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Analysis and Risk Assessment of Insulin-Potentiating Elements in Addua *(Balanites Aegyptiaca)* Leaf, Seed and Bark.

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Abstract

Purpose: This study investigated certain trace elements having therapeutic properties related to diabetes mellitus and to look into the health risk assessment of the elements. The investigated samples were the bark, leaf and seed of *Balanites aegyptiaca*, desert date (Addua). These plants are traditionally used in the management of diabetes in Eritrea, Egypt, and Ethiopia.

Methodology: The elemental analysis was conducted using Flame Emission Photometer and Atomic Absorption Spectroscopy (AAS) techniques. The accuracy of the methods was verified using in-house reference materials (CRMs) and no significant differences were observed between the measured and certified values.

Findings: The analysis displayed variable concentrations of the different trace elements found to be in the permissible limit defined by WHO. The metals are in the order of decreasing concentrations in the bark sample K > Ca > Mg > Co > Fe > Cu > Zn > Mn. In the leaf, the ranking order is K > Ca > Mg > Fe > Zn > Mn. The seed sample appeared in the order K > Ca > Mg > Fe > Zn > Mn. The THQ for the non-carcinogenic risk were all < 1 for all metals and the various exposure pathways. The trend is same for HI for both children and adults. This is a pointer to the fact that no immediate danger due to presence of potential carcinogens. Furthermore, the study revealed the order of pathway in the following decreasing order $HI_{ingestion} > HI_{dermal} > HI_{inhalation}$ and most of all, the HI values for adults generally higher than that of the children. However, this suggests that adults are at greater risks of and could be more susceptible to potential carcinogenic risk from continual exposure.

Recommendation: The findings calls for concern on the regular use of some of the infusion from this plant.

Keywords: *Diabetes, elements, risk assessment, average daily intake, target hazard quotient, carcinogenic*.

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Introduction

Metals are a major category of globally-distributed pollutants and are natural elements that have been extracted from earth and harnessed for human industry and products for millennia. (An exception to metals being "natural" is polonium). Heavy metal is a term used to define metallic elements with atomic weight higher than 40.0 (the atomic mass of Ca) (American Public Health Association (APHA), 1992). Metals are notable for their wide environmental dispersion from activities such as; their tendency to accumulate in selected tissues of human; and their overall potential to be toxic even at relatively minute levels of exposure. Some metals, such as Copper and Iron, are essential to life and play an irreplaceable role in the function of some critical enzyme systems (Ali, Khan, & Ilahi, 2019). Other metals are xenobiotic and, even worse, are the case of lead and mercury, which may be toxic even at trace level of exposure (Jaishankar, Tseten, Anbalagan, Mathew & Beeregowda, 2014).

However, metals that are essential have the potential to be toxic at very high level of exposure. One reflection of the importance of metals relative to other potential hazard is their ranking by the United State Agency for Toxic Substances and Disease Registry (ASTDR, 2005), which lists all hazards present in toxic waste site according to their prevalence and the severity of their toxicity. The first, second, third, and sixth hazards on the list are heavy metals: lead, mercury, arsenic and cadmium respectively. Exposure to metals can occur through a variety of routes. Metals may be inhaled as dust or fume (tiny particulate matter, such as the lead oxide particles produced by the combustion of leaded gasoline). Some metals can be vaporized (e.g. mercury vapour in the manufacture of fluorescent lamps) and inhaled. Metals may also be ingested involuntarily through food and drink. The amount that is actually absorbed from the digestive tract can vary widely, depending on the chemical form of the metal and the age and the nutritional status of the individual. Excretion typically occurs primarily through the kidney and digestive tract, but some metals tend to persist in some storage sites, like the liver, bones, kidneys, for years or decades (Umar, Mohammed, Garba & Faruruwa, 2016). Pollution of soil with heavy metals from polluted irrigation water, atmospheric dust, automobile and industrial exhausts, pesticides and fertilizers play important roles in heavy metal accumulation of medicinal plants/products (ASTDR, 2005).

Metals in medicinal plants

The reasons for the presence of metals in Herbal Medicinal Products (HMPs) are varied. Plants may accumulate heavy metals from the environment during growth on contaminated soil or by deliberate addition (Anim, Laar, Osei, Odonkor & Enti-Brown, 2012; Baye & Hymete, 2010). Whatever the route by which heavy metals are introduced in HMPs, if the level of these metals is high (Bushra, Ghazala & Shahid, 2011; Cooper *et al*., 2007) poisonings may occur (FAO/WHO, 1984). The toxicity of metals most commonly affects the brain and the kidney, but other manifestations occur, and some metals such as arsenic are clearly capable of causing cancer (Fosmire, 1990).

Trace elements have been identified for a long time as potential candidates for improving metabolic disorders including diabetes (Gaur & Agnihotri, 2016). Diabetes mellitus refers to a group of diseases that affect how the body uses blood sugar (glucose). Glucose is vital to health because it's an important source of energy for the cells that make up the muscles and tissues. It's also the brain's main source of fuel (Ferri, 2019). The underlying cause of diabetes varies by type. But, no matter the type of diabetes, it can lead to excess sugar in the blood (Papadakis, 2018).

According to the World Health Organization (WHO, 2011), diabetes mellitus is a disease that affects an estimated 180 million people worldwide, and this number is expected to double by the year 2030. Various forms of hyperglycemia are characteristic of diabetes and are thought to result from a lack of insulin production by the pancreatic β-cells or the inability of the body to efficiently use the insulin that is produced (Gabbe, 2018). Diabetes is typified by hyperglycemia, although the resulting complications are much more serious than simply an elevated level of blood glucose. Interestingly, the observed complications among the various forms of diabetes are remarkably similar and manifold. Diabetes is classified as a single disease, although it results in a wide variety of complications such as retinopathy, which causes blindness in 2% and visual impairment in 10% of patients with diabetes (Cunningham, 2014) and other forms.

It is widely believed that some trace elements, such as Zn, Cr, V, Mg, Mn, and Se serve as cofactors for antioxidative enzymes and play an important role in protecting the insulin secreting pancreatic β-cells which are sensitive to free radical damage (Ngugi, Njagi & Kibiti, 2012; Candilish, 2000). It has also been reported that the imbalance of some essential trace elements might adversely affect pancreatic islet and cause development of diabetes (Khan & Awan, 2014) and thus some trace elements have been recommended as dietary supplement to alleviate the impaired insulin metabolism in diabetic patients (Clark, Deniset, Heyliger & Pierce, 2014; Li, Tan & Sun, 2013). Some researchers have also shown that trace elements beneficially affect the complications of diabetes mellitus (Purnima & Kazi, 2015). Clinical studies suggest that the body's balance of mineral trace elements is disrupted by diabetes and thus diabetic individuals are susceptible to trace element deficiency (Niamat, Khan & Khan, 2012). Even though trace elements are important for the normal functioning of the body, they can be harmful and toxic at high concentrations (Chrzan, 2016). Therefore, profiling the levels of these elements is mandatory in monitoring the safety of herbal preparations employed in the management of diabetes and other ailments.

B. aegyptiaca has been found to possess both neutraceutic and therapeutic potentials all over Africa. In Darfur, the leaves, young sprouted leaves and green thorns are eaten as vegetable salad or may be cooked (Abdoun, 2005). *B. aegyptiaca* leaves are used for the treatment of toothache, stomach complain sterility, epilepsy, yellow fever and syphilis and is used as anti-diabetics (El-Ghazali, El-Tohami & El-Egami, 1994). In Egypt, the fruit is used as an oral hypoglycemic (Kamal, 1998) and antidiabetics (Daya & Vaghasiya, 2010). The fruits are well known for treating dysentary and constipation in Nigeria. The leaves are highly consumed as vegetables, for soup making and salad, its kernel oil for the treatment of wounds while a combination of the leaves and bark is a source of contraception in Nigeria and Somaila. The pure saponin extract from B. aegyptiaca fruit mesocarp has hypoglycermic effect (Kamal, 1998; Mansour & Newairy, 2000).

This study focuses on analysis of the levels of trace elements from the bark, leaf and seed of 'Aduua' plant (desert date) *Balanites aegytical* that potentiate insulin production and their therapeutic role in the management of diabetes. This is to ascertain the risk status of these various elements. This plant has been traditionally used as a vegetable for preparation of soup for meals and for the treatment of diabetes and other ailments (Demoz, Gachoki, Mungai & Negusse, 2015) for centuries.

The contamination of herbal medicine/preparations by excess metals is of great concern because of their toxic and cumulative tendencies. *Balanites aegyptiaca*, desert date (Addua) is known for its potency in the treatment of diabetes and many other ailments. The determination of concentrations of the heavy metals in this important plants should be of regular basis to avail the public a database of the state of clinical and pharmacological fitness of the plant. In order that people keep abreast with the authenticity of what they consume, adsorb and inhale, a regular and persistent check is recommended. Over accumulation of some of these metals in plants portend the risk of deadly diseases such as cancer and the like, hence international organizations set Maximum Permissible Limits to regulate intake of plant or plant products. If these internationally accepted permissible limit are left unsupervised or unmonitored their use could have cumulative effect, which in turn may lead to their toxicity. In order to ascertain that the potent elements in the plant that support its activities against diabetes, a deadly disease in man, is within safety net, this study is conducted. This will guide the general public, government or it agencies and trado-medical practitioners adequately on its safety or otherwise there is risk of gradual self-poisoning.

Materials and Methods

Study Area

Gombe is the capital city of Gombe State. Gombe is estimated to have a population of 268,000 at the 2006 census. The local Government Area has an area 52km^2. Gombe State is one of the 36 states of the Federal Republic of Nigeria, located in the centre of the North-East of the latitude 9°30ˈ and 12°30ˈN, longitude 8ˈˈ45ˈE. It is bordering Borno, Yobe, Adamawa, Taraba and Bauchi States, with a land area of 20,265 SqKm (The World Gazateer, 2007).

Sample Collection and Identification

The samples were collected from a plant which was certified by the Head, Department of Botany, Adamawa State University. The leaves from the plant were carefully harvested manually. The bark of the Addua plant was scraped with the aid of a machete and packed separately in plastic bags. Handful amounts of the fruits were purchase from the market and equally packed in a plastic bag.

Sample Preparation

About 20g of the samples were washed with distilled water to remove sand. The bark was further chopped into smaller sizes. The leaves and the bark were partly air dried and sun dried, ground into a fine powder with mortar and pestle and then sealed in a cellophane plastic bag until ready for use (Salisu, Mohammed & Musa, 2013; JNEFR, 2014). The fruits were soaked in a lukewarm distilled water overnight to soften the epicarp (pulp). This was filter in a 2mm sieve and dried on the laboratory bench. The samples were ground to fine powders with the aid of mortar and pestle (Omale, Olupinyo & Adah, 2011). 1.0 g portion of each of the samples were processed according to the procedures adopted by (Uddin et al., 2016) and analyzed following (Obianjuwa, Adebiyi & Omada, 2005; Hetta, Yassin & EI-Shaer, 2005; Eryomenko, 2018; Emmauel, Omale, Olupinyo, Ada, 2011; Salisu et al., 2013 and Uddin et al., 2016) procedures using Atomic Absorption Spectrophotometer (AAS), Buck Scientific (Model: VPG 210).

Health Risk Assessment Methodology

Health risk is the possibility of harmful effects of pollutants to befall human health (Yaya, Xiaoyun, Zhi, Qin, Houmei & Jie, 2017). The health risk model generated by the United States Environmental Protection Agency (U.S. EPA) is employed to assess the human risk of the metals to humans of all categories. The model is an attempt to predict the possible carcinogenic and non-carcinogenic risks that may arise following the exposure of the elements (Bwatanglang, Alexander & Timothy, 2019) in the plant. The risk assessment method has been used by many researchers (Yaya et al., 2017). The stages of health risk assessment include hazard identification, dose-response assessment, exposure assessment, Average Daily Intake (ADI), exposure pathway, ingestion rate, exposure duration and frequency (Bwatanglang et al., 2019). Human beings can be exposed to metals via the following four main pathways: (1) direct ingestion of soil particles (2) inhalation from air (3) dermal adsorption (4) diet of the plant or vegetables (Yaya et al., 2017). The estimation of the risk assessment in order to predict the probable health risk by integrating possible exposure pathways to quantitatively obtain the average daily intake (ADI) of the toxic metals (mg/kg/day) following either oral ingestion, dermal contact, or inhalation route can be obtain using methods described in the equations 1-3 (Bwatanglang et al., 2019).

$$ADI_{ing} = \frac{10^{-6}\ x\ Cplant\ x\ ing\ R\ x\ EF\ x\ ED}{BW\ x\ AT} \quad \ldots\ldots 1$$

$$ADI_{inh} = \frac{Cplant\ x\ inhR\ x\ EF\ x\ ED}{PEF\ x\ BW\ x\ AT} \quad \ldots\ldots 2$$

$$ADI_{Dermal} = \frac{10^{-6}\ x\ Cplant\ x\ SA\ x\ AF\ x\ ABS\ x\ EF\ x\ ED}{BW\ x\ AT} \quad \ldots\ldots 3$$

The ADI_{ing}, ADI_{inh}, and ADI_{Dermal} represent the average daily intake (ADI) for ingestion, inhalation and dermal exposure pathways respectively. Other parameters and their corresponding functions are described in able 1 below.

Table 1: Exposure factors used for the health risk assessment through different exposure pathways for soil

Factor	Unit	Children	Adult
Body weight(BW)	kg	15	60
Exposure frequency (EF)	days/year	350	350
Exposure Duration (ED)	years	6	30
Ingestion rate ($_{ing}R$)	mg/day	200	100
Inhalation Rate ($_{inh}R_{air}$)	m^3/day	10	20
Skin Surface area (SA)	m^2	2100	5800
Soil Adherence Factor (AF)	mg/cm^2	0.2	0.7
Dermal absorption factor (ABS)	-	0.1	0.1
Particulate emission factor (PEF)	m^2/k	1.3×10^9	$1.3 x 10^9$

Conversion factor (CF)	kg/mg	1.0^{-6}	10^{-6}
Average Time (AT)	days		
i) For carcinogen		365 x 70	365x70
ii) For non-carcinogen		365 x ED	365xED
Ingestion rate (IR_{crop})	g/day	402 (Vegetables)	402

Source: (Bwatanglang et al., 2019; Yaya et al., 2017).

Target Hazard Quotient (THQ)

Non-cancer risk is evaluated by comparing an exposure level over a period of time, with a reference dose derived for a similar exposure period. It can be characterized as a hazard quotient (HQ) and is defined as the ratio of chronic daily intake (CDI) and chronic reference dose (RfD) (Yaya et al., 2017)

This is used to analyze the potential non-carcinogenic effect of the metals in the samples by relating the estimated ADI of each element with their reference dose (RfD) for each exposure pathway as described in equation 4.

$$THQ = \frac{ADI}{RfD} \quad \ldots\ldots 4$$

The oral refence dose for CU, Cr, Zn, Co, Fe and Mn are 0.04, 1.5, 0.3, 0.04, 0.7 and 0.14 mg/kg/day respectively ((Bwatanglang, Alexander and Timothy, 2019 and FAO/WHO. 2011)

Health Index (HI)

The Health Index (HI) is used for the estimation of the overall non-carcinogenic risk posed by more than one potential toxicant. For multiple hazardous substances, the hazard index is the sum of HQ of the individual toxic element. If the THQ or HI value is less than one (THQ or HI < 1), it is unlikely to create adverse health effects for the exposed population. If the THQ or HI exceeds one (THQ or HI > 1), it is not the acceptable range, and the greater the value, the greater the probability of the occurrence of adverse effects (Bwatanglang et al., 2019 and Yaya et al., 2017).

The theoretical representation is given in the equation 5:

$$HI = \sum THQ \quad \ldots\ldots 5$$

Cancer Risk Index (CRI)

The cancer risk index (CRI) represents the probability of developing any type of cancer over a lifetime and it is an integration of the ADI with respect to the respective cancer slope factor CSF for each metal resulting in the linear equation 6 (Bwatanglang et al., 2019). The carcinogenic slope factor (CSF), is the carcinogenicity slope factor in mg/kg/day that converts estimated daily intake averaged over a lifetime of exposure directly to incremental risk of an individual developing cancer (Yaya et al., 2017).

$$CRI = ADI \times CSF \quad \ldots\ldots 6$$

Results and Discussion

Three absorbance values for each of the elements for each plant part were taken. The value and standard deviation for each were calculated to arrive at the values shown in table 2.

Table 2: Result of elemental analysis of the various samples of parts of *Balanites aegyptiaca* with their respective Permissible Limit (PL) and Reference Dose (RfD).

Element	Bark (ppm)	Leaf (ppm)	Seed (ppm)	WHO/FAO PL(mg/kg)	RfD(mg/kg/day)
Cr	N.D.	N.D	N.D	-	1.5
Mg	14.24±0.01	9.99±0.02	12.02±0.01	5.5	
Mn	1.18±0.02	0.90±0.01	0.29±0.01	5.5	0.14
Co	6.71±0.01	N.D.	N.D.	50.0	0.04
Ca	57.3±0.001	44.1±0.002	74.21±0.01	-	-
K	310.2±0.01	492.5±0.03	1170±0.01	-	-
Cu	2.20±0.01	1.80±0.02	N.D.	73.0	0.04
Fe	6.00±0.02	5.40±0.01	4.00±0.01	43.0	0.70
Zn	1.51±0.01	1.50±0.02	0.51±0.01	60.0	0.3

N.D. = Not detected.

(FAO/WHO, 2011 and USEPA, 1989)

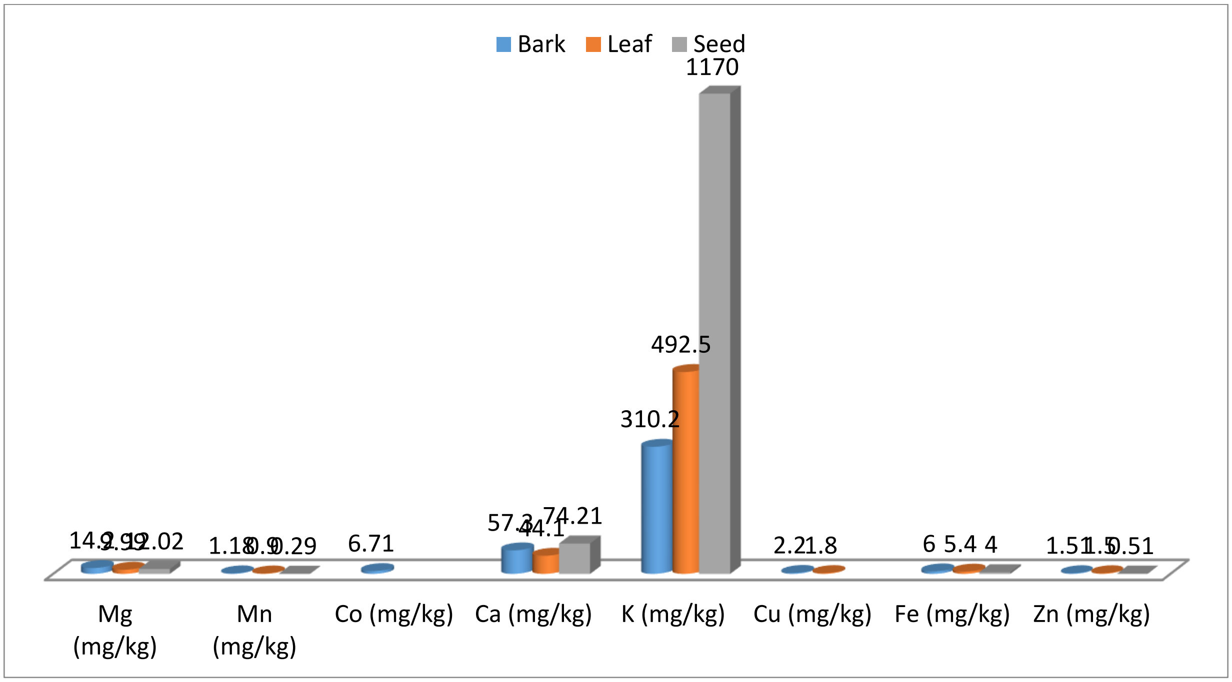

Figure 1: Concentrations (mg/kg) of different elements in the bark, leaf and seed of *B. aegyptiaca* plant.

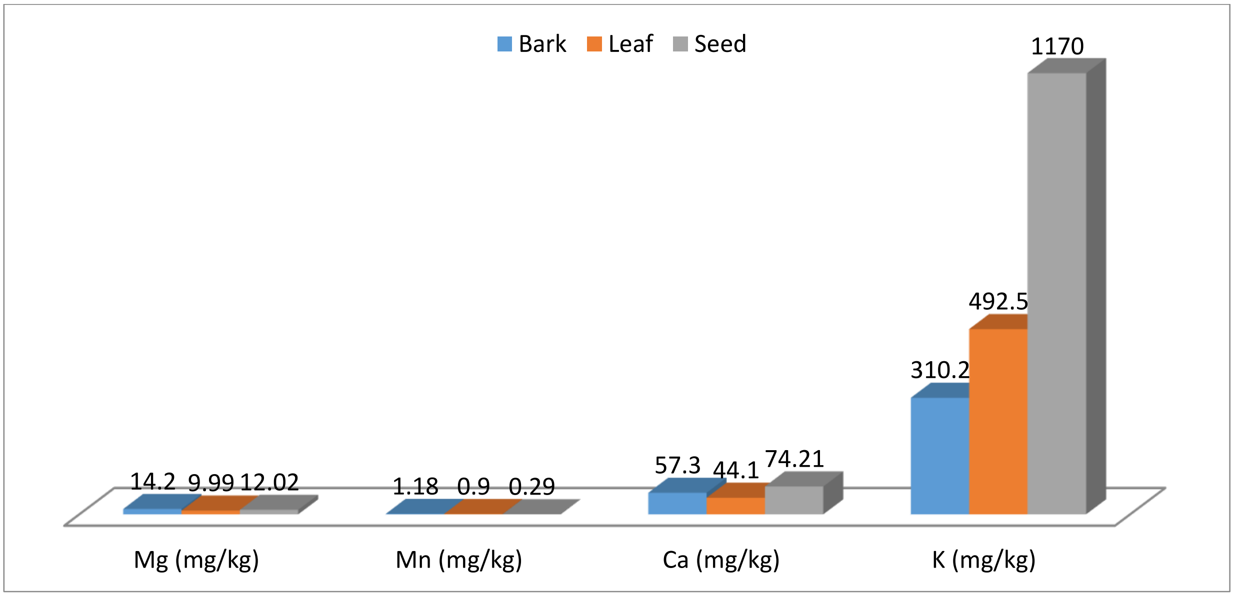

Figure 2: Concetrations {mg/kg) of Mg, Mn, Ca and K in different parts of *B. aegytiaca* plant.

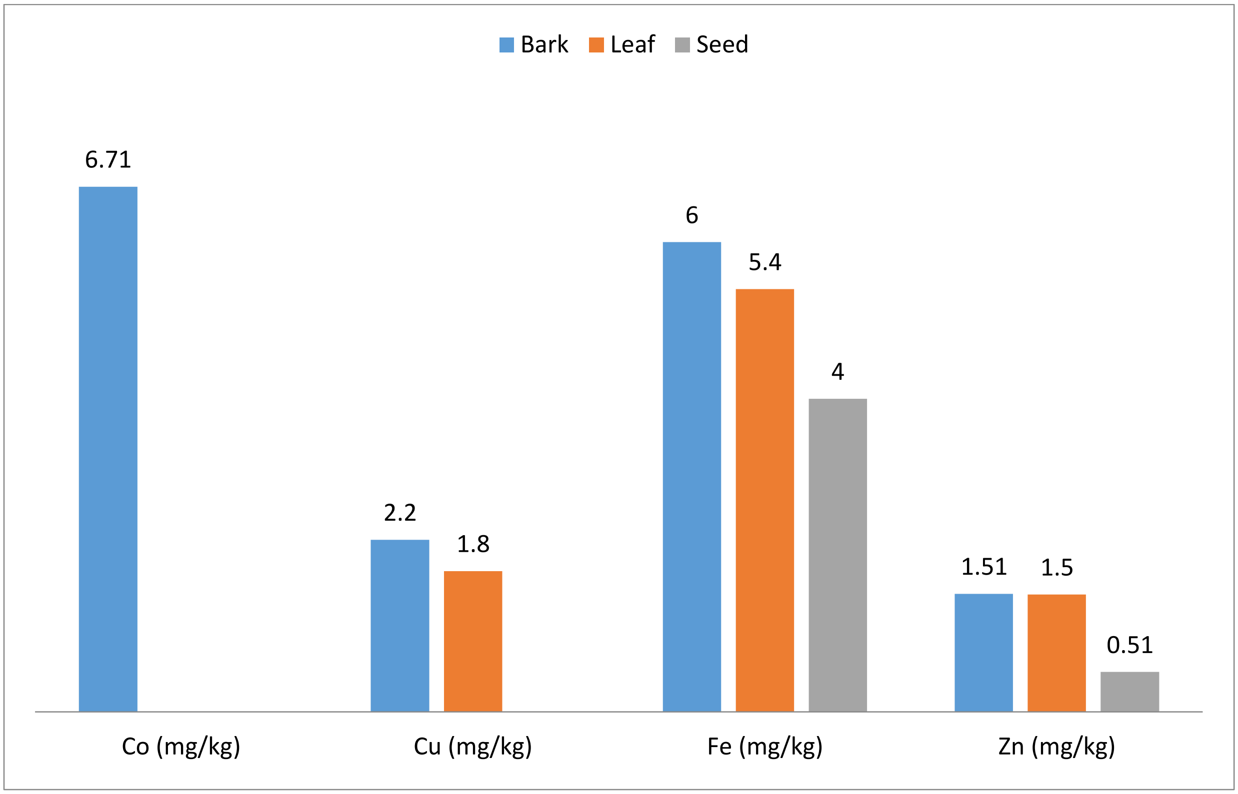

Figure 3: Concentrations (mg/kg) of Co, Cu, Fe and Zn in different parts of *B. aegytiaca plant*

Three samples of the plant comprising the bark, the leaf and the seed were collected to analyze for elemental composition. The elements in focus are those believed by research findings to possess insulin-potentiating ability in the plant as a function of the plant`s potentials in diabetes (Nsonwu, Usoro, Etukudo & Usoro, 2006; Zoroddu, Aashet, Crisponi, Medici, Peana & Nurchi, 2019; MedlinePlus, 2019) and to ascertain their degree of safety and health risk in the discharge of the therapeutic and nutraceutical roles. The health risk model generated by the United States Environmental Protection Agency (U.S. EPA) is employed to assess the human risk of the metals to humans of all categories. The model is an attempt to predict the possible carcinogenic and non-carcinogenic risks that may arise following the exposure of the elements (Bwatanglang et al., 2019; Yaya et al., 2017).

In table 2, the average concentrations of K, Ca, Mg, Co, Fe, Cu, Zn, Mn and Cr were given for the bark, leaf and seed samples. K has the highest recorded mean concentration followed by Ca and the least was Mn and off course Cr that was not detected at all. The ranking of the mineral concentrations in the bark of *B. aegyptiaca* is in the order K > Ca > Mg > Co > Fe > Cu > Zn > Mn. In the leaf sample some elements (Co, and Cr) were not detected. The ranking order is K > Ca > Mg > Fe > Zn > Mn. The seed sample appeared to have the least number of elements detected and is in the order K > Ca > Mg > Fe > Zn > Mn. However, the mean value of elemental concentrations across the three samples of the bark, leaf and seed revealed that the seed (210 mg/kg) had the greatest concentrations of elements followed by the leaf (79.45 mg/kg) and the least average value of mineral composition by the bark with a value of 49.64 mg/kg respectively. In the final analysis, viewing the cumulative concentrations of the element across the three samples K ranked highest with a total value of 1972.7 mg/kg followed from a distance by Ca (175.61 mg/kg), Mg (36.25 mg/kg), Fe (15.4mg/kg), Co (6.71 mg/kg), Cu (4.00 mg/kg), Zn (3.50 mg/kg) and Mn having the lowest value of 2.23 mg/kg respectively.

Potassium (K) is a very important element in human body where along with sodium it helps to regulate the water balance and acid-base balance in the blood tissue (Elfeel, 2010). Potassium recorded the highest average concentration value in the three samples of bark, leaf and seed; 310.2 ± 0.001, 492.5 ± 0.03 and 1170 ± 0.01 mg/kg respectively. Potassium is a systematic electrolyte and is essential in coagulating ATP with sodium. By US Recommended Dietary Allowance (RDA) is 4700 mg (DGA, 2005). It therefore suggests that mean values of potassium recorded from the plant is still way below the international standard and therefore, very safe for both consumption and medicinal infusion. Calcium, Ca helps in the building of bones, supports synthesis and functioning of blood cells. Calcium contributes in regulating osmotic pressure in the body and conducting of nerve impulse (Adamassu, Afework and Jae, 2013). Calcium is also needed for muscles, heart and digestive system. The mean values of calcium in the three sample of the plant were bark (57.3 ± 0.001), leaf (44.1 ± 0.002) and seed (74.21 ± 0.01) mg/kg respectively. According to US regulation, the Recommended Daily Allowance (RDA) for calcium is 1200mg and the Tolerable Upper Intake Level (UL) is 2500 mg (Zoroddu et al., 2019; Diabetes Care, 2018). The concentration of calcium obtained from this study in however, lower than the international bench mark, hence within safe level.

Magnesium (Mg) recorded were bark (14.24 ± 0.01), leaf (9.95 ± 0.02) and seed (12.02 ± 0.01) mg/kg respectively. Magnesium is an active component of many enzymes that are vital to metabolic activities of the body (Daya et al., 2010). It has RDA value of 420mg with a Tolerable

Upper Intake Level (UL) of 350mg EU (UL) of 250mg. FAO/WHO (2011) set the MPL of magnesium at 5.5 mg/kg (FAO/WHO, 2011). The result obtained in this study indicates the recommended value has not been exceeded.

Similar to copper, manganese is the center of manganese superoxide dismutase and plays an important role in the regulation of antioxidant defense functions. Hence, it is usually regarded as cofactor in enzyme function. Manganese has RDA value of 2.3mg and US (UL) of 11mg (Schlenker et al., 2014). FAO/WHO Maximum Permissible Limit (MPL) for Mn is 500 µg/g (FAO/WHO, 2001). The WHO Permissible Limit for Mn is 11mg/kg (World Health Organization, 1998) and the daily intake is set at 200mg/kg/day (Al Zel *et al.,* 2013). Appropriate levels of manganese are required for insulin synthesis and secretion (Naga Raju, Sarita, Ramana Murty, Ravi Kumar and Reddy, 2006) and a deficient level of manganese could result in poor glucose handling. The mean values obtained for manganese were Bark (1.18 ± 0.02), leaf (0.90 ± 0.01) and seed (0.29 ± 0.01) mg/kg respectively.

There is a relation between Mn and K and Ca and Mg that needs explaining in order to place their positions in the proper perspective for better understanding. When plants get adequate supply of Mn, K absorption is tremendously enhanced even without the addition of supply of K. when Mn level increases, the level of K also increases and similar to Ca and Mg without additional supply. Plants which produce fruits with high concentration of carbohydrates such as *B. aegyptiaca* require a great deal of potassium, K for carbohydrate transport into the fruits. The fruits function as storage for sugar and consequently also storage sinks for potassium (Euguene, Benjamin & David, 1969) hence the high concentration of potassium in Addua. High carbohydrate fruits or plants such as tomatoes or potatoes need a great supply of potassium to fill the fruits. K, usually is readily absorbed in plant from the soil (Adeyeye, 2005).

Ca appeared to enhance the rate of Mn absorption, whereas, Mg has a highly depressive effect. The combination of both Ca and Mg are even more inhibitory to Mn absorption than Mg alone. Mg has no effect on the usual negligible Ca absorption by the tissue, but effectively inhibits the absorption of Mg (Euguene et al., 1969).

Copper is an essential metal that is found in various enzymes throughout the body. Importantly, copper is a center in the enzymes cytochrome c oxidase and superoxide dismutase. The RDA (US) for copper is 0.9mg, the US Tolerable Upper Intake Level (UL) is set at 10mg and that of the EU (UL) is 5mg (Zoroddu et al., 2019). The FAO/WHO safe Limit for Cu is 73.0µg/g (Euguene, Benjamin and David, 2001). Copper helps in the absorption of iron from gastrointestinal tract and incorporate same in hemoglobin (Adamassu et al., 2013) and hints that the fruit and leaves showed an average of 0.6mg/kg. The value obtained from this study only revealed for the bark and leaf measuring 2.20 ± 0.01 and 1.80 ± 0.02 mg/kg respectively. The results indicate that the plant does not pose any kind of danger comparing with international bench marks.

The regulatory limits of the WHO Permissible Level for copper in herbal medicines is 10mg/kg (WHO, 1998) and the daily intake is 2 -3mg/day (McGrath and Smith, 1990). But China and Singapore set the permissible limits of 20 ppm and 150 ppm respectively (Jabeen, Shah, Khan, and Hayat, 2010). Copper is an essential component of many enzymes. It has both beneficial and toxic effects depending on its level of consumption.

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Iron is required in the body for the proper functioning of many proteins and enzymes, notably hemoglobin to prevent anemia. The average values of iron reported in this study were bark (6.00 ± 0.02), leaf (5.40 ± 0.01) and seed (4.00 ± 0.01) mg/kg respectively. It has US RDA value of 18mg and US (UL) of 45mg. The Maximum Permissible Limit (MPL) of iron is set at 425.5mg/kg for vegetable (FAO/WHO., 2011). Iron function as hemoglobin in the transport of oxygen (Adamassu et al., 2013). The results for iron obtained as reported (Health Canada, 2005) of some selected medicinal herbs of Egypt as between 261ppm to 1239 ppm. Iron is an essential element that facilitates the oxidation of carbohydrates, protein and fat to control body weight. In the light of the RDA and MPL values, the result presented above still fall short of the ceiling value and therefore, the plant is absolutely in good company.

Cobalt is required for the synthesis of vitamin B_{12}, but the actions of bacteria are needed for the synthesis of vitamin, hence it is usually considered part of vitamin B_{12} which comes from eating animals and animal-sourced foods (Jabeen et al., 2010), in which seven herbal medicines used in Turkey had (0.14 ppm-0.48 ppm) concentration. Excess cobalt causes cobalt toxicity. The mean value of cobalt obtained in the analysis of the bark was 6.71 ± 0.01 mg/kg. Cobalt was not found in other parts of the plant. However, the FAO/WHO as reported by (Elagermi, Edwards, Ala tal, 2012) pegged the Maximum Permissible Limit (MPL) value of cobalt at 50 µg/g. The daily intake as reported that zinc is 11mg/day and 50mg/kg for medicinal plants (WHO, 1998). This is an indication that the consumption of the plant is safe as these limits have not been exceeded by the result.

Zinc is pervasive and is required for several enzymes such as carboxypeptidase, liver alcohol dehydrogenase and carbonic anhydrase. Zinc is a constituent of many enzymes and zinc dependent enzymes are involved in macronutrient metabolism and cell replication (Adamassu et al., 2013) with a record of 252mg/kg. The results in this study falls below any of these values with the bark (1.51 ± 0.01), leaf (1.50 ±0.02) and seed (0.51 ± 0.01) mg/kg respectively. Zinc is an essential element required for normal body growth, proper thyroid function, blood clotting and DNA synthesis. Though there is little information about its toxicity, consumption of zinc beyond the permissible limit may result in toxic effect on the immune system and reduced copper level in the body (Waheed & Fatima, 2013). The permissible limit for zinc in herbal medicine set by WHO/FAO is 50 mg/kg. Zinc has RDA set at 11mg, US(UL) 40mg and EU(UL) of 25mg. Excess zinc results in zinc toxicity (NIH, 2016). The Maximum Permissible Limit (MPL) for Zinc nonetheless is 99.4mg/kg (FAO/WHO, 2011). It is therefore, within the safety nets of world standards.

Human Health Risk Assessment

The results non-carcinogenic risks for various metals through all exposure routes or pathways are presented in Table 3. The non-carcingenic risk posed by K, Ca, Mg, Mn, Co, Cu, Fe and Zn in the bark, leaf and fruit of *Balanites aegyptiaca* (Addua) through different exposure pathways (ingestion, dermal contact and inhalation were assessed. The calculated Average Daily Intake (ADI) values for each exposure pathways for both children and adults were as presented in Table 3. The results the average values of ADI recorded for the various sample parts of the plant decreases in the order leaf > seed > bark. There are however, exceptional cases of magnesium where bark showed a higher value than the seed. The trend is similar moving from ingestion to dermal and then to inhalation for the leaf for iron and zinc (seed > leaf > bark.

The metals are in the following order for the calculated ADI:

Ingestion: K > Ca > Fe > Co > Mg > Mn > Zn > Cu.

Dermal adsorption: K > Ca > Fe > Co > Mg > Mn > Fe >Cu.

Inhalation: Fe > K > Ca > Co > Mg > Mn > Zn > Cu.

The ADI values for K and Ca are relatively high due to their high concentration in the parts which is not far from the fact that they very much absorbed by the plant in part due to their high solubility and availability of alkaline metals and alkali earth metals. The analysis showed that the ADI values descended in the order of ingestion > dermal adsorption > inhalation. Similar findings were reported in previous studies (Yaya et al., 2017; Xiao, Wang, Li, Wang and Zhang, 2017 and Gay & Korre, 2006) for children and dermal adsorption > ingestion > inhalation for adults. The overall results demonstrated that children are at greater risk and more susceptible to higher level of the exposure dose than adults. This is also in tandem with the findings of (Bwatanglang et al., 2019).

Table 3: Results of calculated Average Daily Intake (ADI) of the elements for both Children and Adults

	ADI (ingestion)		**ADI(Dermal)**		**ADI(inhalation)**	
Element	**Children**	**Adults**	**Children**	**Adults**	**Children**	**Adults**
Magnesium (Mg)						
Bark	3.66E-4	3.50E-9	3.62E-5	9.20E-5	7.00E-9	3.50E-9
Leaf	2.57E-10	6.42E-5	2.68E-5	1.85E-5	4.87E-9	2.46E-9
Seed	3.0E-4	7.72E-5	3.23E-5	2.23E-5	6.00E-9	2.96E-9
Average	3.08E-5	4.71E-5	3.24E-5	4.44E-5	5.96E-9	2.97E-9
Manganese						
Bark	3.03E-5	7.58E-6	3.17E-6	2.19E-6	5.80E-10	2.90E-10
Leaf	2.31E-5	5.78E-6	2.42E-6	1.67E-6	4.43E-10	2.21E-10
Seed	7.45E-6	1.86E-6	7.79E-7	5.38E-7	1.47E-10	7.13E-11
Average	2.03E-5	5.07E-6	2.12E-6	1.47E-6	3.90E-10	1.94E-10
Cobalt						
Bark	1.72E-4	4.31E-5	1.80E-5	1.24E-5	3.30E-9	1.65E-9
Leaf	-	-	-	-	-	-
Seed	-	-	-	-	-	-
Average	1.72E-4	4.31E-5	1.80E-5	1.24E-5	3.30E-9	1.65E-9

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Calcium						
Bark	1.47E-3	3.68E-4	1.54E-4	1.06E-4	2.82E-9	1.41E-8
Leaf	1.13E-3	2.83E-4	1.18E-4	8.18E-5	2.17E-8	1.08E-8
Seed	1.90E-3	4.77E-4	1.99E-4	1.38E-4	3.65E-8	1.83E-8
Average	1.50E-3	2.66E-3	1.57E-4	1.09E-4	2.02E-8	1.44E-8
Potassium						
Bark	7.79E-3	1.99E-3	8.33E-4	5.75E-4	1.53E-7	7.63E-8
Leaf	1.27E-2	3.16E-3	1.32E-3	9.13E-4	2.42E-7	1.21E-7
Seed	3.01E-2	7.52E-3	3.14E-3	2.17E-3	5.75E-7	2.88E-7
Average	1.69E-2	4.22E-3	1.76E-3	1.22E-3	3.32E-7	1.62E-7
Copper						
Bark	5.65E-5	1.41E-5	5.91E-6	4.08E-6	1.08E-9	5.41E-10
Leaf	4.63E-5	1.16E-5	4.83E-6	3.33E-6	8.85E-10	4.43E-10
Seed	-	-	-	-	-	-
Average	5.14E-5	1.29E-5	5.37E-6	3.71E-6	9.83E-10	4.92E-10
Iron						
Bark	1.54E-4	3.88E-5	1.61E-5	1.11E-5	2.95E-5	1.48E-9
Leaf	1.39E-4	3.47E-5	1.45E-5	1.00E-5	2.66E-9	1.33E-9
Seed	1.03E-4	2.57E-5	1.07E-5	7.42E-6	1.97E-9	9.84E-10
Average	1.32E-4	3.31E-5	1.38E-5	9.51E-6	9.83E-6	1.26E-9
Zinc						
Bark	3.88E-5	9.70E-6	4.05E-6	2.80E-6	7.43E-10	3.71E-10
Leaf	3.86E-5	9.64E-6	4.03E-6	2.78E-6	7.38E-10	3.69E-10
Seed	1.31E-5	3.28E-6	1.37E-6	9.46E-7	2.51E-10	1.25E-10
Average	3.02E-5	7.54E-6	3.15E-6	2.18E-6	5.77E-10	2.88E-10

The Target Hazard Quotient (THQ)

The THQ for the samples are described in Table 4 for Fe, Cu, Co, Zn and Mn for children and adults using the various pathways of exposure. The results for the THQ were found to be < 1. The THQ for Co, Cu and Fe were found to rank very highest among the others due to their high level of concentrations in the parts of the plant as a result of plant uptake from the soil. The THQ for children ingestion, dermal adsorption and inhalation were observed to follow the ranking Cu > Co

> Zn > Mn > Fe; Cu > Co > Zn > Mn > Fe and Fe > Cu > Co >Zn > Mn respectively. The adults THQ for ingestion, dermal adsorption and inhalation is in the following pattern Co > Cu > Zn > Mn > Fe; Co > Mn > Fe > Cu > Zn and Cu > Co > Mn > Fe > Zn accordingly. The THQ < 1 recorded for all the elements under review further suggest that no associated risk following the ingestion, dermal adsorption or inhalation for both children and adults. This is also supported by a recent study on vehicle-derived heavy metal assessment risk on communities along highway (Bwatanglang et al., 2019).

Health Index (HI)

The HI for various exposure pathways for the elements as presented in table 4 indicated that the human health index (HI) values < 1, which presupposes that there is no associated risk for both children and adults. The HI for adults is generally higher than those of the children across the various exposure pathways, except for the $HI_{inhalation}$ where the children`s value (1.40E-5) pitched higher thn that of the adults (5.78E-8). HI values for $HI_{ingestion}$, HI_{dermal} and $HI_{inhalation}$ is in the following decreasing order $HI_{ingestion}$ > HI_{dermal} > $HI_{inhalation}$.

Table 4: Hazard Quotient (HQ) values for for elements in adults and children for some parts of *Balanites aegpytiaca (Addua)*

	$THQ_{ingestion}$		THQ_{Dermal}		$THQ_{inhalation}$	
Elements	**Children**	**Adults**	**Children**	**Adults**	**Children**	**Adults**
Mn	1.45E-4	3.62E-5	1.51E-5	1.01E-5	2.79E-9	1.39E-9
Cu	1.29E-3	3.23E-4	1.34E-4	9.28E-5	2.46E-8	1.23E-8
Fe	1.89E-4	4.73E-5	1.97E-5	1.36E-5	1.40E-5	1.80E-9
Zn	1.01E-4	2.51E-5	1.05E-5	7.27E-6	1.92E-9	9.60E-10
Co	4.30E-3	1.07E-3	4.50E-4	3.10E-4	8.25E-8	4.13E-8
HI($\sum THQ$)	6.03E-3	1.50E-3	6.29E-4	4.34E-4	1.41E-5	5.78E-8

Conclusion

The contamination of herbal medicine/preparations by excess metals is of great concern because of their toxic and cumulative tendencies. The overall analysis of the three samples of bark, leaf and seed of *Balanites aegyptiaca*, Desert Date (Addua) known for its potency in the treatment of diabetes and nutritive value as a vegetable and snacks, as commonly consumed in Northern Nigeria and Sub-Saharan Africa and Asia, showed the presence of the metals in the order of decreasing concentrations in the bark sample K > Ca > Mg > Co > Fe > Cu > Zn > Mn. In the leaf sample fewer elements were detected which excluded Co, and Cr. The ranking order is K > Ca > Mg > Fe > Zn > Mn. The seed sample appeared in the order K > Ca > Mg > Fe > Zn > Mn. Though the concentrations of the heavy metals in all the tested samples were below the international accepted permissible limit, their unsupervised use could have cumulative effect, which in turn may lead to their toxicity. The THQ for the non-carcinogenic risk were all < 1 for all metals and the various exposure pathways. In the same token, the trend is same for HI for both children and adults. This is a pointer to the fact that no immediate danger to potential non-carcinogenic risk. The results also show that there is no immediate carcinogenic risk of all pathways. Furthermore, the study revealed the order of pathway in the following decreasing order $HI_{ingestion} > HI_{dermal} > HI_{inhalation}$ and most of all, the HI values for adults generally higher than that of the children. This however, suggests that adults are at greater risks of and could be more susceptible to potential carcinogenic risk for continual exposure indicating some concern about the regular use of some of the infusion from the plant.

Recommendations

In view of the above findings, the followings are some suggestions to ensure maximal benefits from the treasure locked within the desert date (addua plant). First, constant and regular evaluation of the plant to ascertain the level of heavy metal concentration in it to avoid exceeding the threshold of the maximum metal concentration in the body when used as vegetable or infusion for medicinal purposes. Secondly, while the fruits, bark and leaves are highly recommended for use as vegetables in food and medicine for treatment, care should be taken to properly screen them using suitable techniques to regulate its elemental components to avoid excess intake of the metals that may bio-accumulate with time. Also, more research is recommended by traditional medical experts in the determination of the safe dosage of the plant parts for adults and children alike either as food or medicine. In addition, due to the rich minerals embedded in the desert date, it is highly recommended for use as food supplement, additive and enrichment in condiments, confectioneries and pastries by food industries. Finally, general awareness of the potentialities of the desert date be made known to the general public.

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