow Fe^{3+} + OH + O$). The excessive free radicals generated via this pathway could precipitate several and adverse medical consequences

within the body system. Although iron is essential for normal body metabolism, yet high iron levels in blood could result in the production of free radicals which in turn could deplete the body's reserve for antioxidant including metal anti oxidants such as zinc and copper, which are essential components of anti oxidant enzymes such as super oxide dismutase and glutathione reductase.

Excessive consumption of iron has been linked to the pathogenesis of Alzheimer's disease; as excessive accumulation of iron in the brain is a consistent observation in patients with Alzheimer's disease [16]. It is believed that increased plasma iron in the circulation could result in the accumulation of iron which is extremely reactive with the beta-amyloid plaques found in the brains of Alzheimer's patients [16,17]. Recent studies in animals have shown that lowering blood levels of iron triggered reduced levels of beta-amyloid and phosphorylated tau protein, which disrupts the ability of neurons to conduct electrical signals to return to normal; thus limiting the risk of Alzheimer's disease [17,18,19]. Based on the relationship between excessive plasma iron and the aetiology of Alzheimer's disease, it is possible to postulate that older subjects who consume this herbal product could be predisposed to the development of Alzheimer's disease. Further studies are therefore required to elucidate this assumption.

Current studies have shown that the herbal product contained about 42 fold of iron more than zinc and copper. This could have a deleterious effect in metal-metal interaction in vivo. Several studies have investigated the interactions between iron and other micronutrients especially zinc when given together in a solution [8,20]. In all, the studies have shown that high concentrations of iron could have a negative effect on zinc absorption in human adults when the zinc and iron are given in solution.

Lead has no known physiological role in the body system, but it is regarded as a highly poisonous chemical when found in excess in the body system. The level of lead detected in this herbal product was within the EPA/WHO recommended limit. This study was consistent with the findings of Adepoju et al. [4] who measured levels of lead in some of the herbal products approved and marketed in Nigeria and reported that their lead content was within the WHO allowable limits. High concentrations of lead are harmful to the environment and the human populace.

## 4. CONCLUSION

From this study, it was evident that the investigated herbal product contained allowable levels of copper and lead, but higher levels of iron and iodine. This could imply that possible iodine and iron toxicities could be associated with heavy use of this herbal product. Excessive consumption of iodine and iodine-containing products has been associated with the development of Iodine Induced Hyperthyroidism (IIH). As with all herbal products, caution should be taken to avoid excessive intake of these micronutrients.

## CONSENT

It is not applicable.

## ETHICAL APPROVAL

It is not applicable.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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