HEALTH RISK ASSESSMENT OF NATURAL RADIONUCLIDE AND HEAVY METALS IN COMMONLY CONSUMED MEDICINAL PLANTS IN SOUTH-WEST NIGERIA

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ABSTRACT

The natural radionuclide and heavy metal contents of five commonly consumed medicinal plants in south-western Nigeria were determined using gamma spectrometry with high purity germanium detector and flame atomic absorption spectrophotometer. The activity concentration of ^{40}K ranged from 315.65 ± 39.17 to 892.04 ± 63.09 $Bqkg^{-1}$. ^{238}U ranged from 1.73 ± 1.95 - 5.41 ± 2.39 $Bqkg^{-1}$ and ^{232}Th ranged from 1.22 ± 1.75 $Bqkg^{-1}$ to 8.49 ± 2.69 $Bqkg^{-1}$ in zobo. The mean annual effective dose was found to be lower than the standard proposed by United Nation Scientific Committee on Energy and Atomic Research. Fatal cancer risk and hereditary cancer risk from ingestion of the plants lie within the safe limit as recommended by United State Environmental Protection Authority and World Health Organization. The mean concentrations of the heavy metals in the samples were compared with the permissible limit in literature and were found to be within the safe limit. The estimated annual daily doses are lower than the recommended daily intake except Zn which is higher. The estimated fractional hazard quotient of the metals is lower than or equal to 1 except for Zinc in garlic and ginger. Total hazard index obtained for all the samples are higher than 1.0 but lower than 3.0. This implies that there is no probable hazard from the consumption of these plants

Keywords
Radionuclide, Heavy metal, Fractional hazard quotient, Average daily doses, Effective dose

INTRODUCTION

Natural radionuclides (^{238}U, ^{232}Th and ^{40}K) and their decay products which originated from the earth's crust are the sources of natural radioactivity in the environment (Kessaratikoon and Awaekechi, 2008). Naturally occurring radioactive materials (NORMS) are found in every constituent of the environment: air, water, soil, food and in humans and according to the International Food Safety Authorities Network (INFOSAN, 2011), plants used as food commonly contain ^{40}K, ^{232}Th and ^{238}U and their progenies. Radionuclides along with other pollutants, like heavy metals can be added into the environment through industrial activities, municipal wastes, automobile exhaust, pesticides and fertilizers used in agriculture (Järup, 2003). Most of the radioactivity in the terrestrial environment whether natural or man-made is bound to the component of the soil. Transportation of this radioactivity from soil to vegetation is possible via dust deposition or root uptake and then to humans through inhalation, breathing and ingestion. Therefore, all pathways of exposure that originate from soil are potentially important for the purpose of radiation risk assessment (Ademola and Obed, 2012).

For more than two decades now, the World Health Organization (WHO) has been encouraging the use of traditional medicine globally by promoting the incorporation of its useful elements into national health care systems. Medicinal plants are administered in their raw form or in formulations such as solutions, tablets or capsules. The health effects of radiation exposures to natural occurring radioactive materials from intake of medicinal plants or herbal preparations may be associated with most forms of leukaemia and with cancer of many organs such as the bone, lung, breast and thyroid in the long term (UNSCEAR, 2000). Many naturally occurring radionuclides, elements or compounds such as metals and metalloids, accumulate along the food chain. The presence of metal pollutant such as cadmium (Cd) and lead (Pb) aids their entry into the food chain and thereby increases the toxicity effects of food in human and animal diet (Ademola *et al.,* 2015). Approximately 10-15% of ^{210}Pb and ^{214}Pb ions, 99% of ^{226}Ra and ^{228}Ra, ^{214}Bi (bone seeker) and ^{210}Po (soluble) reach the blood or the lung and are distributed to the whole body and exchanged with calcium in the mineral of skeletal tissues thereby making blood, bones, lung and other critical

organs to be exposed (UNSCEAR, 1988; 2000).

Many medicinal plants contain heavy metals over a wide range of concentrations and may present a health risk due to the toxicity of heavy metals which depends upon the chemical form of elements. Heavy metals are dangerous in the form of their cations and are highly toxic when bonded to the short chains of carbon atoms (Kirmani *et al.,* 2011). Human exposure to these harmful naturally occurring radioactive materials and heavy metals through human activity is mostly regarded as undesirable at every level due to the harmful effects on human health and the environment.

Medicinal plants are plants used to cure some ailments and are considered to be rich in ingredients which can be used in drug development and synthesis. According to the World Health Organization, about 80% of people in peripheral communities use only medicinal herbs for the treatment of diseases (Sahito *et al.,* 2003). When plants are used in the treatment of certain illnesses, they could be toxic if taken without prescription (Aleksandra *et al.,* 2015). Controlling the heavy metals and radionuclides contents in medicinal plants is imperative in order to ensure safety of their products. Hence, there is the need to carry out a systematic research on some of the most commonly consumed medicinal plants in Nigeria to ascertain the level of natural radionuclides and concentration of heavy metals in these plants. This would also be necessary in establishing policy, rules and regulations relating to processing and manufacturing of medicinal products in Nigeria.

Thus, this study is aimed at determination of the concentration levels of naturally occurring radioactive materials and heavy metals in some commonly used medicinal plants in order to determine their radiological implications as well as their toxicity levels.

MATERIALS AND METHODS
Sample Collection and Preparation
Five samples each of the five commonly consumed medicinal plants in south-western Nigeria, were collected from different local markets in the six states of the region. The commonly consumed medicinal plants sampled are zobo *(Hibiscus sabdariffa)*, turmeric *(Curcuma longa)*, basil *(Occimum basilicum)*, garlic *(Allium sativum)*, and ginger *(Zingiber officinale)*. Samples were collected and packed with identification labels. The samples were taken to the laboratory where they were cleaned with water to remove soil particles, and were then dried in air and weighed. The samples were thereafter oven-dried at $80\,^{\circ}$C to constant weight. The dried samples were then crushed, ground and sieved through a 2 mm mesh. One hundred gram of each of the dried samples was weighed and transferred into a special cylindrical plastic container of dimension (6.5 cm in diameter and 7.0 cm in height) and hermetically sealed with adhesive tape and kept for thirty days which is enough for secular equilibrium to take place (Olomo *et al.,* 1994). The samples were afterwards analyzed for radionuclide concentrations using gamma-ray spectrometry with hyper pure germanium detector.

Radioactivity Determination
The activity concentrations of the samples were determined using hyper pure germanium detector which has 80% relative efficiency and a resolution full width at half maximum of 2.3 keV at energy of 1.33 MeV of ^{60}Co. For effective and reliable shielding against the natural background radiation, the detector was enclosed in a 5 mm thick Lead (Pb) shield. The detector was connected to a pre-amplifier and a multi-channel analyzer with 16000 channels and interfaced to a computer system for data acquisition and analysis. Radiometric measurements were undertaken for qualitative and quantitative determination of different radionuclides present in the sample. The background radiations (which are the additional radioactivity in the environment) were corrected for by first obtaining the background count with the empty container of similar geometry for 10800 s, and then subtracted from the gross count. The activity concentration of ^{238}U was calculated from the average energies of ^{214}Pb (295 keV) and ^{214}Bi (351.9 keV), the activity concentration of ^{232}Th was determined from the average energies of ^{212}Pb (238 keV), ^{208}TI (583) and ^{228}Ac (911.2 keV), respectively while the activity concentration of ^{40}K was measured directly through the gamma line emission of 1460.8 keV. The specific activity (A_{sp})

of the radionuclides in the samples was obtained using equation 1 (Danko *et al.*, 2010; Twesigye *et al.*, 2015).

$$A_{sp} = \frac{N_c \exp(\lambda T_d)}{p T_c M \eta(E)} \qquad 1$$

where A_{sp} is the specific activity concentration in the sample, N_c is the net counts of the radionuclide in the samples, T_d is the decay time between the sampling and counting, p is the gamma emission probability (gamma yield), $\eta(E)$ is the absolute counting efficiency of the detector system, T_c is the sample counting time, M is the mass of the sample, exp (λT_d) is the decay correction factor for decay between time of sampling and counting and λ is the decay constant of the parent radionuclide.

Heavy Metal Analysis Method
Heavy metals (Al, Fe, Cu, Pb, Ni and Cd) contained in five medicinal plant samples obtained in the study area were analyzed using Flame Atomic Absorption Spectrophotometer (FAAS). The samples were prepared using chemicals of analytical grade with double distilled water. As described by Poldoski, (1980), 1 g of fine particles of each medicinal sample was weighed into a 100 ml digestion tube. Each of the tubes was labelled to avoid mix-up. 5 ml each of nitric acid and hydrogen peroxide were added while H_2SO_4 was added in small amount and the mixture was thoroughly stirred until white fumes evolved. The process was continued until the solution was clear. The solution was decanted and diluted with de-ionized water up to 100 ml before being filtered. The procedure was repeated for all the samples

Standard solution of the metals was prepared for calibration for each element being determined on the same day on which the analyses were performed in order to avoid possible deterioration of standard with time (Cantle, 1982). The atomic absorption instrument was set up and flame condition and absorbance were optimized for the analyte. Then blanks (deionized water), standards, sample blank and samples were aspirated into the flame in the flame atomic absorption spectrophotometer. Calibration curves were obtained for concentration versus absorbance. Data were analyzed using fitting of straight line by least square method. Necessary corrections were made during the calculation of concentration of various elements.

RESULTS AND DISCUSSION
Activity Concentrations and Dose Calculations
The activity concentrations of ^{238}U, ^{232}Th and ^{40}K obtained in the medicinal plant samples are presented in table 1. It is obvious that the activity concentration of ^{40}K was highest in all the samples; ranging from 315.65±39.17 to 892.04±63.09 Bqkg^{-1}. Plants absorb potassium from soil in different amounts according to their metabolism and might vary geographically from one place to another. The high activity concentration (See Table1) of ^{40}K may be due to the use of fertilizers by farmers to improve crop yields. The variation of ^{238}U activity concentration in the medicinal plant samples was not significant. The activity concentrations of ^{238}U obtained in this study ranged from 1.73±1.95 Bqkg^{-1} to 5.41±2.39 Bqkg^{-1}The activity concentrations of ^{238}U in the samples are lower than the world average (Table 1).The activity concentrations of ^{232}Th ranged from 1.22±1.75 Bqkg^{-1} in garlic to 8.49±2.69 Bqkg^{-1} in zobo. Also all the activity concentrations of ^{232}Th in the samples are lower than the world average (Table 1).

Table 1: Activity Concentrations of Radionuclides in the Medicinal Plant Samples (Bqkg^{-1})

Plant	A_K	A_U	A_{Th}
Zobo *(Hibiscus sabdariffa)*	541.36±54.32	5.41±2.39	8.49±2.69
Turmeric *(Curcuma longa)*	635.57±60.45	3.15±2.08	3.04±1.99
Basil *(Occimum basilicum)*	658.36±6.18	1.73±1.95	3.17±1.82
Garlic *(Allium sativum)*	301.46±39.18	2.54±1.96	1.22±1.75
Ginger *(Zingiber officinale)*	329.20±41.40	2.14±1.81	1.95±1.65
World Average (UNSCEAR, 2000)	420	33	45

A_K – activity concentration of ^{40}K; A_U - activity concentration of ^{238}U; A_{Th} - activity concentration of ^{232}Th

Calculation of Radiological Parameters
Effective dose

Effective dose is a useful concept which enables the radiation doses from different radionuclides and from different types and sources of radioactivity to be added. It is based on the risks of radiation-induced health effects and the use of the International Commission on Radiological Protection metabolic model that provides relevant conversion coefficient to calculate effective dose from the total activity concentrations of radionuclides measured in foods (ICRP, 1996). Radiation doses resulting from ingestion are obtained by measuring radionuclide activities in foodstuff and multiplying these by the masses of food consumed over a period of time. A dose conversion coefficient can then be applied to give an estimate of ingestion dose. Thus, the annual effective dose due to ingestion is calculated using the expression in equation 2 (Harb, 2015)

$$E_{Dose} = I_p \cdot DCF_{ing} \cdot A_{sp} \qquad 2$$

Where DCF_{ing} is dose conversion factor for ingestion, for each radionuclide (i.e., 2.8 x 10^{-7} Sv/Bq, 2.3 x 10^{-7} Sv/Bq and 6.2 x 10^{-9} Sv/Bq for ^{226}Th, ^{228}U and ^{40}K respectively for adult), I_p is the consumption rate from intake of natural occurring radioactive materials in medicinal plants, (a rate of intake of 1.8 kg/year was assumed for all the medicinal plants used) (Harb, 2015) assuming that a patient needs 100 ml/day of the medicinal plants during the period of treatment. A_{sp} is the activity concentration in the plant samples.

The mean annual effective dose due to ingestion of naturally occurring radioisotopes ^{238}U, ^{232}Th and ^{40}K in the five medicinal plants (zobo, turmeric, basil, ginger, and garlic) are shown in table 2. The largest ingestion dose was from ginger (22.36 μSvy^{-1}) and the lowest ingestion dose was from garlic (10.56 μSvy^{-1}). All the effective doses calculated for the samples are much lower than the world average of 70 μSvy^{-1} proposed by United Nation Scientific Committee on Energy and Atomic Research, (UNSCEAR, 2000) and also lower than the average radiation dose of 0.3 mSvy^{-1} received per person worldwide (WHO, 2007).

Fatal Cancer Risk from Ingestion of Medicinal Plants

A number of models for the calculation of lung cancer risk due to exposure to radionuclides and their short-lived radioactive daughters have been reported (ICRP, 1990; UNSCEAR, 1988; 1993). There is wide variation amongst the estimated value of the fatal cancer risk which is due to the assumed parameter used in the models. In this work, for simplicity of analysis, ICRP, (1990) assumed parameter was used. Fatal cancer risk was estimated from effective dose obtained using the International Commission on Radiological Protection cancer risk assessment methodology (ICRP, 2007) as stated in equation 3.

$$FCR = H_E \times DL \times RF \qquad 3$$

where H_E is the effective dose (μSv/y), DL is life expectancy (70 years) and RF is risk factor (Sv^{-1}). For stochastic effects, International Commission on Radiological Protection uses a value of 0.05 for the public as risk factor (ICRP, 1991). The values of fractional cancer risk obtained in this work are presented in table 2 (column 3). Fatal cancer risk obtained ranged from 36.96 (MPY)$^{-1}$ in garlic to 78.26 MPY^{-1} in ginger. This means that 78 persons out of 1 million people are likely to suffer from some cancer related diseases from intake of ginger. These values lie within the safe limit of 1 x 10^{-6} to 1 x 10^{-4} recommended by United State Environmental Protection Authority (USEPA, 1993) and World Health organization (WHO, 2007).

Hereditary Cancer Risk

To estimate the hereditary cancer risk from the consumption of medicinal plants, the ICRP, (1991) cancer risk assessment methodology was used. According to the ICRP recommendations, assumed parameter for members of the public is 4 x 10^{-2} Sv^{-1} (ICRP, 1991).

$$HCR = H_E \times DL \times RF \qquad 4$$

where HCR is hereditary cancer risk; H_E is the effective dose (Sv/y), DL is life expectancy (70 years) and RF is risk factor (Sv^{-1}). For stochastic effects ICRP uses a value of 0.04 for the public as risk factor (ICRP, 1991). The mean estimated

lifetime hereditary cancer risks in the five medicinal plants are presented in table 2 (column 4). Hereditary cancer risk obtained range from 29.57 MPY[-1] in garlic to 62.61 MPY[-1] in ginger. All the values obtained are much lower than the limit set by USEPA (1993) and WHO, (2007).

Table 2: Mean Values of Effective Dose (E), Fatal Cancer Risk (FCR), Hereditary Cancer Risk (HCR) and Internal Hazard Index (H_{in}) in all Samples of Medicinal Plants.

Plant	E (Svy^{-1})	FCR $(MPY)^{-1}$	HCR$(MPY)^{-1}$	(H_{in})
Zobo *(Hibiscus sabdariffa)*	12.56	43.96	35.17	0.18
Turmeric *(Curcuma longa)*	12.68	44.38	35.50	0.16
Basil *(Occimum basilicum)*	15.85	55.48	44.38	0.16
Garlic *(Allium sativum)*	10.56	36.96	29.57	0.08
Ginger *(Zingiber officinale)*	22.36	78.26	62.61	0.08

Internal Hazard Index

To assess the radiation hazard due to internal exposure from radon and its short-lived decay products, to the respiratory organs from the intake of the medicinal plant samples, it is necessary to calculate the internal hazard index (H_{int}) given by the expression:

$$H_{int} = \frac{A_{Ra}}{159} + \frac{A_{Th}}{259} + \frac{A_K}{4810} \leq 1$$

(Berekta and Mathew, 1985)   5

The average values of H_{int} obtained are 0.18, 0.16, 0.16, 0.08, 0.08 respectively, for zobo, turmeric, basil, garlic and ginger as presented in table 2 (column 5). It is lowest in ginger and garlic and highest in zobo. The values obtained for all the samples are less than unity as required

Heavy Metal Concentration and Risk Assessments

The mean concentrations of the heavy metals analyzed are shown in table 3. Heavy metal concentrations in the samples vary widely due to factors such as: differences between species,

possible contamination from the type of manure or fertilizer used to improve crop yield and method of transportation and storage. It is obvious that the mean concentration of Cadmium (Cd) is lowest in all the samples while Iron (Fe) has the highest concentration in all the medicinal plant samples analyzed except in ginger where the Zn content is highest. Iron is an essential element in human life and it binds with haemoglobin. It is not toxic and hazardous in the amount obtained in this study because all the Fe concentration in the samples are lower compared with World Health Organization recommendations or other published studies (Muhammad and Sreebas, 2012). Lead (Pb) and Cd were detected in all the medicinal plants but their contents are lower than the WHO recommendation (WHO, 1999 and 2004). Turmeric has the highest mean concentration of Fe (7.97 mg/kg) and Cu (26.10 x 10^{-2} mg/kg) while ginger has the highest mean concentration of Ni (5.96 x 10^{-3} mg/kg). The concentrations of the heavy metals in the samples were compared with the permissible limit recorded in literature (FAO/WHO, 1999) and were found to be within the safe limit.

Table 3: Mean Concentrations of Heavy Metals in the Medicinal Plants ($mgkg^{-1}$).

Plant	Zn	Pb	Cd	Ni	Cu	Fe
Zobo *(Hibiscus sabdariffa)*	4.10	0.74	0.10	0.39	0.08	7.9
Turmeric *(Curcuma longa)*	5.20	0.79	0.12	0.37	0.26	9.8
Basil *(Occimum basilicum)*	5.18	0.74	0.16	0.38	0.12	7.5
Garlic *(Allium sativum)*	5.60	0.62	0.13	0.37	0.07	9.3
Ginger *(Zingiber officinale)*	7.20	2.75	0.17	0.63	0.51	0.3

Heavy metal risk calculation in the samples

The health risk from heavy metals intake through the ingestion may be characterized using hazard quotient (HQ), which is the ratio of the average daily dose (ADD in mg/kg of the body weight/day) of a chemical to an oral reference dose (Rf D_0; in mg/kg/day).

Oral Rf D_0 is defined as the maximum tolerable daily intake of specific metal that does not result in any deleterious health effects. According to United States Environmental Protection Agency (USEPA, 1993), Oral Rf Dose are 4×10^{-2} mg kg^{-1} day^{-1} for Pb and Cu, 2×10^{-3} mg kg^{-1} day^{-1} for Ni, 0.3 mg kg^{-1} day^{-1} for Zn, 1×10^{-3} mg kg^{-1} day^{-1} for Cd and 0.7 mg kg^{-1} day^{-1} for Fe.

Average Daily Dose (ADD) is expressed as:

$$ADD = \frac{C_{metal} \times D_{intake}}{B_{average}} \qquad 6$$

Where C_{metal} is the arithmetic mean concentration of metal in the sample; D_{intake} is the chronic daily intake of the metal from the ingestion of the medicinal plants; $B_{average}$ is the average weight of the adults taken as 70 kg.

The world daily average intake of elements by a person of weight 70 kg or recommended daily allowance of elements is taken from United State Environmental Protection Authority, (2006)

Exposure to heavy metal is therefore estimated as:

$$HQ = \frac{ADD}{RfD_0} \qquad 7$$

An index more than 1 implies that the average daily dose of a particular metal exceeds the RfD_0, which means that there is a potential risk associated with that metal and is considered not safe for human health.

The estimated average daily doses for the medicinal plant samples analyzed are shown in table 4. The estimated average daily doses are lower than the recommended daily intake except for Zn in turmeric, garlic and ginger which are higher than the recommended daily intake as shown in column 2 in table 4.

The Fractional Hazard Quotient (FHQ) and the Total Hazard Index (THI) in the samples are presented in table 5. The fractional hazard quotients in zobo and basil are lower than 1 for all the metals analyzed (Zn, Pb, Cd, Ni, Cu and Fe) which imply that there is no potential risk associated with all metals in zobo and basil. In turmeric, the Fractional Hazard Quotient of Zn is 1 while the Fractional Hazard Quotients of other metals analyzed are lower than unity as required. This also implies that there is no potential risk associated with all the metals analyzed in turmeric samples. The estimated Fractional Hazard Quotient of Zn in garlic is slightly higher than 1 and in ginger is higher than 1 by a factor of 40%. This implies that there is potential risk associated with the metal in garlic and ginger.

The total hazard index (THI) of the samples analyzed was estimated using equation 8 (USEPA, 2011)

Table 4: Average Daily Dose (ADD) of Heavy metals in the Medicinal Plant Samples (mgkg^{-1})

Plant	Zn	Pb $\times 10^{-2}$	Cd $\times 10^{-3}$	Ni $\times 10^{-3}$	Cu $\times 10^{-3}$	Fe
Zobo *(Hibiscus sabdariffa)*	0.23	0.51	0.10	0.58	0.46	0.54
Turmeric *(Curcuma longa)*	0.29	0.59	0.12	0.49	1.48	0.67
Basil *(Occimum basilicum)*	0.30	0.50	0.16	0.58	0.94	0.51
Garlic *(Allium sativum)*	0.31	0.41	0.13	0.49	0.46	0.64
Ginger *(Zingiber officinale)*	0.42	2.02	0.17	0.96	4.50	0.02

$$THI = \sum FHQ = HQ_{Pb} + HQ_{Zn} + HQ_{Cd} + HQ_{Ni} + HQ_{Cu} + HQ_{Fe} \qquad 8$$

If THI is <1, it means no hazard, if THI is 1.1 – 3, it means probable hazard from consumption of the medicinal plants. If THI is 3-10, it is likely to cause fatal risk (USEPA, 2011).

The results obtained are presented in table 5 (column 8). Total hazard index obtained for all the samples are higher than 1 but lower than 3. This implies that there is probable hazard from consumption of these medicinal plants especially from Zn. Although Zn is essential for important

biochemical and physiological functions necessary for maintaining human health, the knowledge of Zn toxicity in humans is minimal and the most important information reported is its interference with Cu metabolism (Muhammad and Sreebas, 2012). The symptoms of an acute oral Zn dose may include: tachycardia, vascular shock, dyspeptic nausea, vomiting, diarrhea, pancreatitis and damage of hepatic parenchyma (Adefila *et al.,* 2010).

Table 5: Fractional Hazard Quotient (FHQ mgkg^{-1}) and Hazard Index (HI) of Heavy Metals in the Medicinal Plant Samples

Plant	Zn	Pb	Cd	Ni	Cu	Fe	Hazard Index = ΣFHQ
Zobo *(Hibiscus sabdariffa)*	0.77	0.13	0.10	0.29	0.01	0.77	2.07
Turmeric *(Curcuma longa)*	1.00	0.15	0.12	0.25	0.04	0.96	2.52
Basil *(Occimum basilicum)*	0.99	0.13	0.16	0.27	0.02	0.73	2.30
Garlic *(Allium sativum)*	1.04	0.10	0.13	0.25	0.01	0.91	2.44
Ginger *(Zingiber officinale)*	1.39	0.51	0.17	0.48	0.11	0.03	2.69

CONCLUSION

The activity concentrations of ^{238}U, ^{232}Th and ^{40}K in the samples are lower than the world average. The mean annual effective dose due to ingestion of these naturally occurring radioisotopes were found to be lower than the standard as proposed by UNSCEAR, (2000). Fatal cancer risk and hereditary cancer risk estimated from ingestion of radionuclide in the plants lie within the safe limit of 1×10^{-6} to 1×10^{-4} million person yearly (MP-Y) as recommended by USEPA, (1993) and WHO, (2007).

The analysis of heavy metals in the plant samples revealed that there is presence of Lead (Pb) and Cd in all the medicinal plants but their contents are lower than the WHO recommendation (WHO, 1999 and 2004). The mean concentrations of the heavy metals in the samples were compared with the permissible limit recorded in literature (FAO/WHO, 1999) and were found to be within the safe limit. Therefore, the consumption of these plants is safe.

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