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I.B Bwatanglang & T.S Magili

ABSTRACT

In this study, the longtime dietary exposure of insulin supporting elements in anti-diabetic plants are investigated with a view to establish their essentiality in the management of diabetes mellitus (DM) and potential health risk on consumption. Ten anti-diabetic plants were analyzed for manganese (Mn), iron (Fe), Cobalt (Co), chromium (Cr), zinc (Zn) and vanadium (V) using instrumental neutron activation analysis (INAA) and their respective concentrations were used to estimate their daily intake (EDI) levels. The EDI of Mn was found to be above the reference dose (RfD) of 0.014 mg/kg/day. The highest EDI was found in Hymenocardia acida (HA) (40.43 mg/kg/day). The EDI for Fe shows Ageratum conyzoide (AC) containing the highest EDI of 84.42 mg/kg/day. This value in addition to the EDI of the other species all falls above the RfD for Fe (0.007 mg/kg/day). The EDI for Co in most of the anti-diabetic plants investigated falls below the RfD levels (0.03 mg/kg/day) except for Jatropha gossypiifolia (JG) (0.603 mg/kg/day), Sarcocephalus latifolius (SL) (0.855 mg/kg/day) and Sclerocarya birrea (SB) (0.472 mg/kg/day) respectively.

Keywords: anti-diabetes. trace elements. risk assessment. estimated daily intake. target hazard.

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ABSTRACTS

In this study, the longtime dietary exposure of insulin supporting elements in anti-diabetic plants are investigated with a view to establish their essentiality in the management of diabetes mellitus (DM) and potential health risk on consumption. Ten anti-diabetic plants were analyzed for manganese (Mn), iron (Fe), Cobalt (Co), chromium (Cr), zinc (Zn) and vanadium (V) using instrumental neutron activation analysis (INAA) and their respective concentrations were used to estimate their daily intake (EDI) levels. The EDI of Mn was found to be above the reference dose (RfD) of 0.014 mg/kg/day. The highest EDI was found in Hymenocardia acida (HA) (40.43 mg/kg/day). The EDI for Fe shows Ageratum conyzoide (AC) containing the highest EDI of 84.42 mg/kg/day. This value in addition to the EDI of the other species all falls above the RfD for Fe (0.007 mg/kg/day). The EDI for Co in most of the anti-diabetic plants investigated falls below the RfD levels (0.03 mg/kg/day) except for Jatropha gossypiifolia (JG) (0.603 mg/kg/day), Sarcocephalus latifolius (SL) (0.855 mg/kg/day) and Sclerocarya birrea (SB) (0.472 mg/kg/day) respectively. Furthermore, all the EDI recorded for chromium (Cr) in the respective anti-diabetic plants falls below the RfD (1.5 mg/kg/day) levels except in Sarcocephalus latifolius (LH) (8.66 mg/kg/day). The EDI for Zn in all the respective anti-diabetic plants were found to be above the RfD (0.30 mg/kg/day). The results shows the highest EDI of 2.43 mg/kg/day in Balamites aegyptiacae (BA). Furthermore, the highest EDI for V was found in the extract of SL (0.673 mg/kg/day. However, not all the anti-diabetic plants shows a target hazard quotient (THQ) value less (<1) than one. A THQ greater (>) than one for Cr was observed in LH (12.95). The health index (HI) further shows a high level of concern in LH (13) and in JG (1.36) due to the cumulative effects of the respective metals. Based on the THQ and HI values, it will suffice to conclude that these plants are more or less considered safe for human consumption except from Cr in LH whose THQ and HI values signal potential health risk.

Keywords: anti-diabetes. trace elements. risk assessment. estimated daily intake. target hazard quotient.

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I. INTRODUCTION

Plants are nature-based pharmaceutical laboratory containing active ingredients of great medicinal importance. They are often utilized locally in complementary medicine, with at least 80% of the world population especially in the developing economy exploring its benefits in the primary healthcare services [1]. The renaissance of herbal-based remedy was estimated to account for approximately 25% of pharmaceutical drugs and nearly 60% of anticancer drugs [2, 3]. These unquantifiable benefits has generated entrepreneurship in family-based health care systems, busting the herbal-based rural market and increasing the global trade volume of plant-based pharmaceutical products and other plant-based dietary supplements [4]. These development is expected to expand the global market for plant-based health products to about

$60 billion annually, projected to be driven in part by consumer preference for nature-based materials that are sustainable and affordable [1].

In Nigeria today, one common disease that present it ugly face in both the rural and urban settings is DM which according to the International diabetes federation (IDF), recorded a prevalence rate of 3.9% for Nigeria [5] and projected to take the 7th position in global dead related diseases by 2030 [6-8]. Diabetes mellitus and its related complications is estimated to reach $592 million by 2035, going at a global prevalence rate of 10.1% and is projected to push the global cost of interventions/treatments to about $490 billion by 2030 [5,10]. These scary statistic is projected to grow exponentially considering the poor implementations of government healthcare intervention policies and the corresponding high cost of orthodox medicine [1]. These systemic decay, forces a shift and emphases into plant-based therapy for the treatment and management of DM and its related complications in Nigeria. This however, leads to massive explorations of plants species with active biological components that can support and potentiate insulin metabolism. Thus, the hypoglycemic properties of medicinal plants, in addition to being actively supported by some phytochemicals are also potentiated by some essential micro and macro elements housed within the plants [11, 12].

Using instrumental neutron activation analysis (INAA), we reported in our previous study the presence of some macro elements, micro elements, trace element and some natural radioactive elements in anti-diabetic medicinal plants commonly consumed in Adamawa state, Nigeria [13,14]. And further bring into fore, the elemental bioaccumulation trends in relation to the soil-plant interactions and relates same to the physiochemistry of the elements towards insulin metabolism [15]. The bioavailability of the elements based on the elemental content preponderance was further developed and presented based on elemental hierarchal decision tree to further provide guides on the associated risk that may arise from a particular plant species or plant tissue in the treatment and management of DM [16]. Despite the fact that traditional-based medicine may have fared well within the ambit of Nigeria's home-grown Medicare, the deteriorating condition of the country's healthcare system visa vice lack of standards in herbal-based remedies remains a potential risk requiring serious attention.

Though, the following elements Ca, Mg, Co, Cr, Mn; Zn, and V, found in the anti-diabetic plants were reported to play a bioactive role in potentiating insulin metabolism as presented in our previous studies [13, 14], the complexity and physiochemical interactions of the elements with the biological systems in relations to the degree/or durations of exposure could introduce certain degree of doubt as regards to their safety. Thus, it's imperative that medicinal plants use in herbal preparations for human consumption are filtered through quality-health standards checklist. Such exercises will improve consumer confidence and boost the competitiveness of the market. To support the rising popularity of herbal-based remedies in the primary healthcare services for the management of DM and its complications, human health risk assessment of some insulin supporting trace elements (Fe, Co, Cr, Mn; Zn, and V) found in the anti-diabetic medicinal plants commonly consumed in Adamawa state, Nigeria is conducted and presented in this study. The study is narrowed down to investigate the long time dietary exposure of the above mentioned insulin supporting elements that may arise from the consumption of these medicinal plants. Due to the ubiquitous nature of the essential elements, it's often difficult to present a clear picture and establish a balance between its essentiality and toxicity in risk assessments processes. However, this study is conducted bearing in mind this extreme variations with the view to narrow down the variations to a level were the dietary intake of the anti-diabetic plants presents a likelihood of safety or caution in situations where potential risk may suffice.

II. MATERIALS AND METHODS

2.1 Sampling and Sample Preparations

The following anti-diabetic plants commonly consumed in Adamawa State, Nigeria are used in this study: *Terminalia avicennioides (TA), Hymenocardia acida (HA), Leptadenia hastate (LH), Balamites aegyptiacae (BA), Ageratum conyzoide (AC), Sclerocarya birrea (SB), Anogeissus leiocarpus (AL), Jatropha gossypiifolia (JG), Daniellia oliveri (DO), and Sarcocephalus latifolius* (SL). The plants species are collected from Mubi North, Mubi South and Maiha Local Government Areas of Adamawa State, Nigeria. The dried powdered samples of the plants were respectively heat-sealed and processed following the same methods adapted in our previous work [13].

2.2 Elemental Analysis of the Anti-diabetic Medicinal Plants using INAA

The elemental analysis was conducted using the Nigerian Research Reactor-1 (NIRR-1) facility at the center for energy research and training ABU Zaria. The following reference material SRM NIST-1547 (Peach leaves), and NIST- 1515 (Apple Leaves), were used for quality control test and quantitative analyses. Following the various irradiation regime, the retrieved irradiated samples were then collected for the identification of various elements using gamma ray spectrum analysis software (WINSPAN 2004) [13].

2.3 Health Risk Characterization

For the health risk assessments, the average estimated daily intake (EDI) of the elements was obtained by drawing out a relationship between the metals concentrations in the plants, the average consumption of herbal remedy in Nigeria with the respective body weight using the USEPA recommended procedure described in equation 1 [17,18].

$$EDI = C\frac{F_{IR}}{W_{AB}}\ldots \qquad (1)$$

Where, EDI is the average daily intake (mg/kg body weight/day); C is the concentration of the elements in the medicinal plant; F_{IR} is the daily consumption rate for herbal medicines consumed by the people. Though, the estimation of the exact amount of each herb used traditionally varied from species to species, as well as dosage and by practitioners, an arbitrary value based upon daily consumption of 3 g were thus considered in this study. The W_{AB} is the body weight (kg); set at 60 for an average adult.

Furthermore, target hazard quotient (THQ) as described in equation 2 was used to determine the human health risk posed by the long-time exposure to the elements following the consumption of the herbal medicines

$$THQ = \frac{C \times F_{IR} \times EF \times ED}{BW \times AT \times RfD}\ldots \qquad (2)$$

Where, C is the concentration of the elements in the medicinal plants (mg/kg); F_{IR} is the medicinal plant consumption rate for the respective anti-diabetic plants. EF is the exposure frequency (365 days/year); ED is the exposure duration (70 years); BW is the body weight in kg; and AT is the average time for non-carcinogens (365 days/year × exposure durations). For the study, the oral reference doses (RfDs) of 0.007, 0.009, 1.5, 0.03, 0.30 and 0.014 mg/kg/day were adopted for Fe, V, Cr, Co, Zn, and Mn respectively [19-22]. The description hypothesis a THQ less than 1 to signify no associated risk, meaning the exposed population is unlikely to experience any adverse health hazard. However, if the THQ is equal to or greater than 1, then there is a potential health risk associated [22], thus, calls for concern and interventions.

The health index (HI), expressed as the sum of the hazard quotients THQ as described in equation 3 is used in this study to describe the cumulative effect posed by the combination of the individual metal presents in the medicinal plants. Thus, the greater the value of HI, the greater the level of concern. [17, 18].

$$HI = \Sigma THQ \qquad (3)$$

VI. RESULTS AND DISCUSSION

4.1 Concentrations of insulin supporting elements in the anti-diabetic plants

The average mean concentration of the insulin supporting trace elements Mn, Fe, Co, Cr. Zn and V in the anti-diabetic medicinal plants are presented in Fig 1-3. From the result in Fig.1, the highest concentrations of Mn (808.53±5.00 mg/kg) was found in HA, while the least concentration is recorded in the extract of AL (36.43±0.20 mg/kg). The concentrations follows the ranking HA>AC>DO>TA>JG>LH>SB> BA>SL>AL respectively. The concentration of Mn points directly to its essentiality as a macro elements, a very important insulin supporting elements, a known activator of gluconeogenic enzyme, known also to modulate glucose transport across cell membranes and improve its tolerance under conditions of dietary stress, [23,24].

The availability of Fe content in the respective medicinal plants shows AC containing the highest concentration (1728.33±67.67 mg/kg), while the least concentration (167.33±38.68 mg/kg) was recorded in the extract of HA. The order of availability based on the concentrations follows the ranking AC>BA>JG>LH>SL>AL>TA>SB> DO>HA respectively. Iron is necessary for red blood cell formation and required for transport of oxygen throughout the body and very important for brain function. Apart from being an essential component of hemoglobin, Fe facilitated the oxidation of carbohydrates, protein and fat to control body weight; needed in the reduction of obesity, a component of DM [25]. The uptake of Fe is physiologically stimulated to allow the metallation of enzymes and electron carriers required for oxidative metabolism [26].

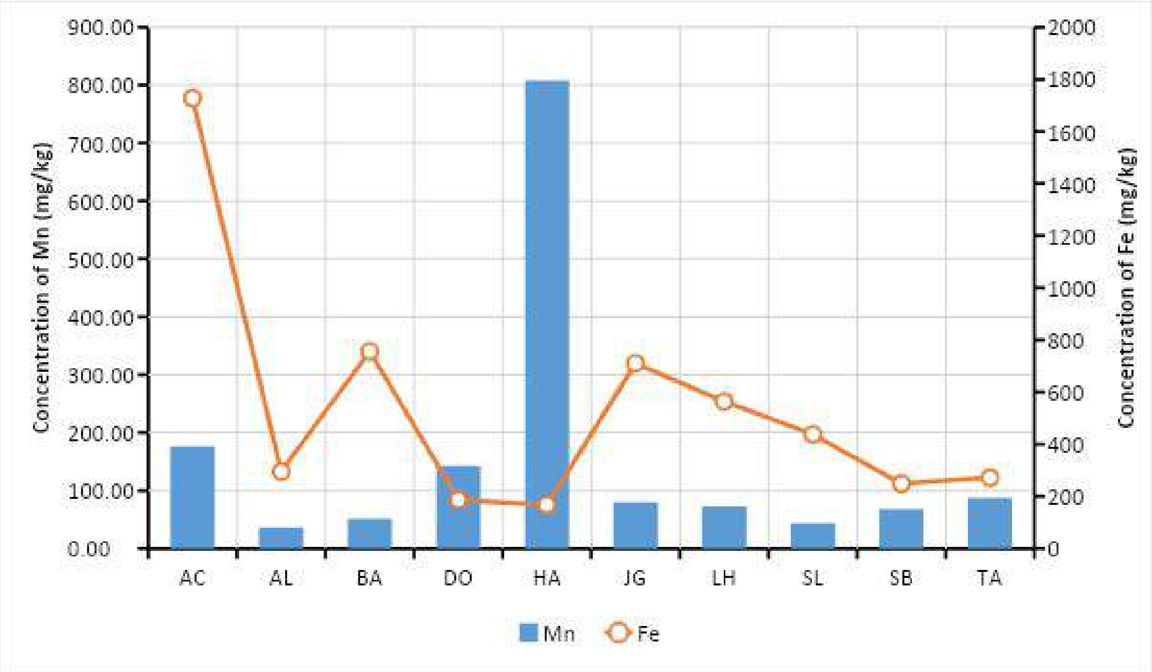

Fig. 1: Average Mean Concentration of Manganese (Mn) and Iron (Fe) in the Anti-diabetic Medicinal Plants. The results are presented as Mean± SD of three replicate analysis

Further analysis of the respective plants species for Co shows higher concentrations of 17.10±2.37 mg kg in the extract of SL follows by 12.06±2.33 mg/kg in JG and 9.43±1.37 mg/kg in SB respectively. Based on the results in Fig 2, the concentrations of Co was found to follow the ranking, SL>JG>SB>AC>AL>TA>BA>HA>LH respectively. Cobalt was reported to possess a glycemia-lowering effect, lowering glucose synthesis and reciprocally increase its cellular uptake. Such cobalt metabolic action were also reported to enhanced the expression of glucose transporter 1 (GLUT1) and inhibition of gluconeogenesis [27, 28]. In addition to the glycemia-lowering effect, Co was also implicated in the observed decrease in lipid peroxidation in diabetic rats [29]. Furthermore, with the exception of AL and BS whose concentrations falls below the detection levels (BDL), the concentration of Cr in the medicinal plants as presented in Fig.2 shows LH containing the highest concentrations (172.67±18.33 mg/kg), while the least values was observed in TA (0.07±0.03 mg/kg). Based on bioavailability, the concentrations of the element in the respective plants species falls in this order, LH>JG>HA>AC>SL>BA>DO>TA. Studies have shown that Cr is an important cofactor that regulate and potentiates the action of insulin, facilitate the cellular uptake of glucose and in the process facilitate in lowing the levels of fasting sugar and restoring glucose tolerance [30, 31]. Similarly, poor Cr status has being single out as a factor contributing to the incidence of impaired glucose tolerance and type II diabetes [32].

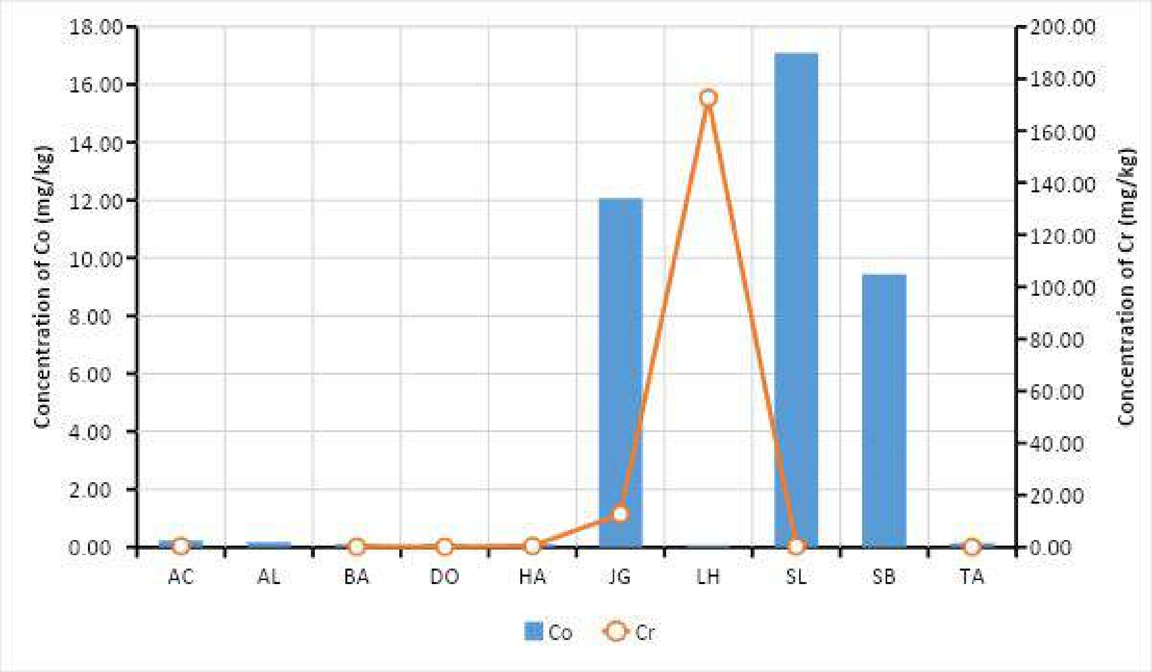

Fig. 2: Average Mean Concentration of Cobalt (Co) and Chromium (Cr) in the Anti-diabetic Medicinal Plants. The results are presented as Mean± SD of three replicate analysis

Zinc is another important insulin actor, activates insulin's secretion in the B-cell and improves the sensitivity of insulin in the management of DM [32, 33]. A necessary cofactor required for the activation of intracellular enzymes needed for glucose metabolism [34, 35]. It has a biphasic effect in that it is required for insulin storage and cellular binding, further reported to mediate glycolysis by influencing the activity of the enzymes, glyceraldehyde-3-phosphate dehydrogenase [34, 35]. The reduction in the intracellular levels of Zn was observed to affects the ability of the islet cell to produce and secrete insulin [33]. It could be observed in Fig.3 that the concentrations of Zn in the extracts of SL and DO are below the detection (BDL) limits. For this element, the highest concentrations of 48.66±4.00 mg/kg was found in the extract of BA and the least in TA (7.10±1.73 mg/kg). The metal contents in the respective plants species falls in this order, BA>AC>SB>JG>LH>HA>AL>TA respectively. Vanadium on the other hand was found to be distributed in all the plants species. As presented in the figure, the highest concentration of V is in

SL (13.47±0.20 mg/kg) and the least value in SB (0.36±0.07 mg/kg). Vanadium is multiphasic in that it's participate in fueling glucose oxidation, glycogen synthesis, carbohydrate metabolism, glycolysis and also serve as a carrier for glucose. Facilitate the upregulation of the insulin receptor and foster the inhibition of hepatic gluconeogenesis [36-38]. In this study, the concentrations of V in the respective plants species were observed to follow the ranking SL>AC>JG>AL>BA>DO>TA>LH>HA>SB.

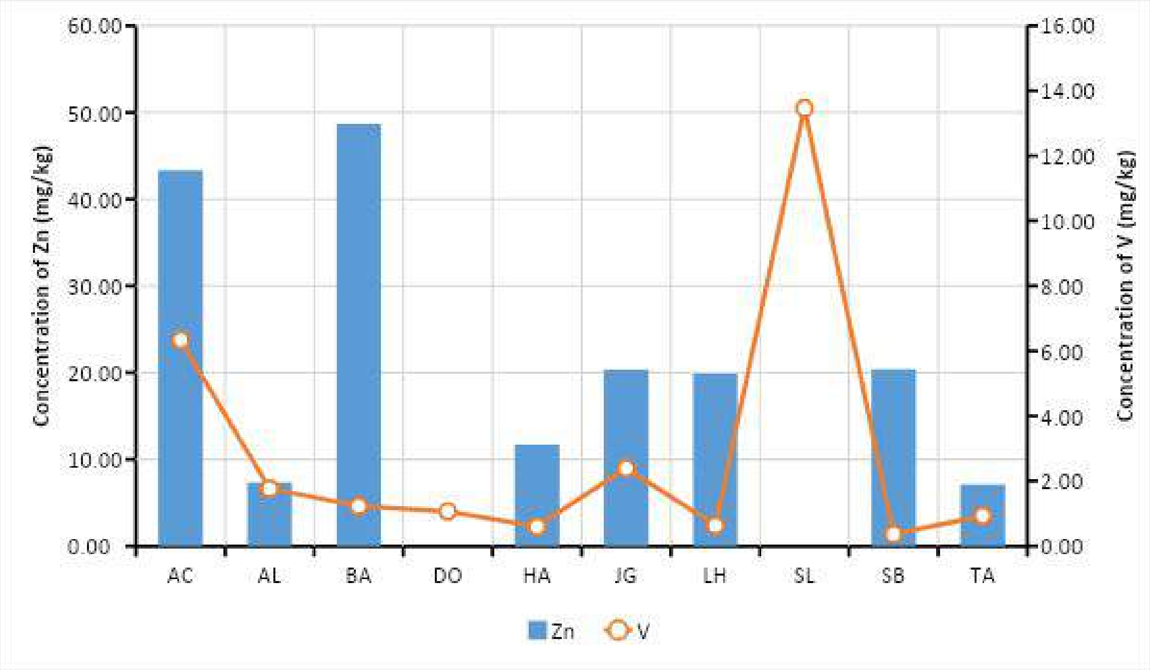

Fig. 3: Average Mean Concentration of Zinc (Zn) and Vanadium (V) in the Anti-diabetic Medicinal Plants. The results are presented as Mean± SD of three replicate analysis

4.4 Estimated daily intake (EDI)

The anti-diabetic plants investigated in this study as presented in Table 1, contains an appreciable amount of Mn which further translates into an estimated daily intake (EDI) greater than its corresponding RfD value. The RfD often used for the assessment of non-carcinogenic health risk is a reference oral dose values set as an estimate for the tolerable daily intake of metals that will pose no health risk during a lifetime [11, 39]. The EDI of Mn was found to be above the RfD of 0.014 mg/kg/day. The highest EDI was found in HA (40.43 mg/kg/day) and the least in AL (1.82 mg/kg/day). Though, these values are observed to be of concern having exceeded the RfD values, dietary studies have demonstrated that daily intake of high doses of Mn can be safely tolerated by healthy individual [40,41]. Thus, it will suffice to say that the EDI values recorded in this study will not necessary translate into toxic levels. This was accredited to the homeostatic control of Mn retention and excretion processes [41]. These mechanism enabled the human body to handle substantial variations in dietary Mn on a daily basis with little or no risk of overload [41, 42]. However, when administering these medicinal plants, factors such as health status should be considered.

The estimated daily intake for Fe in this study as presented in the table shows AC containing the highest EDI of 86.42 mg/kg/day and the least in HA (8.37 mg/kg/day). These values as indicated in the table are all above the RfD for Fe (0.007 mg/kg/day), indicating potential health related implication following the ingestion of Fe via the consumption of these medicinal plants. Physiologically, Fe was observed to exert a causal role in diabetes pathogenesis mediated both by β-cell failure and insulin resistance. [26, 43]. Dietary Fe in excess to the range required for normal erythropoiesis and metabolic function has a direct effect on the secretion of insulin and insulin sensitivity. Such overload could also leads to the activation of stress pathways, mediate adipocyte iron-sensing role and mitochondrial dysfunction [26, 43]. However, the multifactorial role of Fe towards weight regulation are possible route in which excess Fe intake regulates the likelihood of Fe induce toxicity. Essential for lipolysis of adipocytes, thus slows down obesity related biology [44]. High dietary Fe are channel to augment fatty acid oxidation and stimulates lipogenesis [45]. Therefore, the ability of Fe to regulate adiponectin secretion further suggests its essentiality to coordinate metabolism by regulating other hormones important to fuel and energy homeostasis [26]

The EDI for Co in most of the anti-diabetic plants investigated in this study falls below the RfD levels (0.03 mg/kg/day) except for JG (0.603 mg/kg/day), SL (0.855 mg/kg/day) and SB (0.472 mg/kg/day). The results thus suggest that the consumption of AC, AL, BA, DO, HA, LH and TA poised no health risk. However, potential health risk could be associated with the consumption of JG, SL and BS respectively. Though, Co was reported to have low oral toxicity [46], exposure above the safety limits are implicated to number of health related cases such as gastrointestinal complications, liver injury, and allergic dermatitis [47]. Despite the fact that the EDI recorded in this study appeared on a slightly lower sides, caution has to be applied especially in patients with other health complications before administering herbal remedy with high content of cobalt.

The highest EDI of Chromium (8.66 mg/kg/day) was found in LH and the least in TA (0.003 mg/kg/day). From the results it was observed that all the EDI recorded in the respective anti-diabetic plants falls below the RfD (1.5 mg/kg/day) levels except in LH (8.66 mg/kg/day). The EDI values for Cr recorded in the following plants AC, AL, BA, DO, HA, and TA posed no health risk, however, caution should be applied for Cr toxicity when consuming LH as a remedy for diabetes. Chromium toxicity is associated to liver and kidney damage. Other toxic effects includes skin irritation/nose irritation, and lung cancer [48]

From the results in the table, the EDI for Zn in all the respective anti-diabetic plants were found to be above the RfD (0.30 mg/kg/day). The results show the highest EDI of 2.43 mg/kg/day in BA, while the least of 0.35 mg/kg/day was found in TA. Though, Zn plays a vital role in supporting insulin metabolism, excess amount above the RfD levels come with a price. Zinc poisoning as a result of exposure above the RfD levels were reported to induce complications such as nausea, vomiting, diarrhea, fever and lethargy. Physiological, high levels of Zn above the tolerable limits were reported to have the propensity to interfere and in some cases alter the metabolic chemistry of other trace elements [49, 50].

Furthermore, it could be noted that the highest EDI for V was found in the extract of SL (0.673 mg/kg/day), while the lowest EDI of 0.018 mg/kg/day was observed in the extract of SB. Based on the RfD of 0.009 set for V, it is obvious that the EDI recorded for the respective anti-diabetic plants exceeded the RfD levels. Though, the difference between the EDI level and the RfD is minimal, the difference however, suggest that caution should be applied during the consumption of these plants. Oral consumption of V at a very high dose were reported to induce gastrointestinal disturbances in humans. Other complications reported includes kidney lesions, nervous disturbances, neurasthenic or vegetative symptoms [51].

Table 1: Estimated Daily Intake in mg/kg/d for Mn, Fe, Co, Cr, Zn and V in Anti-diabetic Medicinal Plants Commonly Consumed in Nigeria

Elements	AC	AL	BA	DO	HA	JG	LH	SL	SB	TA
Mn	8.79	1.82	2.55	7.15	40.43	4.00	3.61	2.18	3.39	4.36
Fe	86.42	14.76	37.80	9.33	8.37	35.53	28.18	21.90	12.43	13.58
Co	1.15E-02	8.00E-03	5.00E-03	5.00E -03	5.00E-03	6.03E-01	3.00E-03	8.55E-01	4.72E-01	6.50E-03
Cr	1.80E-02	-	6.50E-03	5.00E -03	2.15E-02	6.33E-01	8.63	1.50E-02	-	3.00E-03
Zn	2.17	3.67E-01	2.43	-	5.83E-01	1.02	9.93E-01	-	1.02	3.55E-01
V	3.17E-01	8.80E-02	6.15E-02	5.30E-02	3.00E-02	1.20E-01	3.15E-02	6.73E-01	1.80E-02	4.65E-02

The dose makes the poison is often implied to all chemicals [41], therefore, the ubiquitous nature of the respective elements discussed above has to be factored into the equation in order to draw a line between its essentiality and potential risk. Thus, the underlining EDI however, important towards seating a limit to its exposure does not necessary implies toxicity, as individuals may experience different responses under different conditions, dose and concentrations. As mentioned above, the EDI assessments processes relate the consumption data with the concentrations of the respective elements and its relationship to the bodyweight. These assessment processes, though significant towards understanding the likelihood of toxic related effect associated with the consumption of these medicinal plants, however, falls short of providing the possible health risk effects that may occur over a lifetime relative to the most appropriate limit value. Therefore, to get a realistic health risk picture, the risk characterization processes is made by comparing it with health-based statistical probability. The statistical probability is therefore expressed as a function of the quantified level of concern in the form of THQ, a process developed to estimate the potential health risks associated with long-term exposure to chemical pollutants [20, 21, 52].

4.5 Health risk Assessment

The risk assessment processes involved a concise analysis of the likelihood of harm that may arise following the exposure/or consumption of hazardous materials. The THQ was computed to investigate the potential risk posed by these elements following the consumption of these anti-diabetic plants. The THQs of the six elements analyzed from the ten anti-diabetic medicinal plants are presented in Table 2. From the results presented in the table, the THQ for the individual elements for the individual anti-diabetic plants were observed to be <1, which is considered safe for human consumption. However, not all the anti-diabetic plants shows a THQ value <1 for Cr. A THQ >1 for Cr was observed in LH (12.95). These values is expected as this particular specie (LH) recorded an EDI above the RfD levels for Cr. Thus, this particular species is therefore consider not entirely safe for human consumption. Considering the potential risk to human health, the cumulative effects of the individual metals for a particular species shows a HI values <1 in most of the plant species, except in LH (13.30) and JG (1.36). Its therefore assumed that the magnitude of the effect which is directly proportional to the sum of the multiple metal exposure point towards LH and JG as potential health risk to human and thus, raise the level of concern to their consumptions

From the THQ and HI values derived for the individual elements in most of the anti-diabetic plants and the scenario discussed above to buttress their insulin supporting properties, it will suffice to conclude that these plants are more or less considered safe for human consumption. However, factors such as patience health history should be factored before administering these herbal remedies. In some rare occasions, a combination of more than one medicinal plants such as in concoction could increase the THQ >1, thus, increasing the likelihood for possible human risk. Therefore, carrying out THQ and HI to ascertain the potential human risk that may arise from the consumption of concoctions should be investigated.

Table 2: Target hazard quotient (THQ) for Mn, Fe, Co, Cr, Zn and V in Anti-diabetic Medicinal Plants Commonly Consumed in Nigeria

Elements	AC	AL	BA	DO	HA	JG	LH	SL	SB	TA
Mn	1.23E-01	2.55E-02	3.57E-02	1.00E-01	5.66E-01	5.60E-02	5.06E-02	3.05E-02	4.74E-02	6.10E-02
Fe	6.05E-01	1.03E-01	2.65E-01	6.53E-02	5.86E-02	2.49E-01	1.97E-01	1.53E-01	8.70E-02	9.51E-02
Co	3.45E-04	2.40E-05	1.50E-05	1.50E-05	1.50E-05	1.81E-03	9.00E-06	2.57E-03	1.41E-03	1.95E-05
Cr	2.70E-02	-	9.75E-03	7.50E-03	3.23E-02	9.50E-01	12.95	2.25E-02	-	4.50E-03
Zn	2.17E-01	3.67E-02	2.43E-01	-	5.83E-02	1.02E-01	9.93E-02	-	1.02E-01	3.55E-02
V	2.85E-03	7.92E-04	5.54E-04	4.77E-04	2.70E-04	1.08E-03	2.84E-04	6.06E-03	1.62E-04	4.19E-04
HI	9.75E-01	1.66E-01	5.54E-01	1.73E-01	7.15E-01	1.36	13.30	2.15E-01	2.38E-01	1.97E-01

V. CONCLUSION

The ubiquitous nature of the respective elements as analyzed in this study underscore their essentiality in supporting insulin metabolism against the possible risk. In the study, the underlying EDI shows a level greater than their corresponding RfD in most of the plant species. Iron was observed to show the highest EDI above the RfD, followed by Mn, Zn and finally V. Though, the EDI having exceeded the RfD levels as observed in the study, however important towards seating a limit to its exposure does not necessarily implies toxicity. This observation as demonstrated in the results shows the individual elements for the individual anti-diabetic plants having THQ and HI value <1 safe for human consumption. The results further shows a variation in the LH, the species was observed to have a THQ values >1 for Cr and a very high HI index >1 in the same species. Thus, suggest that this particular species is not entirely safe for human consumption.

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