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COMPARATIVE STUDY OF THE COMPOSITION OF THE MACRO- AND MICRO-NUTRIENTS IN THE LEAVES OF *SYNADENIUM GRANTII* HOOK WITH THE TOLERABLE UPPER INTAKE LEVELS FOR CHILDREN, ADOLESCENTS, PREGNANT WOMAN AND FEMALE

[1]Igor Domingos de Souza, [2]Ana Lucia Alves de Arruda, [1]Elaine Silva de Pádua Melo, [1]Rafaela Henriques Rosa, [1]Ana Carla Gomes Rosa, [1]Joseane Bortolanza de Oliveira, [1]Rita de Cassia Avellaneda Guimarães, [2]Marcos dos Santos Cândido and [1,*]Valter Aragão do Nascimento

[1]Grupo de Espectroscopia e Bioinformática Aplicados a Biodiversidade e a Saúde, School of Medicine, Postgraduation Program in Health and Development in the Middle West Region, Federal University of Mato Grosso do Sul, Brazil, Zipcode: 79070900, Campo Grande, MS, Brazil

[2]Faculdade Unigran Capital, Abrao Júlio Rahe, 325, Zipcode: 7910010, Campo Grande, MS, Brazil

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ABSTRACT

The aim of studies was to compared 14 minerals in *Synadenium grantii* leaves used in the treatment of human diseases with tolerable upper intake levels (ULs) for children, adolescent, pregnancy and female. Concentrations of minerals in samples were determined using induction coupled optical emission spectrometry and the results also were compared to values of FDA and WHO for children, adolescents, pregnancy and female. Comparative results showed that according to UL, the elements Na, P, Cu, Fe, Mn and Zn in *Synadenium grantii* leaves does not represent a risk of adverse health effects. The concentration of Mo is below of limit set by UL only children (4-8 years), adolescent, pregnancy and female. Leaves of these plants accumulate Cr above limit of FAO. The concentration of Ni is high and can be harmful as it exceeds the UL per day. The content of Mo is above the UL for tolerable intake level for children aged 1-3 years. The value Cd obtained is above the guidelines established by the WHO. For elements such as potassium, cadmium, chromium, silicon, cobalt and aluminum, the present study showed that there are gaps regarding knowledge of the levels in which nutrients can be ingested (UL), especially for children, adolescents and pregnancy and female.

Corresponding author:

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INTRODUCTION

Minerals are present in different forms in the nature and are recognized as essential components of certain metabolic processes in the acid-base equilibrium of the human body, animals and plants. Some medicinal plants have therapeutic properties and are nutritionally important because of their high contents of minerals (Preedy *et al*, 2011). According to the World Health Organization (WHO, 2005), in the Africa up to 90% and in India 70% of the population depend on medicinal plants as the only way of access to basic health care.

In China, around 40% of all health care delivered and in the United States, in 2007, about 38% of adults and 12% of children were using some form of traditional medicine (Ernst *et al*, 2005; Barnes *et al*, 2008). In fact, people use medicinal plants as remedies due to the high cost of manufactured drugs, as well as the dissatisfaction with traditional medicine care and difficulties to access the health public system (Canter *et al*, 2004). In recent years, several authors in different countries have focused their study on the concentration levels of traces and toxic elements that cause health problems due to the

prolonged ingestion or overdose of some species of medicinal plants. Their results were compared with permissible limits values of mineral concentration established by FAO/WHO in edible plants or others species of plants (Aziz *et al*, 2016; Dastagir *et al*, 2014; Jabeen *et al*, 2010). Research involving the quantification of mineral concentration in medicinal plants was carried out in Brazil and compared to FAO/WHO values, and daily recommendations of ingestion (Souza *et al*, 2017).
As well as India (De, 2016), Brazilian biodiversity has underexploited medicinal plants which have a promising economic role to local population and pharmaceutical industries, such as *Synadenium grantii* Hook F. (Euphorbiaceae). This is a small tree native to East Central Africa and called African Milk Bush, erect, richly branched from near the base and in its habitat will reach up to 5 m in height. In Brazil in the hot tropical climate with low rainfall, these medicinal plants species grows in the fields and urban area. The leaves are greenish, margins entire or finely toothed towards the apex, more or less spirally arranged, 10-15 cm long and 8-12 cm wide sessile or gradually tapering from above the middle into a short on both sides, cordate at the base and narrowly pointed at the apex, and coarsely toothed, it has short petioles and dark red flowers (Willis, 1997).

In folk medicine, the latex of the stem, leaves and flowers of *S. grantii* are used for the treatments of neoplasic diseases and gastric disorders such as peptic ulcers and gastritis inflammatory. However, toxicity and anti-ulcer activity were also tested in rats, where the data indicate that *S. grantii* latex present gastric protection, and showed low toxicity when dilute in water (Costa *et al*, 2012). The cytotoxicity as well as the antiparasitic activity of the chloroform extract was performed and proved to be active (Hassan *et al*, 2012). Antioxidant properties showed that biological activities may be associated with the presence of flavonoids and terpenes (Munhoz *et al*, 2014). In Brazil, the Board Resolution Collegiate (RDC) nº 10/2010 provides a list of plant species of several species - selected according to its traditional use and methods of use as well the quantities to be eaten (Brasil, 2010). However, some species of Brazilian medicinal plants are not included in this list. Precautions are indispensable when larger amounts of the products are consumed by children, adolescents and pregnant woman during long-term therapy.

In our previous studies, the concentration of micro- and macronutrients in the leaves were determined using inductively coupled plasma optical emission spectrometry (ICP-OES), considering selected wavelengths for the detection of each element. As results, in the leaves of *S. grantii* the content of magnesium (Mg) was reportedly higher than the permissible levels recommended by tolerable upper intake level for adults and Ni, Cu, Cr, Cd above the limit above the permissible limit set by WHO and FAO (Souza *et al*, 2017). There are no comparative studies of macro and micronutrients concentration values obtained in the leaves of *S. grantii* with tolerable upper intake level limits for children, adolescents, pregnant women and female. This plant is used in the treatment of diseases by people that living in Campo Grande, State of Mato Grosso do Sul, Brazil. The constituents of some species of medicinal plants can often pose a risk children, adolescents, pregnant women and female when consumed in large quantities. According the WHO, children are more vulnerable than adults to environmental risks (WHO, 2010). Studies on the continued use of medicinal plants during pregnancy and lactating, show various adverse effects, such as teratogenic, embryotoxic and abortive effects, exposing these women, their fetus and babies to health unknown risks (Macías-Peacok *et al*, 2009). According the dietary reference intake (DRI), the reference values include both recommended intakes and tolerable upper intake levels (ULs) for all age and sex group. The ULs are defined as the highest level of daily nutrients intake that is likely to pose no risk of adverse health to almost all individuals (Otten *et al*, 2006). This is the first study reporting of concentrations of macro- and micronutrients in *S. grantii* leaves compared with tolerable upper intake levels values for children, adolescents, pregnant woman and female. This work is an extension of paper published in ref. (Souza *et al*, 2017) in which macro- and micronutrients in *S. grantii* leaves were obtained by inductively coupled plasma optical emission spectrometry (ICP-OES) and compared with levels recommended by tolerable upper intake level for adults.

MATERIALS AND METHODS

Sample collection

Sample of *Synadenium grantii* leaves was collected in Campo Grande, State of Mato Grosso do Sul, Brazil. The sample was identified by Fábia Alves and deposited (No 53971) in the herbarium of the Federal University of Mato Grosso do Sul (UFMS), Brazil. Details on sample collection are giving in ref. (Souza *et al*, 2017).

Sample preparation and digestion procedure of the *Synadenium grantii* leaves

All recipient as the vessels and flasks were cleaned with HNO_3 and with Milli-Q water. The *Synadenium grantii* leaves were washed with deionized water and then allowed to sundry in the oven dried at the temperature of 45±5 °C for 24 hours. The dried samples were then ground with a manual grinder into powder and sieve to get very fine powder. Digestions procedure of the *S. grantii* leaves in triplicate were prepared with mixture of 0.5 g sample plus 5 mL HNO_3 (65% Merck) and 3 mL H_2O_2 (35%, Merck). Subsequently, the samples were placed on digestion vessels of the microwave digestion equipment (Speed wave Berghof, Germany). After digestion, samples were diluted to 100 mL with ultrapure water. Since the final acid concentration of the samples was quite high (4% HNO_3). After all procedure acid digestion procedure the samples can be introduced into the ICP-OES in liquid form.

Elemental analysis by ICP-OES technique

The contents of macronutrients (K, Na, P) and micronutrients (Cr, Cu, Fe, Mn, Mo, Zn, Si, Ni, Co, Cd, Al) in *Synadenium grantii* leaves were detected by ICP-OES (Thermo Scientific – iCAP 6000 Series). The concentrations of each elements in leaves samples were determined using a corresponding standard calibration curves obtained by using a standard multielement solution with 100 mg L^{-1} of Co, Fe, Mn, Ni, Al, Cd, Cr, Mo and standard solution with 1000 mg L^{-1} of Cu, Zn (both from Sigma Aldrich®, WI, USA). We considering in our work the instrumentation and Techniques in Inductively Coupled Plasma Optical Emission Spectroscopy (Boss and Fredeen, 2004). Conditions of ICP-OES were optimized according to Table 1. As in our other manuscript (Souza *et al*, 2017), the methodology was adopted according to the experimental results of published (Mermet and Poussel, 1995; Trevisan and Nóbrega, 2007).

Table 1. The operating parameters of determination of elements by ICP-OES

Elements	Emission line (nm)*	Correlation
K	766.490	0.9136
Na	589.592	0.7941
P	178.284	0.9988
Cr	267.716	0.9993
Cu	327.396	0.9962
Fe	259.940	0.8722
Mn	259.373	0.9968
Mo	202.030	0.9977
Zn	206.200	0.9957
Si	212.412	0.9987
Ni	231.647	0.9890
Co	228.616	0.9999
Cd	226.502	0.9970
Al	308.215	0.9763

*Date published in Souza *et al* (2017).

Regarding the limit of detection (LOD) in ICP-OES, the concept of concentration equivalent to the background signal (BEC) was used (Thonsen *et al*. 2003). The operating conditions employed for ICP-OES determination were 1150W RF power, 12 L min^{-1} plasma flow, 0.5 L min^{-1} auxiliary flow, 0.8 L min^{-1} nebulizer flow, and 1.5 mL min^{-1} sample uptake rate. Analysis was performed in both the radial and axial mode depending on the element and matrix, while 2-point background correction and 3 replicates were used to measure the analytical signal. The emission intensities were obtained for the most sensitive lines free of spectral interference. The computers and scientific iTEVA software were used as instruments control of the ICP-OES. Thus, iTEva software to construct these curves for quantitation of the elements in the sample. In our case, calibration (standard) curves are generally linear over four orders of magnitude in ICP-OES, it is necessary to measure only one or two standard solutions, plus a blank solution, to calibrate the ICP-OES instrument. The concentration values obtained from the samples must be within the range of this standard curve. The standard curve should cover the entire range of expected concentrations.

Comparative criteria: Nutrient recommendations

The concentration of micro- and macronutrients in the *Synadenium grantii* leaves were compared to the limit specification of the tolerable upper intake levels (ULs) for children, adolescents and pregnant women and female. The Tolerable Upper Intake Level (UL) is based on a process for assessing the risk of adverse effects of nutrients (Dietary Reference Intakes DRI) (Otten *et al*, 2006). In the absence of established data on UL, some values for the concentrations of macroelements and microelements in this manuscript are compared with the permissible limits set by the Food and Agriculture Organization (FAO) and the World Health Organization (WHO) or with evidence from published fruit results.

RESULTS AND DISCUSSION

The concentration of the elements determined in the *Synadenium grantii* leaves collected in Campo Grande - MS are shown in Table 2. Concentration of the macronutrients in the *S. grantii* decreases in the order of: K > Na > P, while those micronutrients were in the order of: Si > Al >Fe > Zn > Ni > Co > Mn > Cu > Mo > Cr > Cd. The results and discussions on the concentration of each element obtained in *S. grantii* leaves in this manuscript are presented in mg/100 g according to Table 2.

Potassium (K)

According to the data in Table 2, the content of K was 1,364 mg/100 g. The UL for potassium in children, adolescents, female and pregnant women has not been established. Potassium is an essential macronutrient for a human, the body excrete excess potassium via the urine when consumption exceeds needs (Young, 2001; Rabelink *et al*, 1990), and there have been no reports of toxicity of potassium from consumption in food or medicinal plants.Therefore, this does not represent a risk of adverse health effects for children, adolescents, female and pregnant woman.

Sodium (Na)

In Table 2, the concentrations of Na obtained in the *Synadenium grantii* leaves have below values than those established by UL values for consuming sodium in children, adolescents and pregnant woman and female (1,500-2,300 mg/day). The Na concentration found in our work is below the values stipulated by the WHO (2 g/day in adults and should be adjusted for children for children relative to those of adults) (WHO, 2012).

Table 2. Elemental concentration (mg/100g) of macro and microelements in the leaves of the *Synadenium grantii* Hook used as medicinal plant in the Brazil compared to Recommended Dietary Allowances/Adequate Intake and values tolerable upper intake level (UL) for children, adolescents, pregnant and female

Elements	*Synadenium grantii** mg/100g	Children 1-3 y mg/day	Children 4-8 y mg/day	Adolescents 9-13 y mg/day	Adolescents 14-18 y mg/day	Pregnancy 19-30 y mg/day	Pregnancy 31-50 y mg/day	Female 19-30 y mg/day	Female 31-50 y mg/day
Macronutrients									
K	1,364	ND	ND	ND	ND	ND	ND	ND	ND
Na	63.833	1,500	1,900	2,200	2,300	2,300	2,300	2,300	2,300
P	50.94	3,000	3,000	4,000	4,000	3,500	3,500	4,000	4,000
Micronutrients									
Cr	0.489	ND	ND	ND	ND	ND	ND	ND	ND
Cu	0.910	1	3	5	8	10	10	10	10
Fe	8.345	40	40	40	45	45	45	45	45
Mn	1.047	2	3	6	9	11	11	11	11
Mo	0.522	0.3	0.6	1.1	1.7	2.0	2.0	2.0	2.0
Zn	3.621	7	12	23	34	40	40	40	40
Si	23.524	ND	ND	ND	ND	ND	ND	ND	ND
Ni	1.951	0.2	0.3	0.6	1.0	1.0	1.0	1.0	1.0
Co	1.723	ND	ND	ND	ND	ND	ND	ND	ND
Cd	0.044	ND	ND	ND	ND	ND	ND	ND	ND
Al	13.498	ND	ND	ND	ND	ND	ND	ND	ND

ND - Not determinable.
*Date published in Souza *et al* (2017).

Therefore, this plant does not represent a risk of adverse health effects for children, adolescents, pregnant women and female.

Phosphorus (P)

In Table 2, the concentration of P detected in *Synadenium grantii* leaves was 50.94 mg/100 g. The phosphorus level determined in the present study (50.94 mg/100 g) is below the UL for consuming P in children (3,000 mg/day), adolescents (4,000 mg/100 g), pregnant woman (3,500 mg/day) and female (4,000 mg/day). Therefore, this does not represent a risk of adverse health effects for children, adolescents, pregnant women and female.

Chromium (Cr)

The content of Cr observed in *Synadenium grantii* leaves was 0.489 mg/100 g (Table 2). The limits have not yet been established by UL for chromium for children, adolescents, pregnancy and female. There are insufficient data to establish a safe upper limit for chromium intake. In addition, special care should be taken with respect to the ingestion of plant in large quantities, as there are no limits established by Brazilian government on intake of this plant. On the other hand, the tolerable limit set by FAO/WHO (1984) for Cr in edible plants is 0.002 g/100 g (FAO/WHO, 1984). From comparison, concentration of Cr in the *S. grantii* leaves with those proposed by FAO/WHO (1984) it is found that this plant accumulates Cr above limit of FAO/WHO; therefore, the consumption should be limited in order to not cause any adverse effects. Information on beneficial effects of chromium and its use in dietary are controversial. According studies, the moderate uptake of chromium (III) through dietary supplements poses no risk (Eastmond *et al*, 2008). However, hexavalent chromium is very toxic and mutagenic when inhaled. The hexavalent chromium compounds is more toxic than the trivalent chromium compounds when both are administered by the oral route (Katz and Salem, 1992).

Copper (Cu)

In Table 2, the concentration of Cu in *Synadenium grantii* leaves was 0.910 mg/ 100 g. From comparison of the concentration of Cu in *S. grantii* with those proposed by the UL for consuming Cu in children (1.0-3.0 mg/day), adolescents (5.0-8.0 mg/100 g), pregnant woman and female (10.0 mg/day), it can be concluded that the concentration of Cu are below the tolerable upper intake level and does not represent a risk of adverse health effects for children, adolescents, pregnant women and female. However the continued use of this plant could cause toxicity. In fact, there cases are related to high exposure to copper due to animal milk stored or heated in copper or copper alloy containers, causing chronic copper toxicity include Indian childhood cirrhosis and Tyrolean infantile cirrhosis (Pandit and Bhave, 1996; *Müller et al, 1996*).

Iron (Fe)

The iron level in Table 2 (8.345 mg/100 g) is below the UL for the consumption of Fe in children (40 mg/day), adolescents (40-45 mg/100 g), pregnant woman and female (45 mg/day). From this comparison of the concentration of iron in *Synadenium grantii* leaves with those proposed by UL, it is concluded that *S. grantti* leaves does not represent a risk of adverse health effects for children, adolescents, pregnant woman and female. However, sufficient data to define a safe lower limit for toxic iron ingestions are not available. As little as 20 mg/ kg of elemental iron has caused toxicity in children, whereas ingestions of more than 50 mg/ kg often produce toxic effects (Fleisher and Ludwig, 2010). In fact, for medicinal plants the WHO (2005) limits not yet been established for Fe, as well as in Brazil, there are no data on limitation of the concentration iron in medicinal plants.

Manganese (Mn)

In Table 2, the concentration of Mn in *Synadenium grantii* leaves was 1.047 mg/100 g. For all age ranges presented in Table 2, the Mn levels for children (2-3 mg/100 g), adolescents (6-9 mg/100g), pregnancy and female (11 mg/100g) were below the UL values. Therefore, the consumption of one portion of *S. grantii* does not confer a risk of adverse effects. According to study on magnesium metabolism in health and disease, magnesium from food does not pose a health risk in healthy individuals, however, high doses of magnesium from dietary supplements or medications often result in diarrhea (Musso, 2009).

Molybdenum (Mo)

The content of Mo observed in the leaves of *Synadenium grantii* was 0.522 mg/100 g (Table 2), which is above the UL for tolerable intake level for children aged 1-3 years (0.3 mg / day), and below the UL for consuming Mo in children aged 4-8 years (0.6 mg/day), and adolescents (1.1-1.7 mg/day), pregnancy and female (2 mg/day). Level of daily nutrient intake that is likely to posse no risk of adverse effects for adolescents, pregnancy and female could cause toxicity in children when ingested in grant quantities. Researches of the consumption medicinal plants containing molybdenum as a mode of treatment of variety of ailments in folk cultures are scarce in the Brazilian literature and those of other countries. However, the toxicity of molybdenum compounds is low in humans. In addition, there only one report of acute toxicity related to molybdenum from a dietary supplement (Momcilovic, 1999).

Zinc (Zn)

The content of zinc in *Synadenium grantii* leaves fruits was 3.621 mg/100 g (Table 2). For all age ranges presented in Table 2, the zinc level (3.621 mg/100 g) is below the UL for the consumption of Zn in children (7-12 mg/day), adolescents (23-34 mg/100 g), pregnancy and female (40 mg/day). There are no limits of zinc concentration in medicinal plants by Brazil and World Health organization (WHO, 2005). However, manifestations of overt toxicity symptoms will occur with extremely high zinc intakes (Fosmire,1990).

Silicon (Si)

According to data in Table 2, the Si content found in *Synadenium grantii* leaves was 23.524 mg/100 g. Safe UL values were not established for silicon in humans. In the recent studies Korean, a mean intake of 37.5 ± 22.2 mg/day showed a positive relationship between dietary silicon intake from vegetables and the bone formation of young adult males with aged 19–25. (Choi and Kim, 2017). In addition, Korean data are in the same range as the mean estimated silicon intakes in the British data, which are estimated to be 20 and 50 mg silicon/day (Bellia *et al*, 1994).

Dietary intake of Si between 140-204 mg/day have been reported in China and India where plant-based foods may form a more predominant part of the diet (Chen *et al*, 1994). In Finland, intake in children (27 mg/day) is closest to adults (29 mg/day) (Kinrade *et al*, 1999). The concentration of silicon obtained in the *S. grantii* is within the stipulated range of values by other countries. We can not concluded that the concentration of Si obtained in our work not represent a risk of adverse health effects for children, adolescents, pregnant women and female.

Nickel (Ni)

The content of Ni observed in the leaves of *Synadenium grantii* was 1.951 mg/100 g (Table 2), which is above the UL for tolerable intake level for children aged 1-3 years (0.2 mg /day), children aged 4-8 years (0.3 mg/day), adolescents (0.6-1.0 mg/day), pregnancy and female (1.0 mg/day). The permissible limits of nickel for medicinal plants have not yet been set by WHO. From the values of UL, we conclude that the leaves are not safe for consumption; due to the continued use of this plant could cause toxicity. Nickel not destroyed in the body, it is e excreted in the urine and feces. However, the acute lethality of nickel following oral exposure is dependent upon the chemical form of nickel (Goyer, 1991).

Cobalt (Co)

According to data in Table 2, the content ofCowas1.723 mg/100 g in *Synadenium grantii* leaves. The limits have not yet been established for the cobalt UL for the studied populations. There is no set limit by WHO or Brazil for cobalt concentration in medicinal plant. According to ref. ATSDR (2004), children may be affected by cobalt the same ways as adults (he average person consumes about 11 micrograms of cobalt a day in their diet). However, high-dose cobalt can cause vomiting, nausea, damage to the thyroid and heart problems ATSDR (2004).

Cadmium (Cd)

The content of Cd observed *Synadenium grantii* leaves was 0.044 mg/100g (Table 2). There is not tolerable upper intake level (UL) for consuming of cadmium in children, adolescents, pregnancy and female. However, in some countries and set by WHO, for medicinal plants the permissible limit for cadmium is 0.03 mg/100g and 0.006 mg/day in finished herbal products (WHO, 2005). The value cadmium obtained in our work is above the guidelines established by the WHO and other countries as Chine, Thailand and Canada (WHO, 2005). Cadmium causes acute and chronic poisoning (Hayes, 1997).

In 2010, for cadmium the Joint FAO/WHO Expert Committee on Food Additives (JECFA) set a provisional tolerable monthly intake of 25 µg/kg body weight which is in the range of the previously set provisional tolerable weekly intake (PTWI) of 7 µg/kg body weight (FAO/WHO, 2010).

Aluminum (Al)

The amount of Al concentration in the leaves of *Synadenium grantii* analyzed was 13.498 mg/100 g. There is not tolerable upper intake level (UL) for consuming of Al in children, adolescents, pregnancy and female. According to Department of Agriculture (USDA) Nationwide Food Consumption Survey, the estimated daily aluminum intakes 0.12 mg Al/kg/day for adult males and females (ATSDR, 2008). There are very few data on oral aluminum bioavailability from foods, or beverages other than water (Krewski *et al*, 2007). All metals can cause disease through excess. Children are regularly exposed to much higher amounts of Al from vaccines than adults (Tomljenovic and Shaw, 2012). In addition, bone disease has also been seen in children taking some medicines containing aluminum (ATSDR, 2008).

Conclusion

New information on the concentration of macro- and micronutrients in the *Synadenium grantii* leaves were obtained and compared with the recommended values for children, adolescents, pregnancy and female. The new information on micro- and macronutrients in *S. grantii* leaves could helpful to determined the dosage to be given to patients considering elemental contents and concentrations. According to UL, the elements Na, P, Cu, Fe, Mn and Zn in *S. grantii* leaves does not represent a risk of adverse health effects for children, adolescents, pregnant women and female. The concentration of Mo is below of limit set by UL only children (4-8 years), adolescent, pregnancy and female. Present study showed that the *S. grantii* leaves accumulate Cr above limit of FAO. The concentration of Ni is high and can be harmful as it exceeds the UL per day. The content of Mo observed in the leaves of *S. grantii* is above the UL for tolerable intake level for children aged 1-3 years. The value cadmium obtained in our work is above the guidelines established by the FAO and WHO. Therefore, larger amounts of the products consumed in the long term should be avoided by children, adolescents, pregnancy and female. For elements such as potassium, cadmium, chromium, silicon, cobalt and aluminum, the present study showed that there are gaps regarding knowledge of the levels in which nutrients can be ingested (UL), especially for children, adolescents and pregnancy and female. Finally, the toxicity of these macro- and micronutrients would depend on their concentration in the plant from which they have been derived. Moreover, some of the elements in these medicinal plants have very important role in health as the presence of Ca, Mg, Fe and Zn indicates their ability to keep the healthy immune system.

REFERENCES

Agency for Toxic Substances and Disease Registry (ATSDR). 2004. Toxicological profile for cobalt. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service.https://www.atsdr.cdc.gov/toxprofiles/tp33.pdf

Agency for Toxic Substances and Disease Registry (ATSDR). 2008. Toxicological profile for Aluminum. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service.https://www.atsdr.cdc.gov/ toxprofiles/ tp22.pdf

Aziz, M.A., Adnan, M., Begum, S., Azizullabm, A., Nazir, R., Iram, S. 2016. A review on the elemental contents of Pakistani medicinal plants: Implication for folk medicines. *Journal of Ethonopharmacology*, 188: 177-192.

Barnes, P.M., Bloom, B., Nahin, R.L. 2008. Complementary and alternative medicine use among adults and children: United States, 2007. *National Health Statistics Reports*, 10(12):1-23.

Bellia, J.P., Birchall, J.D., Roberts, N.B. 1994. Beer: a dietary source of silicon. *The Lancet*, 343(8891): 235.

Boss, C.B., Fredeen, K.J. 2004. Concepts, instrumentation and techniques in inductively coupled plasma optical emission spectroscopy. 3º Edition, Perkin Elmer®.

Brasil. Ministério da Saúde. 2010. Agência Nacional de Vigilância Sanitária. Resolução de Diretoria Colegiada – RDC nº. 10, de 9 de março de 2010. Dispõe sobre a notificação de drogas vegetais junto à Agência Nacional de Vigilância Sanitária (ANVISA) e dá outras providências. Diário Oficial da União, Poder Executivo, Brasília, DF, Seção 1.

Canter, P.H., Ernst, E. 2004. Herbal supplement use by persons aged over 50 years in Britain: Frequently used herbs, concomitant use of herbs, nutritional supplements and prescription drugs, rate of informing doctors and potential for negative interactions. *Drugs & Aging*, 21: 597-605.

Chen, F., Cole, P., Wen, L., Mi, Z., Trapido, E.J. 1994. Estimates of trace element intakes in Chinese farmers. The *Journal of Nutrition*, 124: 196-201.

Choi, M.K., Kim, M.H. 2017. Dietary silicon intake of korean young adult males and its relation to their bone status. *Biological Trace Element Research*, 176(1): 89-104.

Costa, L.L.G., David, V.C., Pinto, R.M.C., Minozzo, B.R., Kozlowski Junior, V.A., Campos, L.A., Silva, R.Z., Beltrame, F.L. 2012. Anti-ulceractivity of *Synadenium grantii* latex. *Revista Brasileira de Farmacognosia*, 22(5): 1070-1078. http://dx.doi.org/10.1590/S0102-695X2012005000050

Dastagir, G., Hussain, F., Rizvi, M.A. 2014. Mineral composition of plants of family Zygophylllaceae and Euphorbiaceae. *Pakistan Journal of Botany*, 46(3): 887-896.

De, L.C. 2016. Medicinal and aromatic plants of northeast India. *International Journal of Development Research*, 06(11): 10104-10114.

Eastmond, D.A., MacGregor, J.T., Slesinski, R.S. 2008. "Trivalent chromium: assessing the genotoxic risk of an essential trace element and widely used human and animal nutritional supplement". *Critical Reviews in Toxicology*, 38(3): 173-190. doi: 10.1080/10408440701845401

Ernst, E., Schmidt, K., Wider, B. 2005. CAM research in Britain: The last 10 years. *Complementary Therapies in Clinical Practice*, 11:17-20. https://doi.org/10.1016/j.ctnm.2004.09.005

FAO/WHO (Food and Agriculture Organisation/World Health Organization), 2010. Joint FAO/WHO
Expert Committee on Food Additives. Seventy-third meeting, Geneva, 8–17 June 2010. Summary
and Conclusions. Issued 24 June 2010. Available from
http://www.fao.org/ag/agn/agns/jecfa/JECFA73%20Summary%20Report%20Final.pd

FAO/WHO (Food and Agriculture Organisation/World Health Organization), 2010. Joint FAO/WHO
Expert Committee on Food Additives. Seventy-third meeting, Geneva, 8–17 June 2010. Summary
and Conclusions. Issued 24 June 2010. Available from
http://www.fao.org/ag/agn/agns/jecfa/JECFA73%20Summary%20Report%20Final.pdf.

Food and Agriculture Organization of United Nations – FAO; World Health Organization – WHO. (1984). Format of codex commodity standards. Codex alimentarius commission: procedural manual. www.fao.org/input/download/report/411/al85_15e.pdf

Food and Agriculture Organization of United Nations – FAO; World Health Organization – WHO. 2010. Joint FAO/WHO Expert Committee on Food Additives. Seventy-third meeting, Geneva, 8-17 June 2010. Summary and Conclusions, Issued 24 June 2010. http://www.who.int/foodsafety/publications/chem/summary73.pdf

Fosmire, G.J. 1990. Zinc toxicity. *The American Journal of Clinical Nutrition*, 51(2): 225-227.

Fleisher, G.R., Ludwig, S. 2010. Textbook of pediatric emergency medicine, Lippincott Williams & Wilkins.

Goyer, R. 1991. Toxic effects of metals. In: Amdur, M.O., Doull, J.D. and Klaassen, C.D., Eds., Casarett and Doull's Toxicology, 4th Edition, Pergamon Press, New York, 623-680.

Hassan, E.M., Mohammed, M.M.D., Mohamed, S.M. 2012. Two new phorbol-type diterpene esters from *Synadenium grantii* Hook F. leaves. *Records of Natural Products*, 6(3): 255-262.
http://www.acgpubs.org/RNP/2012/Volume%206/Issue%201/36-RNP-1102-510.pdf

Hayes, R.B. (1997). The carcinogenicity of metals in humans. *Cancer Causes Control*, 8(3): 371-385. https://www.ncbi.nlm.nih.gov/pubmed/9498900

Jabeen, S., Tahir, M., Khan, S., Hayat, M.Q. (2010). Determination of major and trace elements in ten important folk therapeutic plants of Hapipur basin, Pakistan. *Journal of Medicinal Plants Research*, 47: 559-566.

Katz, S.A., Salem, H. 1992. "The toxicology of chromium with respect to its chemical speciation: A review". *Journal of Applied Toxicology*. 13(3): 217-224. doi:10.1002/jat.2550130314.

Kinrade, S.D., Del Nin, J.W., Schach, A.S. 1999. Stable five- and six-coordinated silicate anions in aqueous solution. *Science*, 285(5433): 1542-1545.

Krewski, D., Yokel, R.A., Nieboer, E., Borchelt, D., Cohen, J., Harry, J., Kacew, S., Lindsay, J., Mahfouz, A.M., Rondeau, V. 2007. Human health risk assessment for aluminium, aluminium oxide, and aluminium hydroxide. *Journal of Toxicology and Environmental Health Part B: Critical Reviews*, 10(Suppl 1):1-269.

Macías-Peacok, B., Pérez-Jackson, L., Suárez-Crespo, M.F., Fong-Domínguez, C.O., Pupo-Perera, E. 2009. Use of medicinal plants during pregnancy. *Revista Médica del Instituto Mexicano del Seguro Social*, 47: 331-4.

Mermet, J.M., Poussel, E. 1995. ICP Emission Spectrometers: 1995 Analytical Figures of Merit. *Applied Spectroscopy*, 49: 12A-18A.

Momcilovic, B. 1999. A case report of acute human molybdenum toxicity from a dietary molybdenum supplement--a new member of the "Lucormetallicum" family. Archives of Industrial Hygiene and Toxicology, 50(3): 289-297.

Müller, T., Feichtinger, H., Berger, H., Müller, W. 1996. *Endemic Tyrolean cirrhosis: an ecogenetic disorder. Lancet,* 347*: 877-80.*

Munhoz, A.C.M., Minozzo, B.R., Cruz, L.S., Oliveira, T.L., Machado, W.M., Pereira, A.V. et al. 2014. Chemical and Pharmacological Investigation of the Stem Bark of *Synadenium grantii*. *Planta Medica*, 80: 458-464. http://dx.doi.org/10.1055/s-0034-1368300

Musso, C.G. 2009. Magnesium metabolism in health and disease. *International Urology and Nephrology*, 41: 357-362.

Otten, J.J., Hellwig, J.P., Meyers, L.D. 2006. United States Department of Agriculture. Dietary Reference Intakes: The Essential Guide to Nutrient Requirements, Washington, US, The National Academies Press: Washington, US.

Pandit, A., Bhave, S. 1996. *Present interpretation of the role of copper in Indian childhood cirrhosis. The American Journal of Clinical Nutrition*, 63*(5):* 830S-*5S.*

Preedy, V.R., Watson, R.R., Martin, C.R. 2011. Handbook of Behavior, Food and Nutrition. Springer New York Dordrecht Heidelberg London.

Rabelink, T.J., Koomans, H.A., Hene, R.J. et al. (1990). Early and late adjustment to potassium loading in humans. *Kidney International*, 38(5): 942-947. http://www.ncbi.nlm.nih.gov/pubmed/2266680

Souza, I.D., Arruda, A.L.A., Silva, A.F., Rosa, R.H., Junior, M.A.F., Nascimento, V.A., Guimarães, R.C. 2017. Identification of macroelements and microelements in the leaves of the *Synadenium grantii Hook* used as medicinal plant in the Brazil. *International Archives of Medicine Section: Toxicology & Therapeutics*, 10(58): 1-12.

Tomljenovic, L., Shaw, C.A. 2012. Mechanisms of aluminum adjuvant toxicity and autoimmunity in pediatric populations. *Lupus*, 21(2): 223-30. doi: 10.1177/0961203311430221

Thonsen, V., Schatzlein, D., Mercuro, D. 2003. Limits of detection in spectroscopy. *Spectroscopy*. 18(12): 112-114.

Trevisan, L.C., Nóbrega, J.A. 2007. Inductively coupled plasma optical emission spectrometry with axially viewed configuration: an overview of application. *Journal of the Brazilian Chemical Society*, 18(4): 678-690.

Willis, J.C. 1997. A Dictionary of the Flowering Plants and Ferns. 8th edition. University Press, Cambridge. DOI: 10.2307/2258437.

World Health Organization (WHO). 2005. National Policy on Traditional Medicine and Regulation of Herbal Medicines. Geneva: Report of WHO global survey. http://apps.who.int/iris/bitstream/10665/43229/1/9241593237.pdf

World Health Organization (WHO). 2010. Children's Health and the Environment Annual Report. http://www.who.int/ceh/publications/ceh_annualreport_2010.pdf?ua=1

World Health Organization (WHO). 2012. Guideline: Sodium intake for adults and children. Geneva, World Health Organization (WHO).

http://apps.who.int/iris/bitstream/10665/77985/1/9789241504836_eng.pdf?ua=1&ua=1

Young, D.B. 2001. Role of potassium in preventive cardiovascular medicine. Basic Science for the Cardiologist Boston, Kluwer Academic Publishers.

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