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Health Hazard Assessment Due to Slimming Medicinal Plant Intake

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Abstract
According to the World Health Organization (WHO), about 80% of people rely on medicinal plants for their primary health needs. Traditional medicine's principal benefits are their vast population knowledge, low severe adverse effects rate, low cost, and the lack of a medical prescription to use them. While obesity has become a global health issue, an increase in finding cheap and fast ways to lose weight escalates medicinal herbs' use for this purpose, both in dietary supplements or in teas. At the same time that Brazil aims to expand traditional medicine, reports regarding toxicology and poisoning put natural products' safety in check. Plants can accumulate heavy metals and metalloids leading to health risks; however, there is a lack of information on that matter, possibly due to a lack of international standardization regarding elemental contamination — this study aimed to determine metal and metalloid concentrations in slimming medicinal plants and their respective teas and evaluate their safety consumption. Metal and metalloid content were determined by inductively coupled plasma optical emission spectrometry (ICP OES). All plants and teas were within the set limits for tolerable upper intake level (UL), *provisional tolerable* daily maximum intake (PTDMI), and *provisional tolerable* weekly intake (*PTWI*). The hazard quotient index (HQ) was above 1 for almost all plants, and the *Hibiscus sabdariffa* tea regarding aluminum content. The arsenic level was above the Brazilian Pharmacopeia limit *in natura* plants demonstrating risk in their consumption. Some herbs also presented detection for elements with no safety limits set, such as lead, cadmium, and arsenic, which could mark as a red flag for consumption once their security intake is not precise yet.

Keywords Heavy metals · Safety · Elemental content · Medicinal plants

Introduction

According to the World Health Organization (WHO), about 80% of people worldwide rely on medicinal plants for their basic health needs [1]. Traditional medicine's principal benefits are regarding their vast population knowledge, low severe adverse effects rate, low cost, and principally the lack of need of a medical prescription to use them [2, 3].

Obesity is a global health problem in developed and developing countries, with rapidly increasing rates, already stated as a pandemic [4, 5]. In this way, the search for fast and cheap ways to lose weight has escalated medicinal plants' use, even without a dietitian or physician prescription. Among these methods is the use of teas and supplements with a slimming purpose [6, 7].

Brazil aims to expand the use of medicinal herbs in the Unified Health System (SUS). A national policy has been created to ensure the population access to this kind of remedy while the traditional medicine distributed is safe [8]. However, there is a lack of information regarding elemental content in medicinal herbs, especially heavy metals and metalloids. The gap in knowledge is even more prominent when street commerce is considered. Although medicinal plants are perceived as harmless, some cases report toxicological effects and poisoning related to herbal medicinal intake [9]. The accumulation of industrial effluents in the soil, air, and water is continuously increasing due to urbanization and environmental pollution [10]. Plants can accumulate heavy metals and metalloid in their parts, like leaves, changing their elemental composition [11], where methods to determine elemental content in teas include ICP OES [7, 12], flame

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atomic absorption spectroscopy (FAAS) [13, 14], and inductively coupled plasma mass spectrometry (ICP MS) [15, 16]. However, even with the use of emerging techniques to expand the investigation on metal and metalloid content in herbs and teas, there is a lack of standardization parameters to evaluate their safety. For once, the limits regarding heavy metals are not internationally established, with countries setting their limits [17].

As a way to evaluate the safe intake of medicinal plants regarding their elemental content, researchers can use parameters such as the threshold limits of the tolerable upper intake level (UL) [18], the provisional maximum daily tolerable intake (PTDMI), the provisional tolerable weekly intake [19], and the hazard quotient [20, 21].

This study aimed at evaluating the elemental content of slimming medicinal herbs commonly used in Brazil and worldwide as tea infusions, dietary supplements, or as food ingredients: *Equisetum giganteum* L. [22]; *Guazuma ulmifolia* Lam. [23, 24]; *Hibiscus sabdariffa* [25–27]; *Quassia amara* L. [28]; *Olea europaea* L. [29]; *Salvia officinalis* [30], and *Moringa oleifera* [31] considering the hazard of heavy metal and metalloid accumulation in medicinal plants and the potential risk their intake can pose.

Materials and Methods

Material Acquisition

The vegetal material from the medicinal plants *H. sabdariffa* (flower), *O. europaea* (leaf), *E. giganteum* L. (stem), *Q. amara* (bark), *G. ulmifolia* (stem), *S. officinalis* (leaf), and *M. oleifera* (leaf) were purchased by direct buy from sellers in an urban area in Campo Grande, Mato Grosso do Sul, Brazil. Once the plants are part of the street commerce, sold by the package, there is no need to deposit them in a herbarium, while the herb-selling companies are responsible for identifying the species. The project was registered in the National Genetic Resource Management System and Associated Traditional Knowledge (SisGen, # A7716EC).

Plant Material Preparation

Five packages were bought and put together to make a sample pool; the samples were grounded and sieved using a stainless steel grinder (100 mesh) before infusion preparation and digestion of plant material and teas.

Infusion Preparation

The teas were prepared using 300 mg of each plant to 30 mL of deionized water, boiled in a heating plate, and muffled in a beaker for 30 min. The infusion prepared respected the water and herb relation as per the instructions of the seller, respective to a 1 L recipe. After cooling down, the teas were filtrated in a quantitative filter. All materials were previously demineralized by soaking for 24 h in a 10% HNO_3 solution. Then the teas were submitted to digestion before ICP OES analysis. All analyses were performed in triplicate.

Microwave-Assisted Digestion

Plant Material Digestion

The *in natura* plant samples were grounded using a Thermomixer processer until fine powder and then sieved in a stainless steel sieve to obtain a homogeneous powder up to 200 μm. Around 250 mg of each grounded sample was directly weighted into a DAP60® tube. To that were add 2 mL of nitric acid (65% - Merck), 1 mL of hydrogen peroxide (30% - Merck), and 1 mL of ultrapure water. The tubes were submitted to microwave-assisted acid digestion (Speedwave four® (Berghof, Germany)), according to the conditions from Table 1 [32]. All analyses occurred in duplicate as well as analytical blanks using the same method.

Tea Digestion

In each tea samples, we added 1 mL of nitric acid (65% - Merck) and 0.5 mL of hydrogen peroxide (30% - Merck). The samples were transferred into a DAP60® tube and submitted to microwave-assisted acid digestion (Speedwave four® (Berghof, Germany)), according to the method described by Tschinkel et al. [32] (Table 1). All analyses occurred in duplicate as well as analytical blanks using the same method.

After digestion, the samples were transferred to a polyethylene tube, and the volume was completed to 10 mL with ultrapure water for the microelements analysis, and an aliquot of this sample was diluted 1:50 (v/v) to macroelement analysis. All procedures of digestion were performed in triplicate, as well as digestion blanks.

Table 1 Microwave conditions for digestion

Stage	Temperature (°C)	Pressure (bar)	Time (min)	Potency (%)
1	170	50	10	90
2	200	50	15	90
3	50	0	10	0

Macroelement and Microelement Detection by ICP OES

Calibration Curves

The contents of macroelements and microelements in medicinal plants were determined by inductively coupled plasma optical emission spectrometry (ICP OES) (Thermo Scientific - series iCAP 6000) according to parameters shown in Table 2. Calibration solutions with ten-point dilution (0.001, 0.0026, 0.005, 0.01, 0.25, 0.05, 0.1, 0.25, 0.5, 1, 2, and 4 mg/mL) were prepared from a multielementar standard solution with 100 mg/L of Al, As, Ca, Cd, Cr, Fe, K, Mg, Mn, Ni, Pb, Se, and Zn (Specsol, São Paulo, Brazil). Preparation of standard solutions for calibration curves was at room temperature (20 °C).

For each analyzed element (Table 3), we determined a limit of quantification (LOQ) and a limit of detection (LOD), and a correlation coefficient (R^2), using the read of ten blanks, according to the recommendations of the International Union of Pure and Applied Chemistry (IUPAC) [33].

Accuracy was defined by adding a known amount of each analyte (1 ppm - spike), being the spike constituted of the addition of a known amount of the analyte in the sample, and measuring the recovery values; this procedure was taken for both plants and teas analysis. The IUPAC acceptable recovery values vary between 80 and 120%. Table 4 shows the recovery (%) for each analyte in the plant and tea readings [34].

Hazard Quotient Calculation

A product consumption may cause risks when its intake surpasses the set values for the Dietary Reference Intakes (DRIs), considering the tolerable upper intake level (UL), which is the highest daily amount of a nutrient intake considered safe for the majority of people. To exceed this intake may cause health hazards [18].

Some elements have no established UL, so that the health risk can be evaluated by simple comparison with a toxicological parameter controlled by regulatory authorities, in this case, the provisional maximum tolerable daily intake (PMTDI) or the provisional tolerable weekly intake (PTWI), when existent. In this matter, for the elements As, Cd, Cu, K, Pb, and Se, there are no established provisional values that indicate safe consumption. There were limits set for lead, cadmium, and arsenic, but they were

Table 3 Obtained calibration parameters using external calibration, correlation coefficient (R^2), limit of detection, and limit of quantification for the ICP OES run

Analyte	R^2	Linear equation	LOD mg/L	LOQ mg/L
Al	0.9648	$y = 1.9714x + 0.0155$	0.2135	0.7118
As	0.9962	$y = 624.43x + 4.7308$	0.0009	0.0029
Cd	0.9937	$y = 26{,}002x + 241.17$	0.00003	0.00009
Ca	0.9693	$y = 3 \times 10^6x + 64{,}248$	0.00004	0.00013
Cr	0.9973	$y = 11{,}501x + 56.392$	0.0020	0.0068
Cu	0.9973	$y = 88{,}803x + 561.92$	0.0001	0.0003
Fe	0.9964	$y = 9151.9x + 67.263$	0.0004	0.0014
K	0.9953	$y = 514{,}646x + 3991.6$	0.0002	0.0006
Mg	0.9944	$y = 208{,}198x + 1954.5$	0.00004	0.0002
Mn	0.9960	$y = 60{,}468x + 471.9$	0.00004	0.00012
Ni	0.9968	$y = 5197.3x + 36.378$	0.00008	0.00025
Se	0.9940	$y = 717.35x + 7.2238$	0.0006	0.0022
Pb	0.9959	$y = 1487.3x + 11.763$	0.0004	0.0012
Zn	0.9939	$y = 9985.8x + 95.532$	0.0001	0.0004

Table 2 Operational conditions on the determination of macroelements and microelements by ICP OES

Parameter (unit)	Settings
Potency (RF W)	1250
Plasma gas flow rate (L/min)	12
Sample uptake rate (L/min)	0.45
Auxiliary flow L (L/min)	0.5
Nebulizer flow (psi)	20
Stabilization time (s)	20
Gas (99.999%)	Argon
Analytical signal measurement	3 replicates
Wavelength (nm)	K 766.490, Ca 393.366, Mg 279.553, Fe 259.940, Ni 221.647, Cr 283.563, Al 396.271, As 189.042, Cd 228.802, Cu 324.754, Pb 220.353, Mn 257.610, Se 196.090, Zn 213.856

Table 4 Analytes add and recovery obtained by ICP OES (n = 3)

Analyte	Spike concentration plant (*in natura*) (mg/kg)	Recovery for plant spike (%)	Spike concentration tea (mg/kg)	Recovery for tea spike (%)
Al	82.5537	97	0.9298	93
As	1.1762	95	0.9212	92
Cd	0.9775	97	0.9883	99
Ca	420.6251	99	5.9927	100
Cr	0.9854	99	0.9865	99
Cu	0.9675	97	1.0178	101
Fe	2.4489	100	0.9698	97
K	192.9977	104	11.6069	100
Mn	1.0838	101	0.9817	98
Ni	0.9307	93	0.9687	97
Se	1.1821	102	0.9456	95
Pb	0.9785	98	0.9925	99
Zn	0.9678	99	0.9542	94

withdrawn once they did not show consumption safety on the proposed levels. For exploratory meaning only, the old set values were used for these elements: 15 μg/kg/week (arsenic), 7 μg/kg/week (cadmium), and 21 μg/kg/week (lead) [35]. The PTWI for aluminum is 2 mg/kg/week [35]. PMTDIs were determined for copper 40 μg/kg/day, chromium 3 μg/kg/day, iron 700 μg/kg/day [36], manganese 140 μg/kg/day [37], nickel 15 μg/kg/day [37], and zinc 0.3 mg/kg/day [36]. While there is no PMTDI for selenium, some authors suggested a limit of 400 μg/day [38], equivalent to the UL [18], the same limit used in this work, while the proposed cadmium limit is 25 μg/kg/month [37]. These latter values are for exploratory and discussion only, once there is no supporting data for a reference amount at the moment. For selenium intake, the difference between beneficial and harmful effects depending on dosage is yet unclear, and the outcomes of selenium exposure are limited [39], while for cadmium, no intake level is considered safe [35].

One other way to assess the associated intake risk from aliments is the hazard quotient index (HQ), which depends on the estimated daily intake (EDI) and inversely proportional to the oral reference dose (RfD) (Eq. 1).

$$HQ = \frac{EDI}{RfD} \quad (1)$$

We used the RfD to determine safety intake in the HQ calculus, with the following values for each element: arsenic 0.3 μg/kg/day, cadmium 1 μg/kg/day, aluminum 0,4 μg/kg/day, iron 700 μg/kg/day, chromium 3 μg/kg/day, manganese 140 μg/kg/day, nickel 20 μg/kg/day, selenium 5 μg/kg/day, and zinc 300 μg/kg/day [40]. In the absence of an RfD, we used the PTWI values to determine the HQ, namely lead 21 μg/kg/week [35].

The HQ calculus evaluates the potential risk to noncarcinogenic chronic damage to human health, where HQ > 1 equals a hazard potential.

In Eq. 1, the term EDI comes from the calculus exposed on equation 2 (Eq. 2), where EDI is directly proportional to the multiplication of the element concentration C_{ele} (μg/kg or mg/kg, according to each element reference) by the intake C_{ali} (kg/day), from the respective food and inversely proportional to the body weight (kg). The HQ and EDI calculus method is used to detect metal and metalloid exposure risk often [20, 21, 41].

$$EDI = \frac{C_{ele} x C_{ali}}{Weight} \quad (2)$$

As instructed by the sellers, the tea consumption is of one tea three times a day, totaling 600 mL/day of the infusion. For this research purpose, it was considered equal to 0.6 kg for 600 mL of tea, which was used on EDI and HQ calculus.

Still, recognizing the possibility of the use of some herbs as food ingredients and the use as a herb supplementation in the form of herb capsules, we considered the standard amount contained in a 500 mg/capsule of the herb, and the intake of 2 capsules a day, totaling the ingestion of 1 g/day. This value was also used to calculate EDI and HQ and compare this ingestion amount with the set values of PTWI and PMTDI. We considered the weight of an average adult to be 60 kg, according to the proposed by the toxicity documents described by FAO/WHO [42].

Results and Discussion

The metal and metalloid detection results in medicinal plants *in natura* form and their respective teas are presented in Table 5. Cobalt and cadmium detection was below the limit of detection in all samples (*in natura* and tea). The ICP OES results for teas are in mg/600 mL due to three cups' intake recommendation (200 mL) a day.

Results expressed in average ± standard deviation

IN in natura

<LOD below the limit of detection

†Above the limit of detection

Elemental Content in Medicinal Herbs and Respective Teas

Except for calcium in *O. europaea* and lead in *Q. amara*, all of the teas showed a reduced amount in elemental quantification compared to *in natura* plants. Some teas can decrease their metal and metalloid concentration during the tea infusion, which depends on the plant and the element studied [43].

The responsible factors for the extract difference are (1) initial elemental concentration in the plant; (2) extraction method; (3) processing method on the plants used in the teas; and (4) extraction efficiency for each element [44]. The initial elemental concentration can vary between and within the same species once the climate and soil differences can impact elemental concentration [45]. Method differences, as the quality of water, can influence the transferred element [46], or if the plant was dried or fresh [47], while efficiency extraction depends on the element itself since the solubility rate in water differs among elements [48].

Aluminum

Aluminum concentration *in natura* plants ranged from 3.14 ± 1.89 to 926.18 ± 57.66 mg/kg (Table 5), where *G. ulmifolia* has the lowest concentration on Al and *H. sabdariffa* the higher. The tea of the plants *E. giganteum*, *G. ulmifolia*, *O. europaea*, *S. officinalis*, and *Q. amara* had concentrations below the limit of detection (<LOD), and the tea of *H. sabdariffa* presented the greatest amount, with 1.62 mg/

Table 5 Quantified metal and metalloid in medicinal plants (*in natura*) (mg/kg) and in their respective teas (mg/600 mL)

Element		*E. giganteum*	*O. europaea*	*M. oleifera*	*G. ulmifolia*	*S. officinalis*	*H. sabdariffa*	*Q. amara*
Al	IN	101.62 ± 0.17	146.33 ± 9.28	308.96 ± 74.06	3.14 ± 1.89	169.63 ± 20.55	926.18 ± 57.66	84.56 ± 17.25
	Tea	<LOD	<LOD	0.02 ± 0.00	<LOD	<LOD	1.62 ± 0.01	<LOD
As	IN	0.30 ± 0.01	0.73 ± 0.04	0.48 ± 0.0001	0.42 ± 0.05	0.67 ± 0.01	0.26 ± 0.04	0.23 ± 0.01
	Tea	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD
Ca	IN	1088.78 ± 10.31	<LOD	1315.62 ± 9.98	†	1142.08 ± 23.37	738.1 ± 7.20	422.84 ± 107.89
	Tea	38.86 ± 0.01	0.22 ± 0.15	7.74 ± 2.86	169.7 ± 6.21	<LOD	206.42 ± 0.79	88.99 ± 0.02
Cr	IN	<LOD	0.12 ± 0.08	<LOD	<LOD	0.23 ± 0.02	0.28 ± 0.04	<LOD
	Tea	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD
Cu	IN	<LOD	6.68 ± 2.70	0.13 ± 0.50	0.04 ± 0.003	0.36 ± 0.01	0.16 ± 0.01	<LOD
	Tea	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD
Fe	IN	3435 ± 0.20	36.75 ± 14.11	26.38 ± 0.05	4.66 ± 0.05	96.85 ± 0.39	46.3 ± 1.10	1.45 ± 0.64
	Tea	<LOD	<LOD	<LOD	<LOD	<LOD	3.60 ± 0.04	<LOD
K	IN	985.56 ± 11.85	625.84 ± 27.49	1085.05 ± 5.96	683.59 ± 6.17	764.04 ± 22.20	791.84 ± 13.52	184.91 ± 30.54
	Tea	194.76 ± 4.95	68.35 ± 0.64	74.99 ± 1.70	304.7 ± 5.08	<LOD	391.58 ± 1.03	189.56 ± 0.55
Mg	IN	319.2 ± 4.90	158.86 ± 1.77	355.85 ± 2.82	342.66 ± 9.77	119.87 ± 2.06	210.78 ± 3.80	15.26 ± 4.35
	Tea	8.66 ± 0.22	<LOD	7.42 ± 0.05	44.14 ± 0.41	<LOD	53.15 ± 1.18	<LOD
Mn	IN	10.77 ± 15.61	3.07 ± 0.57	10.63 ± 0.128	3.22 ± 0.01	4.03 ± 0.07	15.1 ± 0.34	0.07 ± 0.0003
	Tea	0.34 ± 0.01	<LOD	1.10 ± 0.00	0.10 ± 0.34	<LOD	7.16 ± 0.00	<LOD
Ni	IN	<LOD	<LOD	<LOD	<LOD	<LOD	0.04 ± 0.02	<LOD
	Tea	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD
Pb	IN	0.28 ± 0.003	0.17 ± 0.03	<LOD	<LOD	0.26 ± 0.005	0.06 ± 0.007	<LOD
	Tea	0.03 ± 0.0003	0.07 ± 0.00	<LOD	<LOD	0.03 ± 0.0002	<LOD	0.02 ± 0.0003
Zn	IN	1.48 ± 0.41	1.09 ± 0.02	1.11 ± 0.001	0.31 ± 0.01	0.99 ± 0.001	1.6 ± 0.05	<LOD
	Tea	<LOD	<LOD	<LOD	<LOD	<LOD	0.52 ± 0.09	<LOD
Se	IN	<LOD	0.48 ± 0.03	0.34 ± 0.01	0.26 ± 0.05	0.61 ± 0.01	0.19 ± 0.06	0.16 ± 0.08
	Tea	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD

600 mL. The concentration found in *H. sabdariffa in natura* is above than reported in the *C. sinensis* sample of 342.4 mg/kg, also used with a slimming purpose, investigated by Barrela et al. [7]. This aluminum concentration is an elevated amount, and the population should be aware of the excessive exposure from the plant intake [49]. Still, their findings are below the concentrations in this study.

There are neither set values for RDA, AI, and UL for aluminum [50] nor a limit established for pharmaceutical products in the Brazilian Pharmacopeia [51]. However, the elevated levels of aluminum in *H. sabdariffa* might be worrisome. Plants from the genus *Hibiscus* can be consumed in food preparations [52–54], which could increase the exposure to aluminum intake beyond the PTWI of 2 mg/kg [35], that is, 120 mg/week for a 60-kg adult [55].

The vigilance regarding the intake of plants that aggregate aluminum is necessary since aluminum accumulation in human tissues might be linked to the surge of diseases as Alzheimer's, osteopenia, blood-brain barrier dysfunction, and neurotoxicity [56–58].

Arsenic

Arsenic is present in all medicinal herbs studied (Table 5), with a higher concentration in *O. europaea* (0.73 ± 0.04 mg/kg or 730 μg/kg). The herb with the second-largest arsenic amount was *S. officinalis*, which is used as a seasoning, besides tea preparations [59, 60]. The provisional tolerable limit for arsenic consumption is 15 μg/kg/week, that is, 900 μg for a 60-kg adult [38, 55], which makes this exposure for a single font excessive. Although the medicinal plants' teas did not produce detectable arsenic amounts, it is not possible to affirm they do not contain this element once the herbs have concentrations that cannot be neglected.

There are no set values for RDA or AI, owing to arsenic toxicity, but, at the same time, there is no UL either [50]. The Brazilian Pharmacopeia establishes the limit of 1.5 μg/g for arsenic in pharmaceutical products [51], putting the plants in this study above this limit, with possible risks to the consumers.

We did not detect arsenic in the plant teas; however, arsenic was identified in other tea preparations, such as *C. sinensis*, with concentrations ranging from 0.01 to 0.37 μg/g, the transference of this element may happen [61].

Arsenic intoxication is a global health concern, with water or food intake showing risks [62]. Chronic arsenic consumption can trigger several types of câncer (skin, lungs, bladder, kidneys, and liver), besides effects on neurological, respiratory, cardiovascular, endocrine systems, and immunity [63].

Calcium

According to Table 5, the medicinal herbs' calcium concentration varied between 422.84 ± 107.89 and 1315.62 ± 9.98 mg/kg. In *O. europaea*, the concentrations of calcium were below the limit of detection, while in *G. ulmifolia,* it was above the limit of detection. In the teas, the calcium was below the limit of detection in *S. officinalis*, and *H. sabdariffa* has the highest concentration, with (206.42 mg/600 mL). The calcium values are inferior to those found in slimming mix teas, with an average of 819.06 mg/100 g (8190.6 mg/kg), and their respective teas had an average of 3.73 mg/100 mL (which would add to 22.38 mg/600 mL) [6], which infers that our study had a superior metal transference rate.

Calcium is an essential element, with a needed dose (RDA) ranging from 1000 to 1200 mg/day for adults, according to age and gender [64]. Adequate calcium consumption is necessary to bone maintenance, and the plasma homeostasis of calcium is involved in hormonal secretion and neuronal and vascular activities [64–66].

The Brazilian Pharmacopeia does not set limit values for calcium in pharmaceuticals products [51]. The UL for calcium ranges between 2000 and 3000 mg/day for adults, varying with age and gender. Excessive calcium intake is related to symptoms such as hypercalcemia, hypercalciuria, soft tissue and vessel calcification, prostate cancer, and constipation [67]. Therefore, in the presented doses, the medicinal herbs do not offer risks of adverse effects in a healthy population. These results cannot take *G. ulmifolia* into account, once the calcium determination was above the limit of detection; its tea, however, presented safe amounts of calcium.

Chromium

E. giganteum, *M. oleifera*, *G. ulmifolia*, and *Q. amara* plants have chromium below the limit of detection. *O. europaea* was the herb with the lowest detectable chromium (0.12 ± 0.08 mg/kg, while *S. sabdariffa* showed the greatest quantification (0.28 ± 0.04 mg/kg). In all teas, the chromium levels were inferior to the LOD. In samples of black tea plants in India, the chromium concentration in *C. sinensis* displayed an average of 8.33 μg/g (equivalent to 8.33 mg/kg), far superior to those found in this study. In the respective infusions. Chromium values varied from 0.33 to 0.73 (equivalent to 0.33 and 0.73 mg/kg) [61], while we did not detect chromium in the teas.

Chromium concentrations in the plants *O. europaea* (0.12 μg/g) and *S. officinalis* (0.23 μg/g) are within limits established in the Brazilian Pharmacopeia of 25 μg/g [51]. The adequate intake (AI) for chromium varies between 20 and 35 μg/day for adults [50], and this amount can be reached or surpassed by the ingestion of *H. sabdariffa* plant when used in food preparation [52]. However, chromium essentiality is questioned once apparently the health benefits of chromium are achieved in pharmacological doses rather than nutritional, as indicated by the AI [68–70].

So far, there are no PMTDI or PTWI for chromium, as well there is no set UL [55, 71], once there is no evidence that trivalent chromium associated with food intake or supplements have caused adverse effects on a consistent matter [69]. The hexavalent chromium is linked to the development of certain types of cancer [68].

Copper

Copper in *E. giganteum* and *Q. amara* is below the LOD. The highest detectable copper amount was in *O. europaea* (6.68 ± 2.70 mg/kg–6680 μg/kg). This value is still below the average of 12 mg/kg (ranging from 3.37 to 23.7 mg/kg) in 23 medicinal herbs found by Ababneh (2017). The infusion of the herbs of Ababneh's study (2017) had an average of 5.8 mg/kg, while we could not detect copper in our teas (Table 5).

The copper amounts in the plants (Table 5) are below the metal impurity limit for copper (250 μg/g) in pharmaceutical products, medicines, and other products established in the Brazilian Pharmacopeia [51].

Copper requirements are 900 μg/day for adult men and women [72]; therefore, the medicinal plants studied in teas cannot be considered sources of this element. The copper Uls vary between 8000 and 10,000 μg/day for adults of both genders, with variations occurring for gender and age [71]. No PMTDI or PTWI is set for copper once it is not considered a carcinogenic element for humans and animals. Even populations exposed for a long time above the recommendations do not display cumulative effects, except for people with Wilson syndrome [19]. On the other hand, acute exposure to high levels of copper is related to brain tissue inflammation, anorexia, fatigue, hair loss, acne, allergies, depression, premenstrual syndrome, migraines, anxiety, panic attacks, and renal and liver dysfunction [73].

Iron

Iron values in medicinal herbs varied from 1.45 ± 0.64 to 96.85 ± 0.39 mg/kg, with the highest concentration in *S. officinalis* (Table 5). Our results are superior to those found by Samudralwar e Garg (1996) [74] in natural products (herbs, roots, and fruit peels) with quantifications from 0.129 to 0.355 mg/kg. In all teas, except for *H. sabdariffa* (3.60/600 mL), the iron content was below the LOD. Still, the *H. sabdariffa* tea iron amount was below than in black tea samples with 7.749 μg/g (equivalent to 4.65 mg/600 mL) and superior to Oolong tea samples (< 0.001 μg/g) and green tea (< 0.001 μg/g) [75].

Iron is essential, being part of hemoglobin and allowing oxygen exchange in tissue environments. It also takes part in myoglobin, augmenting oxygen diffusion from capillary erythrocytes to the cytoplasm and mitochondria [76]. The recommended daily intake for iron is 8 mg for men and from 8 to 18 mg/day for women, varying according to age [50].

The Brazilian Pharmacopeia does not set limits for iron in pharmaceuticals products [51], while the UL is 45 mg/day [71]. Although it is unlikely to reach this amount by drinking teas or from herb ingestion in food preparation, their use, along with other iron sources, must be observed not to cause chronic intoxications. The PTMDI established for iron, set by the Joint Expert Committee for Food Additives (JECFA), is 0.8 mg/kg/day for adults [36], which means the exposure from these herbs/teas is not prone to cause risks.

Potassium

Potassium detection in the medicinal plants varied between 184.91 ± 30.54 and 1085.05 ± 5.96 mg/kg, where the *Q. amara* showed the lowest concentration and *M. oleifera* the highest (Table 5). *S. officinalis* potassium content was below the LOD in the tea, and the tea from *H. sabdariffa* has the most considerable potassium amount with 391.58 mg/600 mL. The quantified potassium content in slimming herb mixes ranged from 100.14 to 211.11 mg/100 g (ou 1001.4–2111.1 mg/kg), with 1.19 mg/100 mL e 7.14 mg/100 mL quantification in the respective teas [6]. While in the herbs, we had a lower potassium detection, the opposite is true for the teas, where our results showed the highest potassium content in the teas.

There are no upper tolerable levels set for potassium ingestion, neither reference values for weekly or monthly intake [35, 71] nor reference for maximum limit content in pharmaceuticals products set by the Brazilian Pharmacopeia [51]. In healthy populations, the potassium excess is promptly excreted through the kidneys [71]. Therefore, the potassium amount in the herbs and the teas is not likely to cause adverse effects.

Magnesium

The magnesium in medicinal plants *Q. amara* and *M. oleifera* were 15.26 ± 4.35 e 355.85 ± 2.82 mg/kg respectively, below the quantified by Samolinska et al. [6] in slimming herbs, with an average of 265.59 mg/100 g (equivalent to 2655.9 mg/kg). Regarding the teas, the quantification was below the LOD for *O. europaea* and *S. officinalis*. The tea with the lower detectable magnesium content was *M. oleifera* (7.42 mg/600 mL), and the highest concentration was the tea of *H. sabdariffa* (53.15 mg/600 mL). Our results are above Samolińska et al.'s (2017) magnesium detection in slimming tea mixes ranging from 1.12 to 2.89 mg/100 mL (equivalent to 6.72 to 17.34 mg/600 mL).

Magnesium is essential to human health; it is present in over 300 enzymatic systems, participating in the regulation of diverse metabolic processes, such as protein synthesis, muscular and neuronal function, blood glucose control, and blood pressure [50, 77]. The RDA for adults varies between 310 and 420 mg/day, depending on gender and age [50].

The Brazilian Pharmacopeia does not set maximum levels for magnesium concentration in pharmaceuticals products [51], and there is no reference dose for magnesium consumption. However, the UL for magnesium is 350 mg/day for supplementation only, since the kidneys efficiently excrete magnesium excess from food in urine [18], making the consumption of these teas secure for this element once it is below the UL.

Manganese

The lowest and highest manganese content was detected in the medicinal herbs *Q. amara* (0.07 ± 0.0003 mg/kg) and *H. sabdariffa* (15.1 ± 0.34 mg/kg), respectively. The minor manganese content was in *G. ulmifolia* tea (0.10 mg/600 mL) and the major in *H. sabdariffa* tea (7.16 mg/600 mL). Mabuza et al. [78] found greater concentrations in rooibos herbs, with 40.9 to 86.5 μg/g (equivalent to 40.9 to 86.5 mg/kg); equally, rooibos tea manganese detection was superior (11.8 and 30.2 μg/g - equivalent to 7.08 and 18.12 mg/600 mL) than that found in this study (Table 5).

Manganese is an essential element with intake recommendations (AI) of 1.6–2.3 according to gender and age [50]; however, it can be toxic in excessive amounts. Manganese essentiality is due to its participation in enzymatic systems (pyruvate carboxylase, transferases, hydrolases, and kinases) and its antioxidant role (Mn superoxide dismutase). Enzymes are necessary for micronutrient metabolism, bone, and cartilage formation. It is also crucial in wound cicatrization, digestion, reproduction, and energy regulation [79, 80].

Overexposure to manganese induces neurodegeneration, especially in the basal ganglion, a central region in the brain on Parkinson's pathophysiology, but the exact action mechanism is not yet explained [81]. Also, excessive manganese leads to brain oxidative stress [82], prompting mitochondrial dysfunction and apoptosis [83].

The manganese quantified in plants is below the metal impurity level (250 μg/g) in pharmaceuticals, medicines, and other products established by the Brazilian Pharmacopeia [51]. The UL for manganese is 11 mg/day [18], so the concurrent manganese tea containing along with other manganese sources should be monitored to avoid possible intoxication. There are no PMTDI and PTWI for manganese so far.

Nickel

The nickel detection occurred only in the *H. sabdariffa* plant (0.04 ± 0.01 mg/kg). All other samples (herbs and teas) had nickel detection below the LOD. Nickel in other medicinal plants used for weight control ranged from 0.02 μg/g in lemongrass to 0.14 μg/g in yerba mate; the lemongrass nickel content as our samples did not transfer into the tea; however, the transference occurred in yerba mate teas, with the higher detection of 0.04 μg/mL [12].

The elementary nickel is essential to the development of bacteria and plants, while its deficiency can lead to decreased life expectancy in breeding animals and anemia due to reduced iron absorption. However, those symptoms were not observed in humans, once nickel intake usually surpasses this element's primary needs, suggested as 25 e 35 μg/day [84]. It is crucial to notice that these suggested values are not RDA or AI recommendations, which are not set yet [50].

The limit set by the Brazilian Pharmacopeia for metal impurity from nickel is 25 μg/g in pharmaceutical products, medicines, and other products [51], so all samples are within this limit proper for intake considering this element. The UL for nickel is 1 mg/day [18], so it is improbable to occur intoxication by any of the herbs or teas. Also, the PMTDI of nickel is 15 μg/kg/dia [38, 55], so it would be unlikely to surpass this amount with these herbs and teas. The Institute of Medicine itself considers doubtful the oral toxicity for nickel compounds, occurring more frequently by environmental contaminations (occupational hazard) or by contaminated water [18].

Lead

Lead concentration was below the LOD in the herbs of *M. oleifera* and *Q. amara* and the teas of *M. oleifera*, *G. ulmifolia*, and *H. sabdariffa*. In the herbs with lead detection, the quantification varied between 0.06 ± 0.007 and 0.28 ± 0.003 mg/kg, with the highest amount in *E. giganteum.* The teas of *S. officinalis* and *E. giganteum* showed a lead concentration of 0.003 mg/600 mL. Schunk et al. investigated lead detection in herbal teas and infusions. A higher amount of lead was detected in chamomile tea, at the concentration of 0.55 μg/g, well above our findings. In the same way, fennel infusion presented a lead concentration of 0.02 μg/mL, superior to our study's values [12].

The lead impurity limit is 1.0 μg/g in pharmaceutical products, medicines, and other products, according to the Brazilian Pharmacopeia [51]; therefore, the lead in the medicinal plants is below this limit. There is no UL set for lead yet [18].

Considering our method, *S. officinalis* or *E. giganteum* tea's daily intake counts for 21 μg of lead in 1 week. The JECFA withdraws the previous PTWI of 25 μg/kg/week once they found this earlier assessment not enough for health maintenance. It was related to the decrease of 1 point in the intelligence quotient for kids with 0.6 μg/kg/day ingestion. For adults with a dietary exposure of 1.3 μg/kg/day, there was an increase of 1 mmHg in the blood pressure [35].

S. officinalis is used in food preparations [59, 60], so the lead exposure regarding this source could be prejudicial when ingested in high amounts or too often.

Zinc

Zinc concentration in *Q. amara* herb was below the LOD, while the medicinal plant with the highest content was *E. giganteum* (1.48 ± 0.04 mg/kg). The only tea sample that presented quantifiable zinc was the *H. sabdariffa* one (0.52 mg/600 mL). In the rooibos plant, the zinc detection varied from 4.15 to 12.2 μg/g (equivalent to 4,15 and 12,2 mg/kg), and in their respective teas, the zinc amount was 1.51 to 4.59 μg/g (equivalent to 0.91 e 2.75 mg/600 mL) [78], higher than those found in this study (Table 5).

Zinc is essential to several functions, including enzyme and protein activation, and in aiding the absorption of vitamins A, E, and folate [85, 86], with the adequate consumption (RDA) of 8–11 mg/day in adults, according to age and gender [50].

Zinc poisoning is rare once its homeostasis mechanism has a rapid response to high ingestion levels; however, in some cases, it could cause gastrointestinal symptoms and, in severe cases, ataxia and lethargy [87].

The UL for zinc is 40 mg [18], and the PTMDI is 0.3 mg/kg/day [36], which makes the intoxication by using these herbs and teas unlikely. On the other hand, the Brazilian Pharmacopeia does not describe maximum zinc concentrations in pharmaceuticals products [51].

Selenium

Selenium content is below the detection in the plants of *E. giganteum*, while among the other species, it varied from 0.16 ± 0.08 and 0.61 ± 0.01 mg/kg, with the highest concentration in *S. officinalis* (Table 5). All tea samples showed selenium content below the LOD. The selenium quantification in 15 different medicinal herbs in the Central European region ranged from 16.97 to 477.9 μg/kg [88], lower than found in our study.

Selenium is a mineral essential to human health, being part of selenozymes, acting mainly in protecting oxidative stress [89], with a recommended intake of 55 μg/day (RDA) both deficiency or excess are related to adverse health issues. Selenium deficiency is associated with the enhancement of viral virulence, compromised immunity, fertility and thyroid disturbances, type 2 diabetes, prostate cancer risk in men, and colorectal cancer risk in women. On the other hand, the selenium excess or intoxication can lead to dermatitis, alopecia, augmented mortality, enhanced prostate cancer risk, and non-melanoma skin cancer [90].

The Brazilian Pharmacopeia does not set limit values for selenium in pharmaceuticals products [51]. There are no established values of PTMDI and PTWI for selenium so far; however, Deng et al. (2019) proposed a provisional limit of 400 μg/day as PTMDI, the same as UL [18]. According to these references, it is improbable that tea and herb consumption in this study can cause adverse effects.

Hazard Quotient Index for Noncarcinogenic Risk

The results on the HQ for each studied metal and metalloid are available in Table 6.

IN in natura, *ND* not determined

The hazard quotient is determined from reference values of consumption for each element (when available), its amount in the food, the intake, and the individual weight. A particular element is considered a possible chronic noncarcinogenic hazard when the HQ value is superior to 1 [91].

The element with the highest HQ was aluminum, way above the HQ threshold of 1, which shows risk with a long-term intake [91]. The only tea with HQ superior to 1 is the *H. sabdariffa* one, demonstrating risk with the consumption from both *in natura* plant and tea.

Considering that some herbs are also present as food ingredients [59, 92], besides the intake as a supplement and/or teas, this other source should be taken into account to consider a health risk. Although neither herbs nor teas surpassed the proposed limit for arsenic, cadmium, and lead, there is no value set for these elements considered a safe consumption [35], once even at low doses, they can cause damages to health, so the mere presence of lead in the samples is considered a risk itself.

It is necessary to highlight a metal dilution from the herbs during the tea preparations, which is imperative to health risk analysis [93]. In the case of sustained medicinal health effects using the teas, they might present an advantage compared to the *in natura* plants, with a reduced intoxication risk due to dilution.

Conclusions

The use of food preparations with medicinal plants and their respective teas often occurs without clear intake directives to avoid toxicity. Although the analyzed herbs can be consumed chronically, exposing the users to risk, no studied herb or tea had elemental concentrations above the UL, with an acute intoxication being unlikely to happen.

In a possible long-term consumption from the herbs and teas, all studied plants were within the available limit values established for PMTDI and PTWI; however, lead, arsenic, and cadmium are still problems with both forms of ingestion, not having a safety threshold for their

Table 6 HQ for the intake of *in natura* medicinal herbs (1 g/day) and their respective teas (600 mL/day)

Chemical element		*E. giganteum*	*O. europaea*	*M. oleifera*	*G. ulmifolia*	*S. officinalis*	*H. sabdariffa*	*Q. amara*
Al	IN (1 g)	4.2343	6.0971	12.8733	0.1308	7.0679	38.5908	3.5233
	Tea (600 mL)	ND	ND	0.0250	0.0500	ND	2.0250	ND
As	IN (1 g)	0.0167	0.0406	0.0266	0.0233	0.0372	0.0144	0.0129
	Tea (600 mL)	ND	ND	ND	ND	ND	ND	ND
Cr	IN (1 g)	ND	6.67×10^{-4}	ND	0.0013	0.0016	ND	ND
	Tea (600 mL)	ND	ND	ND	ND	ND	ND	ND
Cu	IN (1 g)	ND	0.0028	5.42×10^{-5}	1.67×10^{-5}	0.0002	6.67×10^{-5}	ND
	Tea (600 mL)	ND	ND	ND	ND	ND	ND	ND
Fe	IN (1 g)	0.0008	0.0009	0.0006	0.0001	0.0023	0.0011	3.45×10^{-5}
	Tea (600 mL)	ND	ND	ND	ND	ND	0.0015	ND
Mn	IN (1 g)	0.0013	0.0004	0.0006	0.0004	0.0005	0.0018	8.33×10^{-6}
	Tea (600 mL)	0.0012	ND	0.0039	0.0004	ND	0.0154	ND
Ni	IN (1 g)	ND	ND	ND	ND	ND	4.44×10^{-5}	ND
	Tea (600 mL)	ND	ND	ND	ND	ND	ND	ND
Pb	IN (1 g)	0.0015	0.0009	ND	ND	0.0014	ND	0.0003
	Tea (600 mL)	0.0117	0.0070	ND	ND	0.0113	ND	0.0063
Zn	IN (1 g)	8.22×10^{-5}	6.06×10^{-5}	6.17×10^{-5}	1.72×10^{-5}	5.50×10^{-5}	8.89×10^{-5}	ND
	Tea (600 mL)	ND	ND	1.67×10^{-4}	1.00×10^{-4}	ND	8.67×10^{-4}	ND
Se	IN (1 g)	ND	1.63×10^{-3}	1.33×10^{-3}	8.67×10^{-4}	2.03×10^{-3}	6.33×10^{-4}	ND
	Tea (600 mL)	ND	ND	ND	ND	ND	ND	ND

consumption. Again, almost all plants and *H. sabdariffa* tea showed HQ value above one for aluminum, inferring a potential hazard using this herb in food or preparations. Arsenic was above the set values *in natura* plants, indicating a consumption health hazard for these herbs as a dietary supplement or as a food ingredient. Further studies, such as animal models, are necessary to strengthen or discard these conclusions. In between, caution is advised.

The lack of regulatory measures in medicinal plants and their free and unexceptional use may pose a risk to consumers, being imperative to the fulfillment of quality control directives in Brazil and the surveillance of these products, constituted by the Brazilian Pharmacopeia and regulatory agencies.

Availability of Data and Material Data material is available within the text; raw data is available upon request

Code Availability Not applicable

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Declarations

Conflict of Interest The authors declare no competing interests.

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