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HEALTH RISK ASSESSMENT AND DETERMINATION OF SOME MICROELEMENTS IN COMMONLY USED ANTI-DIABETIC MEDICINAL PLANTS IN MUBI NORTH LOCAL GOVERNMENT AREA, ADAMAWA STATE, NIGERIA

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ABSTRACT

The concentration and health risk assessment of some microelements in commonly consumed antidiabetic medicinal plants in Mubi North Local Government Area, Adamawa State, Nigeria were analysed using Atomic Absorption Spectrometry (AAS). Four anti-diabetic plants were analyzed for concentrations of Lead (Pb), Copper (Cu), Iron (Fe), Chromium (Cr), Zinc (Zn), Manganese (Mn) and Cadmium (Cd) respectively, in the stem bark and leave of the following medicinal plants: (Euphobia Hirta, terminallia Avicenioides, Daniella Oliveri, and Laptadania Hastata).The findings of the study revealed that the investigated antidiabetes medicinal plants contained varying concentrations of elements such as Cu, Fe ,Cr, Zn, Mn and Cd and are within the permissible limits of (WHO), except Pb and Cr which were below detection limits. By calculating risk quotient based on the estimated daily intake (EDI) of 100g the health risk associated with the consumption of the analyzed medicinal plants preparations was also evaluated. However, all the anti-diabetic plants shows a risk quotient (RQ) value less (<1) than one. The potential health risk of the concentration of micro elements in the medicinal plants using 100g as daily intake dose for both adults and children are negligible. Therefore, the consumption of these studied medicinal plants poses no health risk and is safe.

KEYWORDS: anti-diabetes medicinal plants, micro elements, health risk assessment, risk quotient (RQ).

INTRODUCTION

Medicinal plants have been used for centuries to manage different type's ailments such as cardiovascular diseases, dysentery, pile disease, typhoid, yellow fever, toothache, headache, dyspepsia, amenorrhea, venereal diseases, liver diseases, leprosy, wounds, burns, cuts, boils, eczema, mycosis, scabies, sore throat, respiratory diseases, hepatitis, jaundice, rashes, ringworm, inflammation, and diabetes mellitus (Sofowora, 2008). Nature has blessed Nigeria with a wide variety of plants species which are used for the treatment of these ailments. Medicinal plants have been the bases for the development of complex pharmaceuticals for the promotion of health care worldwide (Coria-Tellez et al., 2018). The use of these varieties of plant extracts as crude drugs occupies a unique position in the management of diseases in contemporary communities in Nigeria (Sofowora, 2008). Medicinal plants used to treat diabetes have high concentrations of K, Ca, Cr, Mn, Cu, and Zn that stimulate the action of insulin (Raju et al., 2006) and also Fe, Zn, and Cr that act in the prevention of complications of type 2 diabetes (Mertz,1993). In fact, the macro- and microelements (K, Ca, Mg, Na, Fe, Rb, Sr, Zn, Cu, and Se) play an important role in growth, bone health, fluid balance, and several other processes when ingested in adequate amounts (Rocha, et al., 2019, Haidu et al., L., 2017). The consumption of medicinal plants for therapeutic purposes is recognised as one of the earliest forms of medical practice of mankind. The World Health Organization reported that 80% of the emerging world's population, both in developed and developing countries, relies on traditional medicine for the treatment of different diseases (WHO, 2004). The high demand for traditional and alternative medicines has led to a rapid increase in the medicinal plant applications worldwide (WHO, 2007). Natural products from plants and their derivatives represent more than 25% of all drugs currently in clinical use (Dhaim *et al.*, 2006). The medicinal uses of plants are attributed to their phytochemical constituents (Avoseh, et al., 2015). Apart from the phytochemical constituents inorganic constituents also play an important role in combating these menace. To add value to these plants research on inorganic constituents is vital and critical for the overall development of herbal medicine. It has been reported that both macro and microelements play a critical role in their therapeutic effects. These elements present in medicinal plants contribute to the regulation of glucose metabolism, insulin sensitivity and overall antioxidant capacity which are vital for managing diabetes (Magili et al., 2018). Diabetes mellitus is a chronic condition that requires effective management to prevent complications. Traditional medicinal plants play a significant role in diabetes management (W.H.O, 2019). Diabetes mellitus is of great health concerns in Nigeria due to changes in life styles (Magili et al., 2018). Effective management often involves dietary modifications including the use of mineral supplements that aid the management of this life threatening disease.

In Nigeria today, one common disease that present its ugly face in both the rural and urban settings is Diabetes Mellitus (DM) which according to the International diabetes federation (IDF), recorded a prevalence rate of 3.9% for Nigeria (International Diabetes Federation (IDF).Diabetes Atlas, 2010, Siddiqui, *et al.*, 2014).

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 enthnobotanical survey 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 (Arika *et al.*, 2016, Ngugi *et al.*, 2012). Insulin –supporting micro and macro elements in antidiabetic medicinal plants have traditionally been used in the treatment of diabetes due to their potential to support insulin production and action. Some of these plants may contain micro and macro elements that can play a role in blood sugar regulation (Arika *et al.*, 2016).For example, certain plants may contain minerals like magnesium, zinc and chromium, which are essential for insulin functions and glucose metabolism. However, the specific levels of these elements can vary between different plants species and even within different plant parts (leaves, stems, roots, etc) of the same plants, due to environmental factors.

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 reported by (Magili and Bwatanglang, 2018a, Magili and Bwatanglang, 2018b), 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. These medicinal plants are used as a viable option to improve people's health worldwide. Through research on medicinal plants value can be added to these plants by providing regulatory framework for both the practioners and products on its toxicity and dosage with a view to increase its usage in the primary health care sector.

These plants contain both organic and inorganic constituents and research has been carried out mostly on organic constituents but not much has been achieved on the inorganic aspects (Colagiuri, 2010; Yagi *et al.*, 2013).They have different chemicals in their roots, stems, leaves and fruits. These constituents in one form or another play an important role in the field of medicine in combating diseases as curative or preventive agents. The nutritional and mineral components are also an important factors in determining the quality of medicinal plants. Inorganic elements like calcium, sodium, potassium are essential for a healthy life (Yesufu and Hussaini, 2014). The inorganic elements are very important in trace amounts which play an important role in nutrition, enzyme reaction and also in metabolic processes (Yesufu and Hussaini, 2014). The importance of inorganic constituents in combating diseases is fast spreading (Cesar 2005; David, 1999). Because of this, attention has now been paid on the role of inorganic elements in the medicinal use of plants. This has increased the use of micro and macro elements as dietary supplements derived from plants in recent years. These medicinal plants can act by supplying ß- cells with the necessary micro and macro elements such as Mg, Ca, Zn, V, Cr, Mn,Ni,Se and K which are well known in potentiating insulin and aiding in the management of diabetes mellitus (Ma *et al.*,1995; Candilish,2000).The action of insulin on reducing sugar was reported to be potentiated by some trace elements such as Cr, Mg, V, Zn, Mn, Mo and Se (Candilish, 2000). The proposed mechanism of micro and macro elements enhancing insulin potentiation includes activation of insulin receptor sites, serving as cofactors or components for enzyme systems involved in glucose metabolism ((Masood *et al.*, 2009; Vincent, 2000; Murray *et al.*, 2000). Despite the wide usage of medicinal plants it could cause some health challenges in their consumptions. These challenges could be a result of the mineral contents present in various plants or contamination in the cause of preparations.[6]

Health risk in these medicinal plants, would involve evaluating the levels of essential and potentially toxic elements in these plants as they are widely used for managing diabetes .This study is crucial for determining whether the consumption of these medicinal plants possess any health risks due to the presence of heavy metals or deficiencies in important nutrients. This assessment examines the health risks associated with these elements in diabetes management (*Mohammad, et al.*, 2022)

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. This study aims to explore the concentrations of some microelements in these plants and their therapeutic potential and possible risk that may be associated with the consumption of the medicinal plants using risk quotient (RQ) based on the daily intake of 100g.

MATERIALS AND METHODS

Sampling and Sample Preparations

Plant material

The plant specimens was collected from different locations as listed in Table 1. All plant materials was carefully examined and identified by Prof.C.S.Yusuf at the Botany Department. Faculty of Science Adamawa State University, Mubi. The plant materials were air-dried for 10 days, milled into powder with the aid of a mortar and pestle and stored in air tight bottles before further preparation for analysis.

Table 1: Plant Material.

S/NO	BOTANICAL NAME	FAMILY NAME	COMMON NAME	LOCAL NAME	PARTS USED
1	*Euphorbia Hirta*	Euphorbiaceae	asthma-Plant	Tawa-Tawa	Stem bark, Leaves.
2	*Terminalia Avicennioides*	*Combretaceae*	*Terminalia dictyonuna diels.*	*Baushe*	*Stem bark, Leaves*
3	*Leptadenia hastata*	*Asdepiadaceae hastatum*	*Cyandum*	*Dan barawo*	stem bark, *leaves*
4	*Daniellia oliveri*	*Caesalpinioideae Oliveri*	*daniellia*	*maje*	*Stem bark, leaves*

Sample Digestion

The dried powdered samples (leaves and stem bark) of the plants was processed using standard procedures. The samples were prepared for analysis by wet digestion method using nitric acid and hydrochloric acid treatment (Mihreteab,*et al.*,2020, Indrajan *et al*; 2000)

Sample Analysis: The selected micro elements: Cu, Fe, Cd, Cr, Pb, Mn, and Zn respectively were analysed using Atomic Absorption Spectroscopy-VGD210 in which a proper cathode lamp of the element of interest was allowed to warm up. The instrument was aligned after the lamp level and element was selected. The slit and wavelength was adjusted as was instructed on the screen and the instrument was aligned. The maximum energy was also adjusted and aligned. The machine was zero and the values of the standard was entered. The flow of gas and oxygen was set and the flame was ignited. The nebulizer was immersed into various standard to create the standard calibration curve. The samples were measured in absorbance and then the calibration curve was used in determining the concentration of the various metals in various samples. (Khan, *et al.* 2008).

Health Risk Characterization

The health risk assessment of heavy microelements in the antidiabetes medicinal plant sample were calculated by the risk quotient (RQ) (ATSDR, 2022).

$$DED = \frac{\text{Concentration (mg/kg) x Daily Intake}}{\text{Body Weight in kg}} \quad (1)$$

Where DED is the Daily Exposure Dose in mg/kg-day

$$RQ = \frac{DED}{RFD} \quad (2)$$

Where RFD is the Reference Dose

RQ is the Risk Quotients, if the value of RQ is equal or greater than one it indicate the potential risk of the metal in the sample (W.H.O, 2020).

RESULTS AND DISCUSSION

The results of this study showed that macro and microelements such as (Fe, Zn,Pb, Cr,Mn,Cd and Cu) were present in varying concentrations in the four antidiabetes medicinal commonly used in Mubi north Local Government Area of Adamawa state. The average concentration of the elements in the antidiabetes medicinal plants are shown in Table

Table 2: The concentration of some micro elements in the medicinal plants.

Samples	Zn (mg/kg)	Fe (mg/kg)	Cu (mg/kg)	Mn (mg/kg)	Cd (mg/kg)	Cr (mg/kg)	Pb (mg/kg)
Euphorbia hirta	1.65±0.05	2.89±0.01	1.18±0.01	1.52±0.02	0.06±0.01	BDL	BDL
Terminalia avicenioides							
Stem bark	0.52±0.02	1.62±0.02	0.27±0.02	0.53±0.00	0.11±0.01	BDL	BDL
Leaves.	0.64±0.01	0.74±0.02	0.26±0.01	1.58±0.01	0.07±0.01	BDL	BDL
Daniella oliveri							
Stem bark	0.33 ±0.00	0.33±0.03	0.09±0.01	0.51±0.01	0.07±0.01	BDL	BDL
Leaves.	0.76±0.04	1.38± 0.03	0.23±0.02	2.11±0.01	0.07±0.01	BDL	BDL
laptadania Hastata							
Stem bark.	0.40±0.02	2.52±0.02	0.36±0.03	1.48±0.01	0.06±0.01	BDL	BDL
Leaves.	1.08±0.00	1.97±0.02	0.16±0.01	2.64±0.00	0.08±0.01	BDL	BDL
W.H.O	50	20	10	20	0.3	1.5	0.001

BDL=below detection limit

Table 3: Health Risk Quotient for Adults (RQ).

Metals/Samples	Zn	Fe	Cu	Mn	Cd
Euphorbia-hirta	0.0091	0.0069	0.053	0.018	0.2
Terminalia avicenioides					
Stem bark	0.0029	0.0038	0.012	0.0063	0.36
leaves	0.0035	0.0017	0.012	0.019	0.23
Daniella oliveri					
Stem Bark.	0.0018	0.00079	0.0041	0.0061	0.23
Leaves	0.0013	0.0032	0.010	0.025	0.23
laptadania Hastata					
Stem Bark	0.0022	0.006	0.016	0.017	0.2
Leaves	0.006	0.0046	0.00073	0.031	0.26

Table 4: Health Risk Quotient for Children (RQ).

Metals/Samples	Zn	Fe	Cu	Mn	Cd
Euphorbia hirta	0.018	0.13	0.10	0.036	0.4
Terminalia avicenioides					
Stem bark.	0.0057	0.0077	0.024	0.0013	0.73
Leaves.	0.0071	0.0035	0.023	0.037	0.47
Daniella oliveri					
Stem Bark.	0.0036	0.0015	0.0081	0.012	0.47
Leaves.	0.0084	0.0066	0.021	0.051	0.47
laptadania Hastata					
Stem Bark	0.0044	0.012	0.032	0.035	0.4
Leaves	0.012	0.0093	0.014	0.063	0.53

DISCUSSION

Many medicinal plants with varying concentrations of macro and micro elements also possess bioactive compounds such as polyphenols, flavonoids, alkaloids, and glycosides that synergize with these elements to improve glucose metabolism, reduce oxidative stress, and enhance insulin sensitivity. These elements help, Regulate Blood Glucose Levels. Plants rich in chromium, zinc, magnesium, and manganese are particularly effective in stabilizing blood glucose levels by improving insulin sensitivity and glucose utilization. Macro and micro elements, alongside antioxidants in medicinal plants, can reduce oxidative stress and inflammation, which are common complications in diabetes. This may help prevent complications like neuropathy, nephropathy, and retinopathy. Elements like zinc and chromium directly enhance insulin production and action, while others like magnesium and potassium support cellular processes that allow for better insulin response and glucose uptake((Rabia *et al.*, 2012).

Microelements or trace elements, though required in smaller quantities, are equally critical for managing diabetes. They include zinc (Zn), chromium (Cr), manganese (Mn), copper (Cu), and iron (Fe), among others (Goroya *et al*, 2019).

Zinc (Zn), improve antioxidant defenses, protecting tissues from damage caused by oxidative stress associated with hyperglycemia. The concentration of Zn found in the selected medicinal plants are, *(Ephorbia hirta, (*1.65±0.05,) *Terminalia avicenioides* (0.52±0.02, 0.64±0.01) *Daniella oliveri* (0.33±0.00, 0.76±0.04) and *leptadania hastata (*1.08±0.00, 0.40±0.02)mg/kg for stem barks and leaves, respectively. This shows that the concentration of Zn in all the samples used were appreciable and within the permissible limit set by World health organisation, (Goroya *et al*, 2019). Zinc is important in insulin synthesis and secretion and deficiency may impair glucose metabolism, while excessive supplementation could lead to toxicity. Zinc, is vital for enzyme activity, hormone regulation, and antioxidant defence, influencing diabetes management. The presence of Zn in these plants could be important in insulin synthesis and secretion. Therapeutic insights in the use of these plants with high concentration of these micro element provides potential correlations between element concentrations and the hypoglycemic properties of the plants. Zinc is crucial for the synthesis, storage, and secretion of insulin. Zn is a trace element and is an essential nutrient for humans and animals. Zn is the basic component of a large number of different enzymes. Zn is essential for insulin storage secretion and functions. It also supports immune functions and wound healing. Zn play an important role in structural, regulatory, and catalytic functions, it also play an important role in DNA synthesis, normal growth, brain development and bone formation. However at high concentration Zn can lead to diarrhea, abdominal cramps, fatique, headache, kidney damage, liver damage and reproductive issues. The toxicity of Zn depends on the dose, duration of exposure and individual sustainability. (Khan *et al.*, 2008).

The concentration of iron found in the selected medicinal plants are, *(Ephorbia hirta*, *(*2.89±0.01) *Terminalia avicenioides* (1.62±0.02, 0.74±0.02), *Daniella oliveri* (0.33±0.03, 1.38± 0.03) and *leptadania hastata* (2.52±0.02, 1.97±0.02))mg/kg for stem barks and leaves, respectively. Iron (Fe) is the most abundant and an essential constituent for all plants and animals. Iron at high concentration causes tissue damage and other diseases it is also responsible for anaemia and neurodegenerative condition in humans (Fuotes *et al.*, 2000).

The concentration of iron in all the samples used were not above the permissible limit by the W.H.O (20mg/kg).

The concentration of Cu,found in the selected medicinal plants are, *(Ephorbia hirta*, *(*1.18±0.01) *Terminalia avicenioides* (0.27±0.02, 0.26±0.01), *Daniella oliveri* (0.09±0.01, 0.23±0.02) and *leptadania hastata* (0.36±0.03, 0.16±0.01) mg/kg for both stem barks and leaves, respectively.

Copper is an essential trace element, it is needed for normal growth and development. However high concentration of Cu may lead to hair and skin decolouration, respiratory track diseases and other diseases. The concentration of Cu in all the samples used were within the standard permissible range of the W.H.O, (10mg/kg). Cu is essential for connective tissues health immune function and glucose metabolism.

The concentration of Mn, found in the selected medicinal plants are, *(Ephorbia hirta*, *(*1.52±0.02) *Terminalia avicenioides* (0.53±0.00, 1.58±0.01), *Daniella oliveri* (0.51±0.01, 2.11±0.01) and *leptadania hastate* (1.48±0.01, 2.64±0.00) mg/kg for stem barks and leaves, respectively. Mn is involved in glucose metabolism, antioxidant deficiencies and bone health.

Manganese Mn is a heavy metal with density of 7.21g/cm^3 is an essential heavy metal for both animals and plants growth. The deficiency of this metal in the body lead to severe and productive abnormalities in mammals. The high concentration of Mn causes hazardous effects on lungs and brain of human (Jarup, 2003). It also causes respiratory issues like coughing, wheezing and shortness of breath. Gastrointestinal problems, nausea, diarrhea and vomiting. Neurological symptoms: tremors, muscle spasms, and etc. The concentration of Mn in all the sample are within the range of the permissible intake by the W.H.O standard (20mg/kg).

The concentration of Cd, found in the selected medicinal plants are, *(Ephorbia hirta*, *(*0.06±0.01) *Terminalia avicenioides* (0.11±0.01, 0.07±0.01), *Daniella oliveri* (0.07±0.01, 0.07±0.01) and *leptadania hastate* (0.06±0.01, 0.08±0.01) mg/kg for stem barks and leaves, respectively. Cadmium (Cd) is one of the big three heavy metal poisons and is not known for any essential biological function. In its compounds, Cd occurs as the divalent Cd (II) ion. Cadmium is directly below Zn in the periodic table and has a chemical similarity to that of Zn, an essential micronutrient for plants and animals. Excessive consumption of Cd may lead to chronic diseases like: kidney damage, cancer (lung, prostate, breast), neurological damage and reproductive issues. Chromium and lead was not detected in all of the samples analyzed. However, all of the analyzed samples contained safe levels of all the microelements which do not exceed the WHO permissible limits. Based on the results of this study, there would be a noncarcinogenic health risk to the consumer associated with the consumption of the selected medicinal plants in Mubi North local Government area of Adamawa State Nigeria. Consequently, a continuous and strict regulatory control is required to ensure the safety of the consumption of the medicinal plants in the study area.

Health Risk Assessment of the selected microelements in Medicinal Plants

Health risk assessment based on Risk quotient (RQ) values at 100g daily intake of the micro elements is one of the vital health risk assessment tools. It takes into account the frequency and duration of exposure and the bodyweight of the exposed persons (Mihreteab, *et al*., 2020). In general health risks for Zn, Fe, Mn, Cd, and Cu was within the tolerable daily intake reference limits for all the selected antidiabetes medicinal plants for both adult and children (Table 3 and 4). Health risk assessment for the micro elements in the medicinal plants was calculated by the risk quotient (RQ), and the results are shown in Table 3 and 4. If the RQ value is less than 1, then the exposed consumers are assumed to be safe, and if the RQ value is equal to or higher than 1, it is considered as a level of concern or poses a health risk (ASTDR, 2022, Adefa, and Tefera, 2020, Aschale, et al., 2019, Kohzadi, et al.,2019). The findings showed that the RQ values for Zn, Fe, Mn, Cd, and Cu were all less than 1, suggesting the consumption of these medicinal plants *Euphorbia hirta*, *Terminalia avicenoides*, *Daniellia Oliveri* and *leptadania hastata* in the study area poses no health risk due to these elements. There the study revealed that all the risk quotient (RQ) values for the concentrations of these microelements, Zn,Fe,Cu,Mn and Cd in all the samples are less than one (<1) using 100g as daily intake. This shows that, all the plants used for this research at 100g daily intake for both adults and children has no potential health risk (Pausenbach, 2000).

CONCLUSION

This study highlighted the need for routine health risk assessment and determination of microelements for quality asurance of the antidiabetic medicinal plants used for managing diabetes mellitus in mubi north local Government area. The study further demonstrated the importance of ethnobotanical survey and assessing the safety and efficacy of medicinal plants in terms of microelement content. It also aims to bridge traditional knowledge and scientific inquiry, highlighting the potential of local medicinal plants in diabetes management. Understanding the microelement profiles can inform their use and support sustainable practices in traditional medicine. The micro elements obtained from medicinal plants contribute significantly to the management of diabetes mellitus by regulating blood glucose levels, improving insulin function, and reducing complications. Their presence in medicinal plants enhances the therapeutic potential of these natural remedies and provide a synergy between the phytochemicals and elemental compositions of the medicinal plants, making them valuable adjuncts in the treatment of diabetes mellitus.

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