



Assessment of Carcinogenic and Non-carcinogenic Risk of Exposure to Metals via Consumption of Coffee, Tea, and Herbal Tea in Iranians

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Received: 4 January 2022 / Accepted: 7 April 2022

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Abstract

In the current study, we assessed health risk posed to Iranian consumers through exposure to metals via oral consumption of coffee, tea, and herbal tea of various trademarks collected from Iran market. Level of As, Cd, Cr, Cu, Fe, Hg, Ni, and Pb in 243 samples was quantified by inductively coupled plasma-optical emission spectrometry (ICP-OES). The metal levels in coffee samples from different trademarks of a specific country had statistically similar levels of metals; however, metal levels differed significantly among brand names from different countries. Metal levels in tea samples differed significantly between domestic and imported products, while different trademarks of similar countries did not show significant variations in this respect. Metal level in herbal tea samples did not show significant variations among different trademarks. Nevertheless, it should be highlighted that mean concentrations of metals statistically differed among different herbal tea samples. Deterministic hazard quotients (HQs) were <math><1.0</math> for all non-carcinogenic metals and total hazard index (HI) values indicated no risk; however, probabilistic assessment calculated HI values >1. In both deterministic and probabilistic scenarios, carcinogenic metals As and Ni had an estimated incremental lifetime cancer risk (ILCR) of medium level while that of Pb indicated no cancer risk. Sensitivity analysis showed that the concentration of metals had the most significant effect on non-carcinogenic and carcinogenic risks.

Keywords Stainless clad steel · Multi-pass welding · Mechanical properties · Microstructure · Transition zone · Local hardening zone

Introduction

Food safety has an important role in public health. In this field, the Food and Agriculture Organization (FAO) and World Health Organization (WHO) and European Commission (EC) strictly regulate the allowable concentrations or maximum permitted concentrations of metals in foodstuffs [1, 2].

Metals originating from polluted soil, water, etc. may enter the food chain and they are considered one of the major contaminants. Large zones of global farmlands have been shown to be affected by metals [3]. Ingestion of agricultural crops in which metals are accumulated may result in a considerable health risk to humans. These chemicals are mainly stored in the liver and kidney by binding to metallothioneins. Co-exposure to different metals may lead to serious effects such as oxidative stress, hypertension, kidney dysfunction, diabetes, reproductive dysfunction, and hepatic, cardiovascular, and peripheral nervous conditions [4, 5]. Several metals are also classified as human carcinogens by

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the International Agency for Research on Cancer (IARC). Concerning carcinogenicity, the International Agency for Research on Cancer (IARC) categorized different metals as follows: group 1, carcinogenic to humans; group 2A, probably carcinogenic to humans; group 2B, possibly carcinogenic to humans; group 3, not classified as a carcinogen to humans; and group 4, probably not carcinogenic to humans. IARC has classified As, Cd, and Ni as group 1, and Cr, Cu, Fe, and Hg in group 2B [6].

Oral absorption of metals may vary significantly among different food products, and it depends on potential interactions among food components in the food matrix. Also, the extent of absorption depends on the gastrointestinal tract traits (e.g., stomach pH and the rate of gastric transit); a recent review article discusses matrix effect on calcium absorption [7].

Among *Coffea* species (Rubiaceae), only the following three species are cultivated for commercial purposes: *Coffea arabica*, *Coffea robusta*, and *Coffea liberica* [8]. Tea (*Camellia sinensis*, from the family Theaceae) is the oldest and most popular non-alcoholic beverage, and it has different phytoconstituents such as polyphenols, flavonol glycosides (quercetin, kaempferol, and myricetin), tannins, vitamins, and minerals, which attribute to its potential health benefits including immune-enhancing, hypoglycemic, anticancer/antimutagenic, and hypotensive effects [9, 10]. Tea and herbal teas are commonly used in traditional medicine for therapeutic purposes. Different plant species (e.g., echium, lavender, thyme, chamomile, fenugreek, stinging nettle, spearmint, and hibiscus) as herbal teas are used for treatment of heart diseases and diabetes and to lose weight [11].

With a mean annual consumption of 500 billion cups per year or 9.4 million tons per year, coffee is one of the most popular drinks in the world. Due to its pleasant flavor and benefits for human health, coffee drinking especially in Western countries has been a part of lifestyle [8, 12, 13]. Tea is another popular beverage of which 18 to 20 billion cups are globally consumed per day and it is widely produced throughout the world [14]. Annually, the amount of black tea produced in Guilan Province, Iran, is about 61,000 ton per 34000 ha [15]. Herbal teas are usually used to make tea solutions due to their aroma and potential health benefits. The annual production of tea in the world is 3.6 million tons. Of note, 78% of the consumed tea is fully fermented black tea, 20% is non-fermented green tea, and 2% is semi-fermented oolong tea [16].

Considering the popularity of coffee, tea, and herbal tea in Iran and as recommended by the FAO, regular monitoring of metal levels in these product is necessary to ensure consumers health. Therefore, in this study, we (i) determined concentrations of eight metals (i.e., As, Cd, Cr, Cu, Fe, Hg, Ni, and Pb) in a total of 243 coffee, tea, and herbal tea samples collected from retail markets of Iran, and (ii) assessed

carcinogenic and non-carcinogenic risks posed to Iranian consumers via oral consumption of these products.

Materials and Methods

Collection of Samples

We randomly selected 29 coffee trademarks imported from 6 countries (A, B, C, D, E, and F), and for each trademark, 3 samples from different batches were collected, making a total of 87 coffee samples ($29 \times 3 = 87$). Also, 60 tea samples (7 trademarks imported from various countries and 3 different batches for each trademark ($7 \times 3 = 21$) and 13 domestic trademarks and 3 batches for each trademark ($13 \times 3 = 39$)) were purchased. A total of 96 herbal tea samples from 8 herbs (*Thymus vulgaris*, *Maticaria chamomilla*, *Hibiscus sabdariffa*, *Camellia sinensis*, *Echium amoenum*, *Rosa damascene*, *Menthe spicata*, and *Crocus sativus*, 3 different batches of 4 trademarks ($8 \times 3 \times 4 = 96$)) were also collected (Fig. 1). All samples were obtained under a randomized design from random markets in Iran. Samples were collected from August 2020 to November 2020.

Chemicals

All standards (of 99% purity) for metals As, Cd, Cr, Cu, Fe, Hg, Ni, Pb, and HNO_3 were purchased from Sigma-Aldrich (Steinheim, Germany).

Instrumentation

Microwave Digestion System

To determine the metal content of the samples, a microwave digestion system Milestone Ethos MicroSYNTH Oven (Milestone Srl. Sorisole, Italy) with 1000 W maximum power was used. Table 1 reports the digestion conditions [17].

ICP-OES

ICP-OES (Spectro Arcos, Germany) was used for As, Cd, Cr, Cu, Fe, Hg, Ni, and Pb detection with Torch type of Flared End EOP Torch, 2.5 mm. The specifications of ICP-OES are given in Table 2 [18].

Analytical Performance

Limit of detection (LOD) and limit of quantification (LOQ) for each metal were determined (Table 2). For each analytical batch, a fresh blank sample was considered. Next, a calibration curve was plotted for standard

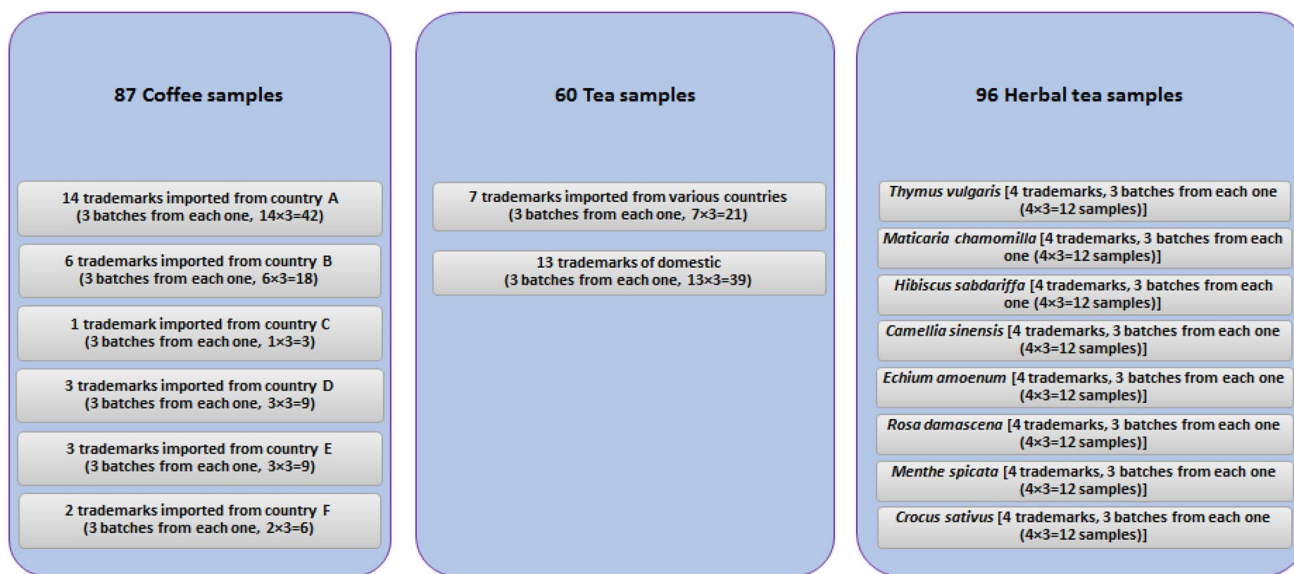


Fig. 1 Detailed description of samples analyzed in the present work. For all samples, analysis was done in triplicate

Table 1 Operating program used for microwave digestion in the present work

Phase	Initial temperature (°C)	Final temperature (°C)	Time (min)	Power (W)
1	25	90	5	700
2	90	90	3	600
3	90	170	10	600
4	170	170	7	600

solutions (0.625 to 1000 mg/L concentrations), and based on linear regression equations, As, Cd, Cr, Cu, Fe, Hg, Ni, and Pb levels in samples were determined. Additionally, recovery value for metals was calculated by comparing As, Cd, Cr, Cu, Fe, Hg, Ni, and Pb concentrations in the spike samples with those of standard solutions (5 to 800 mg/kg for each metal solution) (Fig. 2). Since nutrients Cu and Fe were also present in the tested matrices and are usually abundantly found in food samples, it was necessary to consider a wide range first. Therefore, a range of 5–800 was considered and then, according to the measured of metal level, the concentration of standard solution ranged 0.1–4 mg/kg ($n=3$ replicates of each samples were run) [19].

Metals Extraction

Wet ashing was done using a microwave digestion system to digest the samples. In this stage, 20 g of each sample was

dissolved in 120 ml of HNO_3 and 40 mL of H_2O_2 (40%) and the solution was then diluted to 200 mL 2% HNO_3 . The same method was used to prepare the blank. The clear liquid obtained was subjected to ICP-OES [4].

Quantitative Risk Analysis

In this study, we estimated the risk chronic exposure to carcinogenic (As, Ni, and Pb) and non-carcinogenic metals (Cd, Cr, Cu, Fe, and Hg), by calculation of daily intake (EDI) (mg/kg bw, Equation 1) of each metal found in the collected coffee, tea, and herbal tea (Fig. 3) [19].

$$EDI_i = \frac{C \times IRI}{BW} \quad (1)$$

C: Concentration of each metal in coffee, tea, and herbal tea samples (mg metal/kg dry weight (dw) of each sample)

IR: Ingestion rate; daily coffee, tea, or herbal tea consumption (kg); coffee: 0.002 kg/day [20], tea: 0.004 kg/day [21], and herbal tea: 0.002 kg/day [22].

BW: Body weight for an Iranian adult (70 kg) [23].

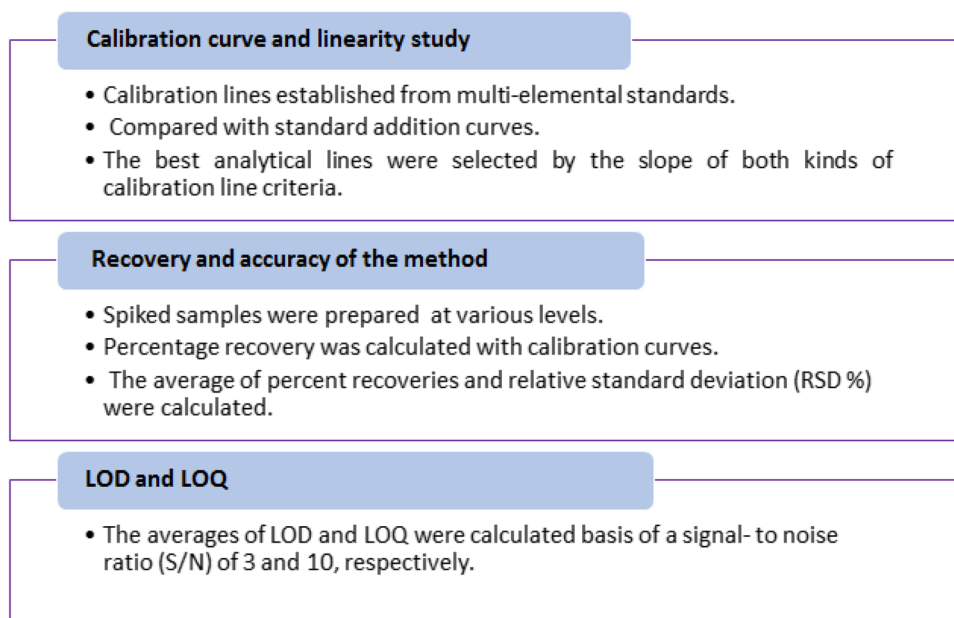
Non-carcinogenic Metals

We assessed health risk for oral exposure to non-carcinogenic metals (Cd, Cr, Cu, Fe, and Hg,) by calculating HQs (Equation 2) [24].

$$HQ = \frac{EDI}{ADI} \quad (2)$$

Table 2 Specification of ICP-OES employed in the present work

ICP specifications	Condition
Plasma power	1.2 kW
Carrier gas	Argon
Flow rate	15.0 L/min
Auxiliary flow rate	1.50 L/min
Read time	60 s
Nebulizer pressure	250 kPa
Operating optimal parameters	Radio-frequency generator (1400 W)
Uptake time	240 s
Rinse time	45 s
Initial stabilization time	45 s
Delay time	0
Time between replicate analysis	0
Type of detector	Solid state
Spray chamber	Charge coupled device (CCD)
Prewash pump speed (rpm)	60 (for 15 s) and 30 (for 30 s)
Injection pump speed	30 rpm
LOD for As, Cd, Cr, Cu, Fe, Hg, and Pb	1.0 µg/kg
LOQ for As, Cd, Cr, Cu, Fe, Hg, and Pb	3.0 µg/kg
LOD for Ni	7.0 µg/kg
LOQ for Ni	21.0 µg/kg
Replicates	3

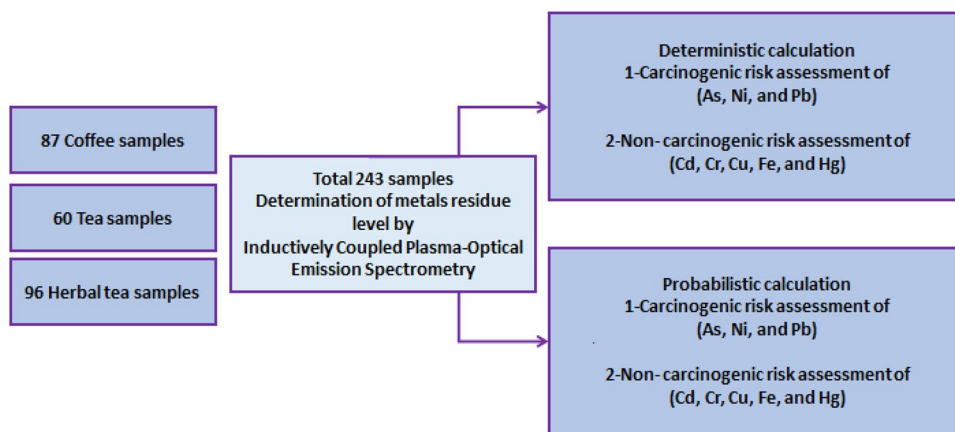
Fig. 2 The flowchart presenting the analytical performance

ADI: Acceptable daily intake for Cd, Cr, Cu, Fe, and Hg are, respectively, 0.001, 0.005, 0.5, 0.8, and 0.0005 mg/kg bw/day [25].

We calculated the total hazard index (HI) for non-carcinogenic metals by using the HQ [26].

$$HI = \sum_{i=1}^n HQ_i \quad (3)$$

Fig. 3 Schematic presentation of samples collected, metals residue level determination and risk assessment done for non-carcinogenic and carcinogenic metals



As indicated by the EPA, an HI < 1 indicates the absence of significant non-carcinogenic health risk, but an HI > 1 indicates a possibility of adverse health effects [27].

Carcinogenic Metals

Since, the IARC regards As, Pb, and Ni as carcinogens [28], by considering the cancer slope factors (CSFs), carcinogenic risk of oral exposure to As (group 1), Pb (group 2B), and Ni (group 1) [6] was assessed using the ILCR (Equation 4). It should be noted that although Cd is classified as group 1 carcinogens, but because no CSF for its oral exposure was found, it was included in non-carcinogenic scenario [17].

$$ILCR = EDI \times CSF \tag{4}$$

CSF: Cancer slope factor for As, Ni, and Pb was 1.5, 0.91, and 0.0085 mg/kg body weight/day, respectively [28, 29].

The findings were interpreted as follows: < 10⁻⁶ a very low level, 10⁻⁶-10⁻⁵ a low level, 10⁻⁵-10⁻⁴ a medium level, 10⁻⁴-10⁻³ a high level, and > 10⁻³ a very high level of carcinogenic risk [28].

Probabilistic Calculations

Monte Carlo simulation (MCS) enabled us to (I) specify dependent and independent variables, (II) identify independent variables distribution, and (III) perform simulations using the values of independent variables. Accordingly, we conducted MCS with 10,000 iterations or evaluation of non-carcinogenic and carcinogenic risks associated with oral exposure to metal content determined in coffee, tea, and herbal tea samples. In the current calculations, distribution mode was chosen as “log-normal” by SAS software JMP 8 (Campus Drive, Cary, NC 27513) [30].

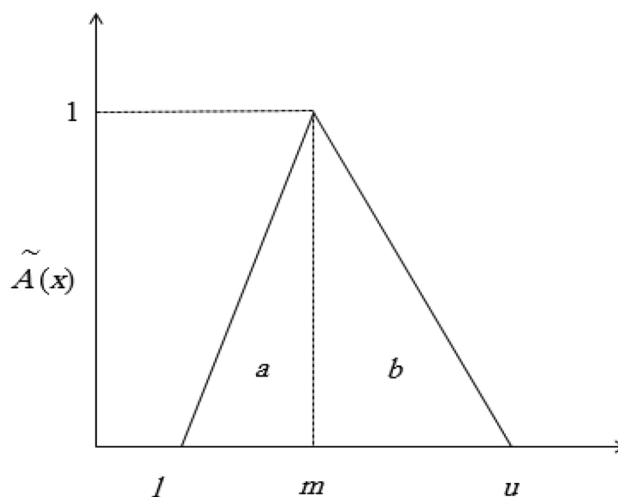


Fig. 4 The triangular fuzzy number for sensitivity analysis

Sensitivity Analysis

The probability of basic events was defined as a triangular fuzzy number $\tilde{A}(l, m, \text{ and } u)$ (Fig. 4). To investigate the variables that critically influence the accuracy of the assessed risk, we employed the median method for sensitivity analysis. The median number T_z represented \tilde{A} . The operation rules were as follows [31, 32]:

$$T_z = m - \sqrt{a^2 - ba}, a > b$$

$$T_z = m + \sqrt{b^2 - ba}, a < b$$

$$T_z = m, a = b$$

$$a = m - l$$

$$b = u - m$$

Statistical Analysis

In order to examine statistical differences among mean values, SAS software JMP 8 (Campus Drive, Cary, NC 27513)

was used. Significant differences among mean values were determined by using LSD at a probability of 0.05.

Results

Analytical Performance

Recoveries from the three matrices were determined at three concentrations and they were found to be within the range of 90.1–100%, with an associated RSD of $\leq 3.5\%$. The obtained recoveries confirmed the appropriateness of extraction, indicating no significant loss of metals. Coefficients of determination (R^2) exhibited significant linear relationships (99.6–99.9%) for all the calibration curves (Table 3).

Concentrations of Metals in the Collected Samples

As shown in Table 4, the metal levels in coffee samples from different trademarks of a specific country had statistically similar levels of metals; however, metal levels differed significantly among brand names from different countries. As and Pb levels were below LOD in all coffee samples of different trademarks from countries A and C. Also, similar pattern was found for Hg and Ni in all coffee samples of different trademarks from countries C and F (Table 4).

Metal levels in tea samples differed significantly between domestic and imported products, while different trademarks of similar countries did not show significant variations in this respect. The average level of Hg in our samples was lower than LOD in both imported and domestic tea samples. Nevertheless,

carcinogenic metals had significantly higher levels in imported products compared to domestic tea samples (Table 5).

As summarized in Table 6, metal level in herbal tea samples analyzed did not show significant variations among different trademarks. Nevertheless, it should be highlighted that mean concentrations of metals statistically differed among different herbal tea samples. In different species of herbal tea, except for *T. vulgaris* and *M. chamomilla*, Hg levels were below LOD. In *R. damascene* and *C. sativus* herbal tea samples, As, Cd, Hg, and Pb levels were below LOD (Table 6).

Health Risk Assessments

Risk Posed by Exposure to Metal Residue in Coffee Samples

As shown in Table 7, we calculated the HQs, HIs, and ILCRs under both carcinogenic and non-carcinogenic risk scenarios. Based on results, we found that HI for non-carcinogenic metals in coffee samples was below one (i.e., 0.01), while the ILCRs for carcinogenic metals (As, Ni, and Pb) were 3.84×10^{-6} , 2.83×10^{-5} , and 2.71×10^{-8} , which indicates medium level and no cancer risk, respectively.

Risk Posed by Exposure to Metal Residue in Tea Samples

For the non-carcinogenic metals content of tea samples, the estimated HI was 0.02 (reflecting absence of significant non-carcinogenic health risk), while for carcinogenic metals, we found ILCRs of 4.08×10^{-5} , 4.88×10^{-5} , and 5.13×10^{-9} (reflecting a medium and no carcinogenic health risk), respectively (Table 8).

Table 3 Mean recoveries, relative standard deviation (RSD, %) and coefficients of determination (R^2) for eight metals at three spiked concentrations ($\mu\text{g}/\text{kg}$ dw)

Metal	As	Cd	Cr	Cu	Fe	Hg	Ni	Pb
Coffee								
50 $\mu\text{g}/\text{kg}$	93.5 (2.4)	98.1 (1.4)	97.1 (2.3)	97.5 (2.0)	96.4 (2.2)	91.2 (3.1)	97.1 (2.1)	96.0 (3.1)
100 $\mu\text{g}/\text{kg}$	97.4 (3.2)	100 (1.1)	98.2 (3.3)	99.4 (1.3)	98.0 (3.5)	94.4 (3.1)	98.4 (3.0)	99.4 (1.3)
150 $\mu\text{g}/\text{kg}$	98.2 (3.1)	97.1 (2.0)	93.5 (2.2)	100 (2.3)	99.4 (2.5)	95.3 (1.5)	99.1 (2.3)	98.2 (2.2)
R^2	0.999	0.998	0.999	0.999	0.999	0.996	0.999	0.998
Tea								
50 $\mu\text{g}/\text{kg}$	91.2 (3.3)	97.4 (2.5)	95.1 (2.5)	91.2 (1.1)	93.4 (3.1)	90.1 (3.5)	97.4 (3.5)	91.2 (2.1)
100 $\mu\text{g}/\text{kg}$	96.1 (2.3)	99.5 (2.1)	97.1 (2.2)	96.2 (3.1)	95.3 (1.5)	96.4 (1.3)	99.1 (1.3)	94.4 (3.1)
150 $\mu\text{g}/\text{kg}$	98.2 (2.1)	98.0 (2.4)	100 (1.1)	99.2 (3.1)	98.2 (3.3)	98.2 (2.4)	100 (2.1)	99.3 (1.5)
R^2	0.999	0.997	0.999	0.998	0.999	0.997	0.999	0.999
Herbal tea								
50 $\mu\text{g}/\text{kg}$	96.1 (2.2)	97.4 (1.5)	93.1 (2.0)	94.5 (2.0)	91.4 (3.1)	91.2 (3.1)	97.5 (2.2)	94.4 (3.1)
100 $\mu\text{g}/\text{kg}$	98.2 (2.1)	100 (2.1)	99.5 (2.0)	95.3 (1.0)	95.3 (1.1)	94.4 (3.1)	98.2 (1.3)	100 (2.4)
150 $\mu\text{g}/\text{kg}$	100 (1.1)	96.0 (2.3)	98.2 (3.3)	99.4 (2.3)	98.1 (2.0)	98.3 (2.5)	100 (2.0)	97.1 (2.3)
R^2	0.999	0.999	0.999	0.999	0.999	0.998	0.999	0.998

Table 4 Levels of metals in different coffee samples

Coffee samples	As	Cd	Cr	Cu	Fe	Hg	Ni	Pb
Country A								
Trademarks								
A1	≤LOD	≤LOD	0.32±0.05	2.20±0.60	1.83±0.14	≤LOD	1.22±0.21	≤LOD
A2	≤LOD	≤LOD	0.22±0.01	2.31±0.55	1.67±0.10	0.01±0.002	0.91±0.20	≤LOD
A3	≤LOD	≤LOD	0.11±0.04	1.95±0.30	1.74±0.10	0.04±0.003	0.90±0.10	≤LOD
A4	≤LOD	≤LOD	0.14±0.02	1.01±0.14	1.55±0.11	≤LOD	≤LOQ	≤LOD
A5	≤LOD	≤LOD	0.22±0.05	2.01±0.40	1.36±0.21	0.05±0.002	1.18±0.21	≤LOD
A6	≤LOD	≤LOD	0.32±0.01	1.86±0.12	1.62±0.20	≤LOD	0.93±0.20	≤LOD
A7	≤LOD	≤LOD	0.29±0.01	1.73±0.15	1.75±0.15	≤LOD	0.87±0.25	≤LOD
A8	≤LOD	≤LOD	0.18±0.04	1.64±0.10	1.90±0.10	≤LOD	1.16±0.10	≤LOD
A9	≤LOD	≤LOD	1.38±0.12	1.92±0.12	1.70±0.30	0.01±0.002	1.55±0.13	≤LOD
A10	≤LOD	≤LOD	0.03±0.005	1.61±0.15	1.31±0.15	≤LOD	1.61±0.15	≤LOD
A11	≤LOD	≤LOD	0.01±0.005	1.82±0.12	1.44±0.11	≤LOD	1.43±0.10	≤LOD
A12	≤LOD	≤LOD	0.03±0.005	1.73±0.10	1.28±0.10	0.01±0.002	1.45±0.20	≤LOD
A13	≤LOD	≤LOD	0.85±0.05	2.02±0.12	1.75±0.20	0.06±0.001	1.76±0.30	≤LOD
A14	≤LOD	≤LOD	1.03±0.11	1.66±0.22	1.45±0.30	≤LOD	1.68±0.31	≤LOD
Country B								
Trademarks								
B1	0.12±0.02	1.64±0.31	1.26±0.10	2.00±0.15	1.41±0.11	≤LOD	1.85±0.33	0.01±0.001
B2	0.21±0.04	0.21±0.02	1.23±0.11	2.11±0.12	1.84±0.12	≤LOD	≤LOQ	0.03±0.005
B3	0.32±0.02	0.32±0.05	1.74±0.13	1.83±0.20	1.78±0.20	≤LOD	≤LOQ	0.01±0.002
B4	0.21±0.02	0.21±0.03	1.52±0.08	1.53±0.13	1.46±0.10	0.01±0.003	≤LOQ	≤LOQ
B5	0.07±0.005	0.11±0.03	1.46±0.10	1.73±0.11	1.94±0.30	≤LOD	1.56±0.20	≤LOD
B6	0.18±0.03	0.18±0.02	1.64±0.10	1.50±0.15	1.90±0.30	0.05±0.005	≤LOQ	≤LOD
Country C								
Trademarks								
C1	≤LOD	1.00±0.23	≤LOD	2.01±0.30	1.96±0.32	≤LOD	≤LOQ	≤LOD
Country D								
Trademarks								
D1	0.22±0.02	0.01±0.005	1.04±0.05	2.14±0.13	2.21±0.42	≤LOD	1.62±0.23	≤LOD
D2	0.25±0.02	0.01±0.004	1.04±0.05	2.03±0.10	2.50±0.30	≤LOD	2.02±0.30	≤LOD
D3	0.30±0.05	≤LOD	1.03±0.03	1.72±0.23	2.40±0.35	≤LOD	2.04±0.15	0.16±0.02
Country E								
Trademarks								
E1	0.15±0.01	≤LOD	0.04±0.005	2.15±0.20	0.78±0.05	0.94±0.005	1.95±0.24	1.24±0.10
E2	0.21±0.05	≤LOD	0.01±0.003	1.70±0.14	0.70±0.05	0.50±0.005	1.84±0.31	0.93±0.13
E3	0.32±0.04	≤LOD	0.01±0.003	1.50±0.13	0.20±0.03	≤LOD	1.93±0.25	0.90±0.11
Country F								
Trademarks								
F1	≤LOD	1.70±0.14	1.72±0.22	1.61±0.22	0.70±0.04	≤LOD	≤LOQ	0.01±0.11
F2	≤LOD	0.80±0.11	1.03±0.15	1.64±0.15	0.74±0.05	≤LOD	≤LOQ	≤LOD

Data expressed as mean of metals content (mg/kg) of samples ±SD (standard deviation) in three replicates

LOD limit of detection; LOQ limit of quantification

Risk Posed by Exposure to Metal Residue in Herbal Tea Samples

Concerning the content of eight metals in herbal tea samples, our calculations showed an HI of 0.01 and in

non-carcinogenic scenario; ILCRs were 2.95×10^{-5} , 3.84×10^{-5} , and 8.34×10^{-8} , for As, Ni, and Pb, respectively, that indicated the medium and no level of risk, respectively (Table 9).

Table 5 Levels of metals in different tea samples

Tea samples	As	Cd	Cr	Cu	Fe	Hg	Ni	Pb
Imported products								
Trademarks								
IP1	1.02±0.24	0.61±0.05	0.22±0.03	3.40±0.33	2.41±0.12	†LOD	0.12±0.01	0.03±0.004
IP2	1.10±0.11	0.50±0.03	0.25±0.01	3.44±0.32	2.55±0.13	†LOD	0.46±0.02	†LOD
IP3	1.35±0.13	0.64±0.02	0.30±0.01	3.35±0.31	2.42±0.10	†LOD	1.01±0.10	0.04±0.005
IP4	1.50±0.15	0.32±0.02	0.21±0.01	3.45±0.25	2.31±0.12	†LOD	1.12±0.10	0.01±0.003
IP5	1.04±0.10	0.60±0.02	0.30±0.05	3.41±0.30	4.15±0.22	†LOD	1.46±0.11	0.02±0.004
IP6	1.10±0.15	0.45±0.03	0.22±0.01	3.45±0.33	2.47±0.11	†LOD	1.30±0.10	†LOD
IP7	1.44±0.10	0.73±0.02	0.12±0.03	3.42±0.33	2.30±0.10	†LOD	1.37±0.15	0.02±0.005
Domestic products								
Trademarks								
DP1	0.10±0.03	0.10±0.03	0.12±0.01	1.84±0.10	7.24±0.53	†LOD	1.34±0.13	0.01±0.003
DP2	0.09±0.004	0.06±0.005	0.21±0.05	1.70±0.10	7.52±0.51	†LOD	1.54±0.15	0.01±0.003
DP3	0.03±0.002	0.10±0.02	0.22±0.03	1.17±0.12	6.30±0.55	†LOD	1.50±0.10	†LOD
DP4	0.11±0.03	0.05±0.001	0.24±0.02	1.30±0.15	5.08±0.51	†LOD	0.46±0.02	0.02±0.005
DP5	0.12±0.03	0.03±0.005	1.43±0.12	1.24±0.15	7.40±0.55	†LOD	0.78±0.02	†LOD
DP6	0.12±0.03	0.08±0.004	1.40±0.11	1.37±0.20	7.80±0.50	†LOD	0.90±0.02	†LOD
DP7	0.10±0.02	0.11±0.02	1.06±0.10	1.96±0.14	8.01±0.55	†LOD	0.93±0.02	†LOD
DP8	0.09±0.005	0.12±0.02	1.73±0.12	2.01±0.15	5.50±0.32	†LOD	0.31±0.05	0.01±0.003
DP9	0.06±0.003	0.13±0.03	1.73±0.11	1.97±0.11	5.17±0.32	†LOD	1.31±0.10	0.01±0.003
DP10	0.09±0.002	0.07±0.002	1.62±0.10	1.81±0.10	7.31±0.50	†LOD	1.65±0.11	†LOD
DP11	0.08±0.004	0.10±0.01	1.44±0.21	1.70±0.10	7.95±0.53	†LOD	1.71±0.01	0.02±0.005
DP12	0.13±0.02	0.08±0.002	1.48±0.15	1.62±0.15	6.55±0.41	†LOD	0.47±0.01	†LOD
DP13	0.17±0.03	0.10±0.01	1.48±0.25	1.84±0.10	5.66±0.35	†LOD	0.55±0.01	†LOD
DP14	0.07±0.005	0.06±0.002	1.84±0.10	1.66±0.10	4.92±0.23	†LOD	0.37±0.05	†LOD

Data expressed as mean of metals content (mg/kg) of samples ±SD (standard deviation) in three replicates

LOD limit of detection

Probabilistic Health Risk Assessments for Metal Contents of Coffee Samples

At the 50th, 75th, and 95th centiles, the ILCRs for As were, respectively, 1.33×10^{-4} , 5.38×10^{-4} , and 2.54×10^{-7} ; for Ni were, respectively, 9.85×10^{-4} , 1.08×10^{-3} , and 1.40×10^{-3} ; and for Pb were, respectively, 9.50×10^{-7} , 1.72×10^{-6} , and 2.04×10^{-6} . Based on the MCS model, at the 50th, 75th, and 95th centiles, HIs were 0.60, 1.40, and 4.41, respectively (Table 10).

Probabilistic Health Risk Assessments for Metal Contents of Tea Samples

For the carcinogenic metal residue in tea samples, ILCRs for As at the 50th, 75th, and 95th centiles were 1.44×10^{-3} , 4.03×10^{-3} , and 6.45×10^{-3} , respectively. ILCRs for Ni at the 50th, 75th, and 95th centiles were 1.23×10^{-3} , 1.53×10^{-3} , and 1.70×10^{-3} , respectively. Moreover, ILCRs for Pb at the 50th, 75th, and 95th centiles were 1.25×10^{-7} , 3.51×10^{-7} , and 5.62×10^{-7} ,

respectively. For non-carcinogenic metals, HIs at the 50th, 75th, and 95th centiles were 0.86, 1.30, and 1.82, respectively (Table 11).

Probabilistic Health Risk Assessments for Metal Contents of Herbal Tea Samples

At the 50th, 75th, and 95th centiles, the ILCRs for As were, respectively, 1.11×10^{-3} , 2.04×10^{-3} , and 4.30×10^{-3} ; for Ni were, respectively, 1.35×10^{-3} , 1.51×10^{-6} , and 1.72×10^{-3} ; and for Pb were, respectively, 3.20×10^{-6} , 5.67×10^{-6} , and 1.21×10^{-5} . Based on the MCS model, at the 50th, 75th, and 95th centile, HI values were 1.43, 2.58, and 5.68, respectively (Table 12).

Sensitivity Analysis

Based on the sensitivity analysis done by MCS, concentration was the input parameter with the greatest impact on HQ and ILCR estimations in assessment of risk of exposure to metals in coffee, tea, and herbal

Table 6 Levels of metals in different herbal tea samples

Herbal tea samples	As	Cd	Cr	Cu	Fe	Hg	Ni	Pb
<i>Thymus vulgaris</i>								
Trademarks								
Tv1	1.16±0.11	∠LOD	∠LOD	2.31±0.33	10.01±1.10	0.01±0.002	∠LOD	∠LOD
Tv2	1.02±0.10	0.01±0.013	0.01±0.001	1.46±0.32	10.80±1.13	∠LOD	∠LOD	0.81±0.03
Tv3	1.48±0.13	0.01±0.002	1.02±0.12	1.38±0.30	10.32±1.10	∠LOD	∠LOD	0.87±0.03
Tv4	1.35±0.10	0.01±0.002	2.24±0.21	1.45±0.20	11.35±1.10	0.01±0.01	1.72±0.13	∠LOD
<i>Maticaria chamomilla</i>								
Trademarks								
Mc1	1.90±0.10	∠LOD	2.12±0.22	1.24±0.32	9.27±1.11	∠LOD	1.40±0.13	1.03±0.15
Mc2	2.30±0.10	∠LOD	1.92±0.15	1.18±0.30	9.26±1.10	∠LOD	1.60±0.10	∠LOD
Mc3	2.46±0.10	∠LOD	0.96±0.03	1.85±0.22	9.88±1.10	0.01±0.002	1.63±0.10	1.14±0.11
Mc4	1.65±0.13	∠LOD	0.83±0.02	1.83±0.20	9.96±1.33	∠LOD	1.67±0.10	0.02±0.002
<i>Hibiscus sabdariffa</i>								
Trademarks								
Hs1	0.50±0.02	0.10±0.002	1.93±0.11	1.73±0.20	10.00±1.25	∠LOD	1.50±0.10	0.97±0.02
Hs2	0.56±0.03	∠LOD	1.90±0.12	1.63±0.21	9.78±1.21	∠LOD	1.01±0.11	1.04±0.02
Hs3	∠LOD	∠LOD	1.88±0.12	1.55±0.25	9.25±1.35	∠LOD	1.14±0.11	1.28±0.03
Hs4	∠LOD	0.10±0.004	0.91±0.03	1.41±0.21	9.60±1.30	∠LOD	1.01±0.10	∠LOD
<i>Camellia sinensis</i>								
Trademarks								
Cs1	0.31±0.02	0.27±0.02	0.54±0.02	1.46±0.15	9.14±1.22	∠LOD	1.72±0.11	0.01±0.003
Cs2	∠LOD	0.34±0.03	0.61±0.02	1.38±0.10	11.77±1.22	∠LOD	∠LOD	0.40±0.10
Cs3	0.46±0.02	0.34±0.02	0.64±0.02	1.10±0.10	9.52±1.30	∠LOD	∠LOD	0.24±0.10
Cs4	0.30±0.02	0.12±0.01	0.76±0.02	1.06±0.11	9.34±1.33	∠LOD	∠LOD	0.87±0.12
<i>Echium amoenum</i>								
Trademarks								
Ea1	1.65±0.14	0.41±0.01	0.82±0.03	1.83±0.13	10.23±1.25	∠LOD	1.61±0.12	0.73±0.12
Ea2	1.71±0.11	0.58±0.02	0.44±0.02	1.52±0.12	9.41±1.23	∠LOD	1.64±0.11	∠LOD
Ea3	0.76±0.04	0.33±0.02	0.53±0.02	1.68±0.23	10.00±1.10	∠LOD	3.70±0.21	0.97±0.14
Ea4	1.02±0.13	0.93±0.03	0.63±0.02	1.01±0.21	10.07±1.10	∠LOD	3.14±0.20	0.77±0.12
<i>Rosa damascena</i>								
Trademarks								
Rd1	∠LOD	∠LOD	1.00±0.22	1.44±0.30	10.38±1.10	∠LOD	3.32±0.21	∠LOD
Rd2	∠LOD	∠LOD	0.70±0.05	1.48±0.31	10.11±1.10	∠LOD	3.07±0.21	∠LOD
Rd3	∠LOD	∠LOD	1.86±0.31	1.47±0.25	10.06±1.12	∠LOD	3.07±0.21	∠LOD
Rd4	∠LOD	∠LOD	2.01±0.11	1.33±0.21	10.04±1.12	∠LOD	∠LOD	∠LOD
<i>Menthe spicata</i>								
Trademarks								
Ms1	0.31±0.02	∠LOD	2.00±0.14	1.78±0.25	9.10±1.05	∠LOD	3.78±0.25	0.01±0.005
Ms2	0.31±0.02	∠LOD	0.81±0.03	1.16±0.23	9.85±1.05	∠LOD	3.11±0.25	0.02±0.005
Ms3	0.38±0.03	∠LOD	2.07±0.12	2.15±0.40	9.96±1.04	∠LOD	3.32±0.25	∠LOD
Ms4	0.48±0.02	∠LOD	0.64±0.10	1.90±0.24	9.84±1.04	∠LOD	3.13±0.25	∠LOD
<i>Crocus sativus</i>								
Trademarks								
Cs1	∠LOD	∠LOD	∠LOD	1.42±0.20	9.84±1.04	∠LOD	∠LOD	∠LOD
Cs2	∠LOD	∠LOD	∠LOD	1.38±0.23	9.55±1.03	∠LOD	∠LOD	∠LOD
Cs3	∠LOD	∠LOD	0.80±0.02	1.10±0.15	9.40±1.04	∠LOD	∠LOD	∠LOD
Cs4	∠LOD	∠LOD	1.04±0.10	1.10±0.15	9.91±1.03	∠LOD	∠LOD	∠LOD

Data expressed as mean of metals content (mg/kg) of samples ±SD (standard deviation) in three replicates

LOD limit of detection

Table 7 HQs, HIs, and ILCRs calculated for carcinogenic and non-carcinogenic metals content of the collected coffee samples

Coffee samples	As ILCR	Cd HQ	Cr HQ	Cu HQ	Fe HQ	Hg HQ	Ni ILCR	Pb ILCR
Country A								
Trademarks								
A1	2.14×10^{-8}	1.42×10^{-5}	1.84×10^{-3}	1.25×10^{-4}	6.61×10^{-5}	2.85×10^{-5}	3.17×10^{-5}	1.18×10^{-10}
A2	2.14×10^{-8}	1.42×10^{-5}	1.27×10^{-3}	1.32×10^{-4}	5.97×10^{-5}	5.71×10^{-4}	2.38×10^{-5}	1.18×10^{-10}
A3	2.14×10^{-8}	1.42×10^{-5}	6.66×10^{-4}	1.11×10^{-4}	6.21×10^{-5}	2.36×10^{-3}	2.35×10^{-5}	1.18×10^{-10}
A4	2.14×10^{-8}	1.42×10^{-5}	8.38×10^{-4}	5.80×10^{-5}	5.55×10^{-5}	2.85×10^{-5}	2.73×10^{-5}	1.18×10^{-10}
A5	2.14×10^{-8}	1.42×10^{-5}	1.30×10^{-3}	1.11×10^{-4}	4.85×10^{-5}	3.00×10^{-3}	3.07×10^{-5}	1.18×10^{-10}
A6	2.14×10^{-8}	1.42×10^{-5}	1.84×10^{-3}	1.06×10^{-4}	5.80×10^{-5}	2.85×10^{-5}	2.42×10^{-5}	1.18×10^{-10}
A7	2.14×10^{-8}	1.42×10^{-5}	1.70×10^{-3}	9.92×10^{-5}	6.27×10^{-5}	2.85×10^{-5}	2.28×10^{-5}	1.18×10^{-10}
A8	2.14×10^{-8}	1.42×10^{-5}	1.06×10^{-3}	9.37×10^{-5}	6.80×10^{-5}	2.85×10^{-5}	3.02×10^{-5}	1.18×10^{-10}
A9	2.14×10^{-8}	1.42×10^{-5}	7.88×10^{-3}	1.10×10^{-4}	6.05×10^{-5}	6.28×10^{-4}	4.03×10^{-5}	1.18×10^{-10}
A10	2.14×10^{-8}	1.42×10^{-5}	1.82×10^{-4}	9.23×10^{-5}	4.67×10^{-5}	2.85×10^{-5}	4.19×10^{-5}	1.18×10^{-10}
A11	2.14×10^{-8}	1.42×10^{-5}	6.66×10^{-5}	1.04×10^{-4}	5.16×10^{-5}	2.85×10^{-5}	3.72×10^{-5}	1.18×10^{-10}
A12	2.14×10^{-8}	1.42×10^{-5}	1.84×10^{-4}	9.88×10^{-5}	4.58×10^{-5}	7.23×10^{-4}	3.77×10^{-5}	1.18×10^{-10}
A13	2.14×10^{-8}	1.42×10^{-5}	4.87×10^{-3}	1.15×10^{-4}	6.26×10^{-5}	3.75×10^{-3}	4.58×10^{-5}	1.18×10^{-10}
A14	2.14×10^{-8}	1.42×10^{-5}	5.90×10^{-3}	9.48×10^{-5}	5.20×10^{-5}	2.85×10^{-5}	4.38×10^{-5}	1.18×10^{-10}
Country B								
Trademarks								
B1	5.42×10^{-6}	4.68×10^{-2}	7.21×10^{-3}	1.14×10^{-4}	5.04×10^{-5}	2.85×10^{-5}	4.81×10^{-5}	2.76×10^{-9}
B2	9.00×10^{-6}	6.00×10^{-3}	7.02×10^{-3}	1.12×10^{-4}	6.58×10^{-5}	2.85×10^{-5}	2.73×10^{-7}	7.58×10^{-9}
B3	1.40×10^{-5}	9.00×10^{-3}	9.96×10^{-3}	1.04×10^{-4}	6.36×10^{-5}	2.85×10^{-5}	2.73×10^{-7}	2.37×10^{-9}
B4	9.00×10^{-6}	6.00×10^{-3}	8.70×10^{-3}	8.74×10^{-5}	5.22×10^{-5}	6.66×10^{-4}	2.73×10^{-7}	3.55×10^{-10}
B5	3.04×10^{-6}	3.00×10^{-3}	8.36×10^{-3}	9.92×10^{-5}	6.94×10^{-5}	2.85×10^{-5}	4.06×10^{-5}	1.18×10^{-10}
B6	7.85×10^{-6}	5.00×10^{-3}	9.41×10^{-3}	8.53×10^{-5}	6.80×10^{-5}	3.23×10^{-3}	2.73×10^{-7}	1.18×10^{-10}
Country C								
Trademarks								
C1	2.14×10^{-8}	2.87×10^{-2}	2.85×10^{-6}	1.14×10^{-4}	7.01×10^{-5}	2.85×10^{-5}	2.73×10^{-7}	1.18×10^{-10}
Country D								
Trademarks								
D1	9.71×10^{-6}	2.00×10^{-4}	5.96×10^{-3}	1.12×10^{-4}	7.91×10^{-5}	2.85×10^{-5}	4.21×10^{-5}	1.18×10^{-10}
D2	1.10×10^{-5}	3.00×10^{-4}	5.98×10^{-3}	1.15×10^{-4}	8.92×10^{-5}	2.85×10^{-5}	5.25×10^{-5}	1.18×10^{-10}
D3	1.27×10^{-5}	1.42×10^{-5}	5.90×10^{-3}	1.82×10^{-5}	8.57×10^{-5}	2.85×10^{-5}	5.32×10^{-5}	3.87×10^{-8}
Country E								
Trademarks								
E1	6.42×10^{-6}	1.42×10^{-5}	2.32×10^{-4}	1.12×10^{-4}	2.80×10^{-5}	5.40×10^{-2}	5.08×10^{-5}	2.95×10^{-7}
E2	9.14×10^{-6}	1.42×10^{-5}	5.71×10^{-5}	9.67×10^{-5}	2.48×10^{-5}	2.28×10^{-2}	4.78×10^{-5}	2.20×10^{-7}
E3	1.37×10^{-5}	1.42×10^{-5}	5.71×10^{-5}	8.53×10^{-5}	6.90×10^{-6}	2.85×10^{-5}	5.04×10^{-5}	2.13×10^{-7}
Country F								
Trademarks								
F1	2.14×10^{-8}	4.86×10^{-2}	9.86×10^{-3}	9.20×10^{-5}	2.52×10^{-5}	2.85×10^{-5}	2.73×10^{-7}	2.37×10^{-9}
F2	2.14×10^{-8}	2.28×10^{-2}	5.90×10^{-3}	9.37×10^{-5}	2.66×10^{-5}	2.85×10^{-5}	2.73×10^{-7}	1.18×10^{-10}
HI = 0.01	-	-	-	-	-	-	-	-
ILCR	3.84×10^{-6}	-	-	-	-	-	2.83×10^{-5}	2.71×10^{-8}

tea (Fig. 5). Under the non-carcinogenic scenario, the influence of concentration was, respectively, near 13.42, 18, and 14% for coffee, tea, and herbal tea, and, respectively, 15.45, 15, and 15 under carcinogenic scenario (Fig. 5).

Discussion

In the present study, we assessed the potential health risks posed to Iranian consumers by oral exposure to residues of eight metals through consumption of coffee, tea, and herbal

Table 8 HQs, HIs, and ILCRs calculated for carcinogenic and non-carcinogenic metals content of the collected tea samples

Tea samples	As ILCR	Cd HQ	Cr HQ	Cu HQ	Fe HQ	Hg HQ	Ni ILCR	Pb ILCR
Imported products								
Trademarks								
IP1	8.80×10^{-5}	3.52×10^{-2}	2.60×10^{-3}	3.88×10^{-4}	1.72×10^{-4}	5.71×10^{-5}	6.60×10^{-6}	1.43×10^{-8}
IP2	9.48×10^{-5}	2.80×10^{-2}	2.93×10^{-3}	3.93×10^{-4}	1.82×10^{-4}	5.71×10^{-5}	2.42×10^{-5}	2.37×10^{-10}
IP3	1.16×10^{-4}	3.67×10^{-2}	3.46×10^{-3}	3.83×10^{-4}	1.73×10^{-4}	5.71×10^{-5}	5.25×10^{-5}	1.97×10^{-8}
IP4	1.28×10^{-4}	1.84×10^{-2}	2.43×10^{-3}	3.94×10^{-4}	1.65×10^{-4}	5.71×10^{-5}	5.82×10^{-5}	5.70×10^{-9}
IP5	8.91×10^{-5}	3.46×10^{-2}	3.31×10^{-3}	3.90×10^{-4}	2.97×10^{-4}	5.71×10^{-5}	7.63×10^{-5}	1.12×10^{-8}
IP6	9.48×10^{-5}	2.60×10^{-2}	2.55×10^{-3}	3.94×10^{-4}	1.77×10^{-4}	5.71×10^{-5}	6.76×10^{-5}	2.37×10^{-10}
IP7	1.23×10^{-4}	4.20×10^{-2}	1.44×10^{-3}	3.91×10^{-4}	1.65×10^{-4}	5.71×10^{-5}	7.16×10^{-5}	1.24×10^{-8}
Domestic products								
Trademarks								
DP1	8.57×10^{-6}	5.33×10^{-3}	1.44×10^{-3}	2.10×10^{-4}	5.17×10^{-4}	5.71×10^{-5}	6.97×10^{-5}	4.90×10^{-9}
DP2	8.28×10^{-6}	3.54×10^{-3}	2.40×10^{-3}	1.94×10^{-4}	5.37×10^{-4}	5.71×10^{-5}	8.03×10^{-5}	5.53×10^{-9}
DP3	3.20×10^{-6}	5.52×10^{-3}	2.60×10^{-3}	6.72×10^{-5}	2.25×10^{-4}	5.71×10^{-5}	7.78×10^{-5}	2.37×10^{-10}
DP4	1.00×10^{-5}	2.85×10^{-3}	2.81×10^{-3}	1.50×10^{-4}	3.63×10^{-4}	5.71×10^{-5}	2.43×10^{-5}	9.96×10^{-9}
DP5	1.05×10^{-5}	2.01×10^{-3}	1.63×10^{-2}	1.41×10^{-4}	5.30×10^{-4}	5.71×10^{-5}	4.10×10^{-5}	2.37×10^{-10}
DP6	1.08×10^{-5}	5.02×10^{-3}	1.60×10^{-2}	1.56×10^{-4}	5.56×10^{-4}	5.71×10^{-5}	4.63×10^{-5}	2.37×10^{-10}
DP7	8.85×10^{-6}	6.28×10^{-3}	1.21×10^{-2}	2.24×10^{-4}	5.72×10^{-4}	5.71×10^{-5}	4.87×10^{-5}	2.37×10^{-10}
DP8	7.85×10^{-6}	6.85×10^{-3}	9.90×10^{-3}	2.30×10^{-4}	3.93×10^{-4}	5.71×10^{-5}	1.61×10^{-5}	5.37×10^{-9}
DP9	5.22×10^{-6}	7.61×10^{-3}	2.00×10^{-2}	2.25×10^{-4}	3.70×10^{-4}	5.71×10^{-5}	1.63×10^{-5}	6.00×10^{-9}
DP10	8.28×10^{-6}	4.38×10^{-3}	1.85×10^{-2}	2.07×10^{-4}	5.22×10^{-4}	5.71×10^{-5}	8.60×10^{-5}	2.37×10^{-10}
DP11	7.48×10^{-6}	5.71×10^{-3}	1.65×10^{-2}	1.94×10^{-4}	5.68×10^{-4}	5.71×10^{-5}	8.92×10^{-5}	1.01×10^{-8}
DP12	1.17×10^{-5}	5.00×10^{-3}	1.70×10^{-2}	1.85×10^{-4}	4.68×10^{-4}	5.71×10^{-5}	2.45×10^{-5}	2.37×10^{-10}
DP13	1.51×10^{-5}	5.23×10^{-3}	1.70×10^{-2}	2.10×10^{-4}	4.04×10^{-4}	5.71×10^{-5}	2.90×10^{-5}	2.37×10^{-10}
DP14	6.34×10^{-6}	3.88×10^{-3}	2.10×10^{-2}	1.90×10^{-4}	3.52×10^{-4}	5.71×10^{-5}	1.94×10^{-5}	2.37×10^{-10}
HI = 0.02		-	-	-	-	-	-	-
ILCR	4.08×10^{-5}						4.88×10^{-5}	5.13×10^{-9}

tea samples collected from Iran market, in terms of HQ method (for non-carcinogenic metals) and ILCR (for carcinogenic metals).

Mean metal concentration in coffee, tea, and herbal tea samples showed statistically significant variations among different trademarks. Of note, samples from different producing countries had different metal residue content. Our health risk assessment in terms of HI indicated that consumption of the collected samples poses no risk to Iranian consumer's health. Several pre- and post-harvest factors including soil and water contamination (e.g., due to mismanagement of waste), as well as manufacturing and cooking processes, can contaminate foods with metals. The use of different fertilizers and plant protection products may cause toxic metal accumulation in food chain [33]. Acidic soils that are suitable for tea cultivation were shown to contribute to accumulation of metals in this plant [34]. It was previously shown that the degree of roasting affects the level of metals in resulting drinks [8].

A study from China assessed four different types of tea (black, dark, green, and oolong) for rare earth metals (Ce, La, Sc, Nd, and Y) and reported that tea leaves accumulated these rare metals with Ce being the most abundant one [35]. A study from India reported content of As and Cr in 497 black tea samples and indicated HQs < 1 based on non-carcinogenic risk assessment, reflecting no health risk [14]. Ferrara et al. collected tea samples from Italy and reported that Cr in black tea was in the range of 17.9–115.4 mg/kg, while the concentrations of Cr among the imported tea samples were 19.8–129.1 mg/kg [36]. Another study from China showed that mean concentration of Cr in a total of 801 tea samples from China retail markets was 16.10 mg/kg [37]. A comparison of Indian, Chinese, and Japanese green tea indicated that Chinese and Japanese green tea contained a higher mean content of Cr (0.4–1.4 and 1.0–3.4 mg/kg, respectively) than Indian samples (0.3–1.0 mg/kg) [38]. The mean concentration of Cr in black teas from Iran, India, and Ceylon in the retail markets of Tehran, Iran, was 1.54, 1.56, and < 1.21

Table 9 HQs, HIs, and ILCRs calculated for carcinogenic and non-carcinogenic metals content of the collected herbal tea samples

Herbal tea samples	As ILCR	Cd HQ	Cr HQ	Cu HQ	Fe HQ	Hg HQ	Ni ILCR	Pb ILCR
<i>Thymus vulgaris</i>								
Trademarks								
Tv1	4.98×10^{-5}	1.42×10^{-5}	2.85×10^{-6}	1.32×10^{-4}	3.58×10^{-4}	6.28×10^{-4}	9.10×10^{-8}	1.18×10^{-10}
Tv2	4.37×10^{-5}	3.80×10^{-4}	7.61×10^{-5}	8.36×10^{-5}	3.85×10^{-4}	2.85×10^{-5}	9.10×10^{-8}	1.93×10^{-7}
Tv3	6.34×10^{-5}	3.14×10^{-4}	5.82×10^{-3}	7.88×10^{-5}	3.70×10^{-4}	2.85×10^{-5}	9.10×10^{-8}	2.07×10^{-7}
Tv4	5.78×10^{-5}	3.14×10^{-4}	1.28×10^{-2}	8.30×10^{-5}	4.05×10^{-4}	8.00×10^{-4}	4.50×10^{-5}	1.18×10^{-10}
<i>Maticaria chamomilla</i>								
Trademarks								
Mc1	8.10×10^{-5}	1.42×10^{-5}	1.21×10^{-2}	7.12×10^{-5}	3.31×10^{-4}	2.85×10^{-5}	3.64×10^{-5}	2.45×10^{-7}
Mc2	9.82×10^{-5}	1.42×10^{-5}	1.10×10^{-2}	6.76×10^{-5}	3.31×10^{-4}	2.85×10^{-5}	4.15×10^{-5}	1.18×10^{-10}
Mc3	1.05×10^{-4}	1.42×10^{-5}	5.52×10^{-3}	1.06×10^{-4}	3.53×10^{-4}	5.71×10^{-4}	4.25×10^{-5}	2.71×10^{-7}
Mc4	7.10×10^{-5}	1.42×10^{-5}	4.74×10^{-3}	1.04×10^{-4}	3.56×10^{-4}	2.85×10^{-5}	4.34×10^{-5}	5.30×10^{-9}
<i>Hibiscus sabdariffa</i>								
Trademarks								
Hs1	2.11×10^{-5}	3.04×10^{-3}	1.10×10^{-2}	9.90×10^{-5}	3.57×10^{-4}	2.85×10^{-5}	3.88×10^{-5}	2.31×10^{-7}
Hs2	2.41×10^{-5}	1.42×10^{-5}	1.08×10^{-2}	9.35×10^{-5}	3.50×10^{-4}	2.85×10^{-5}	2.63×10^{-5}	2.48×10^{-7}
Hs3	2.14×10^{-8}	1.42×10^{-5}	1.07×10^{-2}	8.90×10^{-5}	3.31×10^{-4}	2.85×10^{-5}	2.96×10^{-5}	3.03×10^{-7}
Hs4	2.14×10^{-8}	3.04×10^{-3}	5.20×10^{-3}	8.10×10^{-5}	3.43×10^{-4}	2.85×10^{-5}	2.63×10^{-5}	1.18×10^{-10}
<i>Camellia sinensis</i>								
Trademarks								
Cs1	1.32×10^{-5}	7.80×10^{-3}	3.12×10^{-3}	8.34×10^{-5}	3.27×10^{-4}	2.85×10^{-5}	4.47×10^{-5}	2.37×10^{-9}
Cs2	2.14×10^{-8}	9.71×10^{-3}	3.48×10^{-3}	7.90×10^{-5}	4.21×10^{-4}	2.85×10^{-5}	9.10×10^{-8}	9.64×10^{-8}
Cs3	2.00×10^{-5}	9.90×10^{-3}	3.65×10^{-3}	6.22×10^{-5}	3.40×10^{-4}	2.85×10^{-5}	9.10×10^{-8}	5.84×10^{-8}
Cs4	1.27×10^{-5}	3.42×10^{-3}	4.34×10^{-3}	6.05×10^{-5}	3.34×10^{-4}	2.85×10^{-5}	9.10×10^{-8}	2.07×10^{-7}
<i>Echium amoenum</i>								
Trademarks								
Ea1	7.10×10^{-5}	1.20×10^{-2}	4.68×10^{-3}	1.04×10^{-4}	3.65×10^{-4}	2.85×10^{-5}	4.20×10^{-5}	1.73×10^{-7}
Ea2	7.35×10^{-5}	1.16×10^{-2}	2.55×10^{-3}	8.70×10^{-5}	3.36×10^{-4}	2.85×10^{-5}	4.26×10^{-5}	1.18×10^{-10}
Ea3	3.25×10^{-5}	9.61×10^{-3}	3.06×10^{-3}	9.63×10^{-5}	3.57×10^{-4}	2.85×10^{-5}	9.61×10^{-5}	2.31×10^{-7}
Ea4	4.40×10^{-5}	9.61×10^{-3}	3.60×10^{-3}	5.77×10^{-5}	3.60×10^{-4}	2.85×10^{-5}	8.18×10^{-5}	1.83×10^{-7}
<i>Rosa damascena</i>								
Trademarks								
Rd1	2.14×10^{-8}	1.42×10^{-5}	5.65×10^{-3}	8.26×10^{-5}	3.71×10^{-4}	2.85×10^{-5}	8.63×10^{-5}	1.18×10^{-10}
Rd2	2.14×10^{-8}	1.42×10^{-5}	4.00×10^{-3}	8.50×10^{-5}	3.61×10^{-4}	2.85×10^{-5}	8.00×10^{-5}	1.18×10^{-10}
Rd3	2.14×10^{-8}	1.42×10^{-5}	1.06×10^{-2}	8.43×10^{-5}	3.60×10^{-4}	2.85×10^{-5}	7.98×10^{-5}	1.18×10^{-10}
Rd4	2.14×10^{-8}	1.42×10^{-5}	1.15×10^{-2}	8.63×10^{-5}	3.60×10^{-4}	2.85×10^{-5}	9.10×10^{-8}	1.18×10^{-10}
<i>Menthe spicata</i>								
Trademarks								
Ms1	1.32×10^{-5}	1.42×10^{-5}	1.14×10^{-2}	1.01×10^{-4}	3.25×10^{-4}	2.85×10^{-5}	9.84×10^{-5}	2.37×10^{-9}
Ms2	1.34×10^{-5}	1.42×10^{-5}	4.66×10^{-3}	6.62×10^{-5}	3.52×10^{-4}	2.85×10^{-5}	8.10×10^{-5}	5.84×10^{-9}
Ms3	1.62×10^{-5}	1.42×10^{-5}	1.18×10^{-2}	1.23×10^{-4}	3.56×10^{-4}	2.85×10^{-5}	8.63×10^{-5}	1.18×10^{-10}
Ms4	2.07×10^{-5}	1.42×10^{-5}	3.70×10^{-3}	1.08×10^{-4}	3.52×10^{-4}	2.85×10^{-5}	8.16×10^{-5}	1.18×10^{-10}
<i>Crocus sativus</i>								
Trademarks								
Cs1	2.14×10^{-8}	1.42×10^{-5}	2.85×10^{-6}	8.15×10^{-5}	3.52×10^{-4}	2.85×10^{-5}	9.10×10^{-8}	1.18×10^{-10}
Cs2	2.14×10^{-8}	1.42×10^{-5}	2.85×10^{-6}	7.90×10^{-5}	3.41×10^{-4}	2.85×10^{-5}	9.10×10^{-8}	1.18×10^{-10}
Cs3	2.14×10^{-8}	1.42×10^{-5}	4.60×10^{-3}	6.22×10^{-5}	3.36×10^{-4}	2.85×10^{-5}	9.10×10^{-8}	1.18×10^{-10}
Cs4	2.14×10^{-8}	1.42×10^{-5}	5.94×10^{-3}	6.28×10^{-5}	3.54×10^{-4}	2.85×10^{-5}	9.10×10^{-8}	1.18×10^{-10}
HI = 0.01	-	-	-	-	-	-	-	-
ILCR	2.95×10^{-5}	-	-	-	-	-	3.84×10^{-5}	8.34×10^{-8}

Table 10 Probabilistic HQs, HIs, and ILCRs for carcinogenic and non-carcinogenic metals contents of coffee samples

Percentiles	As ILCR	Cd HQ	Cr HQ	Cu HQ	Fe HQ	Hg HQ	Ni ILCR	Pb ILCR
Country A								
50th	3.60×10^{-7}	2.20×10^{-4}	3.25×10^{-2}	1.60×10^{-3}	8.80×10^{-4}	1.23×10^{-2}	5.20×10^{-4}	1.82×10^{-9}
75th	6.60×10^{-7}	5.06×10^{-4}	7.50×10^{-2}	3.68×10^{-3}	2.02×10^{-3}	2.84×10^{-2}	5.73×10^{-4}	3.65×10^{-9}
95th	7.80×10^{-7}	1.67×10^{-3}	5.70×10^{-2}	1.21×10^{-2}	6.68×10^{-3}	9.40×10^{-2}	7.45×10^{-4}	4.31×10^{-9}
Country B								
50th	4.85×10^{-5}	8.45×10^{-2}	5.57×10^{-2}	6.73×10^{-4}	4.06×10^{-4}	4.42×10^{-3}	1.07×10^{-4}	1.46×10^{-8}
75th	2.33×10^{-4}	1.94×10^{-1}	1.28×10^{-1}	1.54×10^{-3}	9.35×10^{-4}	1.01×10^{-2}	1.20×10^{-4}	2.93×10^{-8}
95th	1.25×10^{-4}	6.41×10^{-1}	4.23×10^{-1}	5.11×10^{-3}	3.08×10^{-3}	3.35×10^{-2}	1.54×10^{-4}	3.46×10^{-8}
Country C								
50th	2.57×10^{-8}	3.16×10^{-2}	3.14×10^{-6}	1.26×10^{-4}	7.71×10^{-5}	3.14×10^{-5}	3.27×10^{-7}	1.30×10^{-10}
75th	1.03×10^{-7}	7.27×10^{-2}	7.22×10^{-6}	2.91×10^{-4}	1.77×10^{-4}	7.22×10^{-5}	3.60×10^{-7}	2.60×10^{-10}
95th	5.57×10^{-8}	2.40×10^{-1}	2.38×10^{-5}	9.60×10^{-4}	5.85×10^{-4}	2.40×10^{-4}	4.68×10^{-7}	3.08×10^{-10}
Country D								
50th	4.01×10^{-5}	7.07×10^{-4}	1.96×10^{-2}	3.70×10^{-4}	2.80×10^{-4}	9.42×10^{-5}	1.77×10^{-4}	4.71×10^{-8}
75th	1.61×10^{-4}	1.62×10^{-3}	4.51×10^{-2}	8.50×10^{-4}	6.43×10^{-4}	2.16×10^{-4}	1.95×10^{-4}	8.57×10^{-8}
95th	8.70×10^{-4}	5.36×10^{-3}	1.50×10^{-1}	2.80×10^{-3}	2.12×10^{-3}	7.16×10^{-4}	2.54×10^{-4}	1.01×10^{-7}
Country E								
50th	3.51×10^{-5}	4.71×10^{-5}	3.81×10^{-4}	3.35×10^{-4}	6.57×10^{-5}	9.07×10^{-2}	1.78×10^{-4}	8.82×10^{-7}
75th	1.41×10^{-4}	1.08×10^{-4}	8.77×10^{-4}	7.72×10^{-4}	1.51×10^{-4}	2.08×10^{-1}	1.97×10^{-4}	1.60×10^{-6}
95th	4.04×10^{-5}	3.58×10^{-4}	2.90×10^{-3}	2.54×10^{-3}	5.00×10^{-4}	6.88×10^{-1}	2.56×10^{-4}	1.90×10^{-6}
Country F								
50th	5.14×10^{-8}	7.86×10^{-2}	1.73×10^{-2}	2.04×10^{-4}	5.70×10^{-5}	6.28×10^{-5}	6.55×10^{-7}	3.01×10^{-9}
75th	2.07×10^{-7}	1.80×10^{-1}	4.00×10^{-2}	4.70×10^{-4}	1.31×10^{-4}	1.44×10^{-4}	7.21×10^{-7}	5.47×10^{-9}
95th	1.11×10^{-7}	5.97×10^{-1}	1.31×10^{-1}	1.55×10^{-3}	4.33×10^{-4}	4.77×10^{-4}	9.37×10^{-7}	6.47×10^{-9}
HI (50th)	-	1.95×10^{-1}	1.25×10^{-1}	3.31×10^{-3}	1.76×10^{-3}	1.07×10^{-1}	-	-
HI = 0.43	-	-	-	-	-	-	-	-
HI (75th)	-	4.50×10^{-1}	2.90×10^{-1}	7.61×10^{-3}	4.06×10^{-3}	2.47×10^{-1}	-	-
HI = 1.00	-	-	-	-	-	-	-	-
HI (95th)	-	14.8×10^{-1}	7.63×10^{-1}	2.51×10^{-2}	1.34×10^{-2}	8.17×10^{-1}	-	-
HI = 3.10	-	-	-	-	-	-	-	-
ILCR (50th)	1.33×10^{-4}	-	-	-	-	-	9.85×10^{-4}	9.50×10^{-7}
ILCR (75th)	5.38×10^{-4}	-	-	-	-	-	1.08×10^{-3}	1.72×10^{-6}
ILCR (95th)	2.54×10^{-7}	-	-	-	-	-	1.40×10^{-3}	2.04×10^{-6}

$\mu\text{g/g}$, respectively [39]. A report from China determined Cr (III), Cr (VI), and total Cr levels in 128 domestic teas and found that drinking tea could be the main route for Cr intake and poses risk to human health [40]. A report from China showed that the calculated HQs indicated no risk; this study indicated that the storage years had no effect on metal exposure risk and the metals in tea samples were originated from the atmosphere and soil [9]. In another study, HQs and HI for Fe, Zn, As, Cd, and Pb levels in black, green, and white tea samples were <1 that revealed no potential risk to human health; however, the carcinogenic risk for As was $> 10^{-6}$ [34]. A report from Poland

determined the concentrations of Cd, Pb, As, and Hg in 240 tea, coffee, and herbal tea samples, and conducted probabilistic carcinogenic (in terms of ILCR) and non-carcinogenic (in terms of HQ) risk assessment; the HQs for tea, coffee, spices, and herbal tea samples were 4.03×10^{-2} , 1.25×10^{-1} , and 2.51×10^{-1} , respectively, reflecting no probability of non-carcinogenic risk via consumption of these products. Also, ILCR for As was 1.29×10^{-5} which is less than the maximum acceptable level (i.e., 1.00×10^{-4}) suggested by the United States Environmental Protection Agency (USEPA). Several studies revealed that certain species of plants due to their anatomical structure

Table 11 Probabilistic HQs, HIs, and ILCRs for carcinogenic and non-carcinogenic metals contents of tea samples

Percentiles	As ILCR	Cd HQ	Cr HQ	Cu HQ	Fe HQ	Hg HQ	Ni ILCR	Pb ILCR
Imported products								
50th	1.44×10^{-3}	2.65×10^{-1}	2.24×10^{-2}	3.28×10^{-3}	1.60×10^{-3}	4.80×10^{-4}	4.28×10^{-4}	1.25×10^{-7}
75th	4.03×10^{-3}	4.00×10^{-1}	3.37×10^{-2}	4.92×10^{-3}	2.40×10^{-3}	7.20×10^{-4}	5.36×10^{-4}	3.51×10^{-7}
95th	6.45×10^{-3}	5.57×10^{-1}	4.72×10^{-2}	6.90×10^{-3}	3.35×10^{-3}	1.00×10^{-3}	5.90×10^{-4}	5.62×10^{-7}
Domestic products								
50th	2.40×10^{-4}	8.31×10^{-2}	2.08×10^{-1}	3.10×10^{-3}	7.65×10^{-3}	9.60×10^{-4}	8.02×10^{-4}	8.58×10^{-8}
75th	6.72×10^{-4}	1.24×10^{-1}	3.12×10^{-1}	4.65×10^{-3}	1.14×10^{-4}	1.44×10^{-3}	1.00×10^{-3}	2.40×10^{-7}
95th	1.07×10^{-3}	1.74×10^{-1}	4.37×10^{-1}	6.52×10^{-3}	1.60×10^{-2}	2.01×10^{-3}	1.10×10^{-3}	3.84×10^{-7}
HI (50th)	-	3.48×10^{-1}	2.30×10^{-1}	6.38×10^{-3}	9.24×10^{-3}	1.44×10^{-3}	-	-
HI = 0.60	-	-	-	-	-	-	-	-
HI (75th)	-	5.22×10^{-1}	3.46×10^{-1}	9.58×10^{-3}	1.38×10^{-2}	2.16×10^{-3}	-	-
HI = 0.90	-	-	-	-	-	-	-	-
HI (95th)	-	7.31×10^{-1}	4.84×10^{-1}	1.34×10^{-2}	1.94×10^{-2}	3.02×10^{-3}	-	-
HI = 1.25	-	-	-	-	-	-	-	-
ILCR (50th)	1.44×10^{-3}	-	-	-	-	-	1.23×10^{-3}	1.25×10^{-7}
ILCR (75th)	4.03×10^{-3}	-	-	-	-	-	1.53×10^{-3}	3.51×10^{-7}
ILCR (95th)	6.45×10^{-3}	-	-	-	-	-	1.70×10^{-3}	5.62×10^{-7}

are more prone to accumulation of some metals [41, 42]. Also, interactions between the plant organ and metals, based on their chemical properties, as well as the exposure time were found to play critical roles in metal accumulation in plants. Concerning metals absorbed from the atmosphere by plants, various environmental conditions such as precipitation and air humidity are influential. Of note, in this regard, the role of biochemical properties of the plant such as the amounts of chlorophyll or secondary metabolites cannot be simply ignored [43].

The international regulatory authorities such as European Food Safety Authority (EFSA) and WHO determined the maximum permitted concentrations of As, Cd, Hg, and Pb (5.0, 0.3, 0.2, 10.0 mg/kg, respectively) in herbal raw materials [33]. In a previous study of metal level in several medicinal plants, the HQs calculated for Cd and Pb were 1.50×10^{-2} and 1.60×10^{-2} , respectively [44]. Consistently, several reports showed similar values for HQs for oral exposure to the mixture of metals via consumption of herbal tea (HQ < 1.0) [45–49].

Application of strategies on more restrict use of the agricultural inputs such as fertilizers and pesticides maybe a good solution to reduce metal content of the soil and irrigation water/aquatic ecosystems. Moreover, limiting the use of nitrogen and phosphorus can also help to reduce metal accumulation as some toxic pollutants may alter the soil pH, thus predisposing metals accumulation [50]. Environmental policies such as soil/plant remediation can be considered

alternative approaches of further developments. Furthermore, considering other methods for final preparation of these products may reduce the levels of such contaminants.

Conclusions

In this work, we assessed carcinogenic and non-carcinogenic risk of exposure to eight metals via oral intake of coffee, tea, and herbal tea, for Iranian consumers. Following determination of metal levels in a total of 243 samples collected, we found HIs of < 1.0 for non-carcinogenic metals. We speculate a medium and no risk to consumers' health based on the calculated ILCRs for As, Ni, and Pb, respectively. It seems that chronic consumption of the collected coffee, tea, and herbal tea samples poses no non-carcinogenic health risk to Iranian consumers, while exposure to As, Ni, Pb indicated medium and no cancer risk, respectively. Our assessments showed that levels of metals determined in tea/coffee/herbal tea samples were within the standard limits and the calculated risk were de minimis. However, to have a more insightful estimation of these risks, the overall contribution of tea/coffee/herbal tea to the total diet should be determined. Our results indicate the necessity of taking appropriate number of samples and the need to re-assay the health risk based on cumulative exposure.

Table 12 Probabilistic HQs, HIs, and ILCRs for carcinogenic and non-carcinogenic metals contents of herbal tea samples

Herbal tea samples	As ILCR	Cd HQ	Cr HQ	Cu HQ	Fe HQ	Hg HQ	Ni ILCR	Pb ILCR
<i>Thymus vulgaris</i>								
Trademarks								
50th	2.57×10^{-4}	1.63×10^{-3}	3.00×10^{-2}	6.04×10^{-4}	2.42×10^{-3}	2.37×10^{-3}	4.96×10^{-5}	4.81×10^{-7}
75th	4.64×10^{-4}	2.94×10^{-3}	5.40×10^{-2}	1.08×10^{-3}	4.37×10^{-3}	4.27×10^{-3}	5.56×10^{-5}	8.66×10^{-7}
95th	9.74×10^{-4}	6.48×10^{-3}	1.18×10^{-1}	2.40×10^{-3}	9.61×10^{-3}	9.41×10^{-3}	6.33×10^{-5}	1.81×10^{-6}
<i>Maticaria chamomilla</i>								
Trademarks								
50th	4.27×10^{-4}	1.46×10^{-4}	8.54×10^{-2}	6.27×10^{-4}	3.51×10^{-3}	1.68×10^{-3}	1.80×10^{-4}	6.25×10^{-7}
75th	7.68×10^{-4}	2.63×10^{-4}	1.53×10^{-1}	1.61×10^{-3}	6.31×10^{-3}	3.02×10^{-3}	2.01×10^{-4}	1.12×10^{-6}
95th	1.61×10^{-3}	5.80×10^{-4}	3.38×10^{-1}	3.54×10^{-3}	1.38×10^{-2}	6.66×10^{-3}	2.30×10^{-4}	2.36×10^{-6}
<i>Hibiscus sabdariffa</i>								
Trademarks								
50th	5.43×10^{-5}	1.60×10^{-2}	9.85×10^{-2}	9.42×10^{-4}	2.70×10^{-3}	2.97×10^{-4}	1.33×10^{-4}	9.40×10^{-7}
75th	9.80×10^{-5}	2.86×10^{-2}	1.77×10^{-1}	1.70×10^{-3}	6.45×10^{-3}	5.35×10^{-4}	1.50×10^{-4}	1.70×10^{-6}
95th	2.05×10^{-4}	6.30×10^{-2}	3.90×10^{-1}	3.73×10^{-3}	1.42×10^{-2}	1.17×10^{-3}	1.70×10^{-4}	3.55×10^{-6}
<i>Camellia sinensis</i>								
Trademarks								
50th	5.52×10^{-5}	8.02×10^{-2}	3.80×10^{-2}	7.42×10^{-4}	3.70×10^{-3}	2.97×10^{-4}	4.94×10^{-5}	4.37×10^{-7}
75th	9.94×10^{-5}	1.44×10^{-1}	6.83×10^{-2}	1.33×10^{-3}	6.64×10^{-3}	5.35×10^{-4}	5.53×10^{-5}	7.87×10^{-7}
95th	2.08×10^{-4}	3.17×10^{-1}	1.50×10^{-1}	2.93×10^{-3}	1.46×10^{-2}	1.17×10^{-3}	6.31×10^{-5}	1.65×10^{-6}
<i>Echium amoenum</i>								
Trademarks								
50th	2.65×10^{-4}	1.24×10^{-1}	3.61×10^{-2}	9.00×10^{-4}	3.68×10^{-3}	2.97×10^{-4}	2.88×10^{-4}	7.06×10^{-7}
75th	4.77×10^{-4}	2.23×10^{-1}	6.50×10^{-2}	1.61×10^{-3}	6.63×10^{-3}	5.35×10^{-4}	3.23×10^{-4}	1.27×10^{-6}
95th	1.00×10^{-3}	4.92×10^{-1}	1.43×10^{-1}	3.55×10^{-3}	1.46×10^{-2}	1.17×10^{-3}	3.68×10^{-4}	2.67×10^{-6}
<i>Rosa damascena</i>								
Trademarks								
50th	1.02×10^{-7}	1.50×10^{-4}	8.26×10^{-2}	8.54×10^{-4}	3.77×10^{-3}	2.97×10^{-4}	2.70×10^{-4}	5.70×10^{-10}
75th	1.85×10^{-7}	2.67×10^{-4}	1.48×10^{-1}	1.53×10^{-3}	6.78×10^{-3}	5.35×10^{-4}	3.03×10^{-4}	1.02×10^{-9}
95th	3.88×10^{-7}	5.88×10^{-4}	3.27×10^{-1}	3.38×10^{-3}	1.50×10^{-2}	1.17×10^{-3}	3.45×10^{-4}	2.15×10^{-9}
<i>Menthe spicata</i>								
Trademarks								
50th	7.64×10^{-5}	1.50×10^{-4}	8.23×10^{-2}	1.03×10^{-3}	3.60×10^{-3}	2.97×10^{-4}	3.82×10^{-4}	1.01×10^{-8}
75th	1.37×10^{-4}	2.67×10^{-3}	1.48×10^{-1}	1.36×10^{-3}	6.48×10^{-3}	5.35×10^{-4}	4.27×10^{-4}	1.80×10^{-8}
95th	2.90×10^{-4}	5.85×10^{-4}	3.25×10^{-1}	4.11×10^{-3}	1.42×10^{-2}	1.17×10^{-3}	4.87×10^{-4}	3.83×10^{-8}
<i>Crocus sativus</i>								
Trademarks								
50th	1.02×10^{-7}	1.50×10^{-4}	2.74×10^{-2}	7.43×10^{-4}	3.60×10^{-3}	2.97×10^{-4}	4.00×10^{-7}	5.70×10^{-10}
75th	1.85×10^{-7}	2.67×10^{-4}	4.94×10^{-2}	1.33×10^{-3}	6.47×10^{-3}	5.35×10^{-4}	4.48×10^{-7}	1.02×10^{-9}
95th	3.88×10^{-7}	5.85×10^{-4}	1.08×10^{-1}	2.94×10^{-3}	1.42×10^{-2}	1.17×10^{-3}	5.10×10^{-7}	2.15×10^{-9}
HI (50th)	-	2.22×10^{-1}	4.80×10^{-1}	6.71×10^{-3}	2.78×10^{-2}	5.84×10^{-3}	-	-
HI = 0.74	-	-	-	-	-	-	-	-
HI (75th)	-	4.00×10^{-1}	8.64×10^{-1}	1.20×10^{-2}	5.00×10^{-2}	1.05×10^{-2}	-	-
HI = 1.33	-	-	-	-	-	-	-	-
HI (95th)	-	8.81×10^{-1}	19.0×10^{-1}	2.65×10^{-2}	1.10×10^{-1}	2.31×10^{-2}	-	-
HI = 2.94	-	-	-	-	-	-	-	-
ILCR (50th)	1.11×10^{-3}	-	-	-	-	-	1.35×10^{-3}	3.20×10^{-6}
ILCR (75th)	2.04×10^{-3}	-	-	-	-	-	1.51×10^{-3}	5.76×10^{-6}
ILCR (95th)	4.30×10^{-3}	-	-	-	-	-	1.72×10^{-3}	1.21×10^{-5}

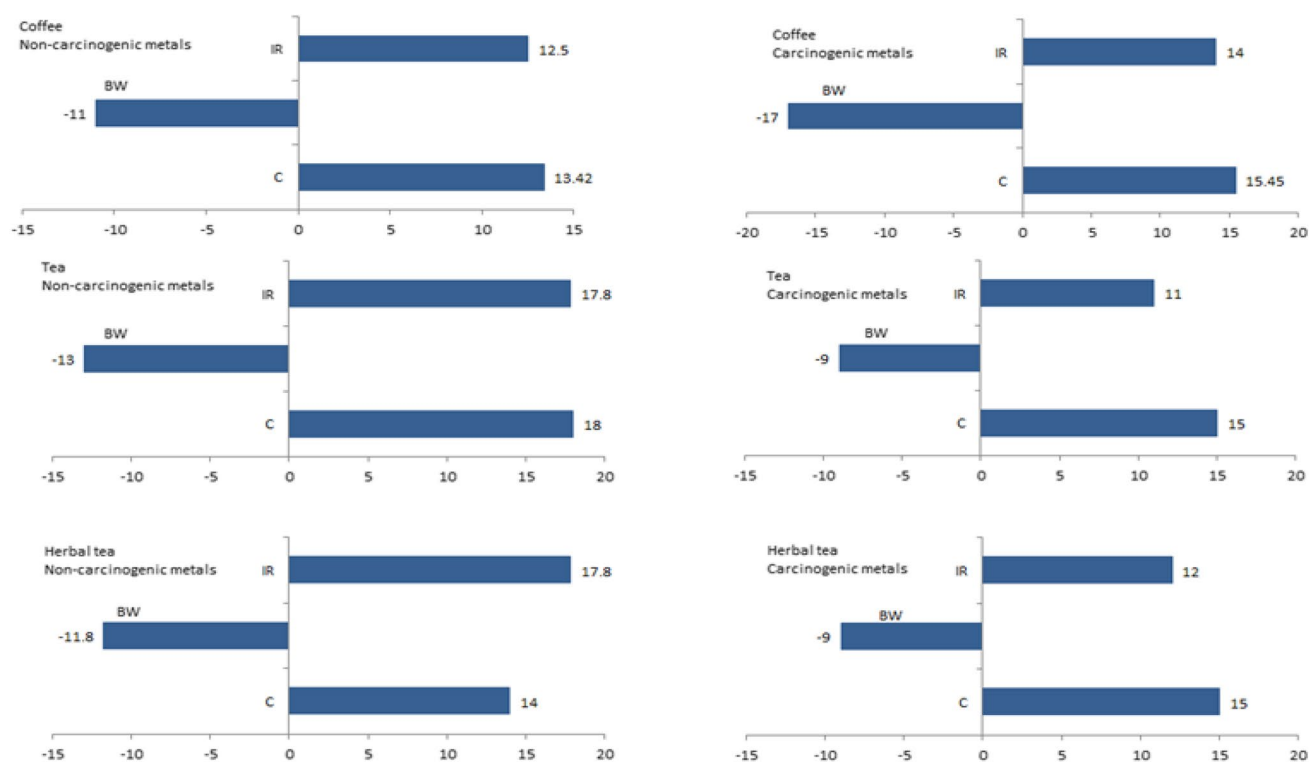


Fig. 5 Parameters that influenced (%) HQ and ILCR calculation in the present work

Acknowledgements The authors are thankful to Vice chancellor for research, Mashhad University of Medical Sciences, Mashhad, Iran, for financial support and appreciate the assistance of Clinical Research Development Unit, Imam Reza Hospital, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran (No. 981682). Also, Majid Azizi was partially supported by a grant from Ferdowsi University of Mashhad (No. FUM-40949).

Funding This work was supported by the Clinical Research Development Unit, Imam Reza Hospital, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran (project No. 981682 and ethics approval No. IR.MUMS.MEDICAL.REC.1399.220).

Declarations

Ethical Approval Ethical approval was obtained from the Ethics Mashhad University of Medical Sciences, Mashhad, Iran (No. IR.MUMS.MEDICAL.REC.1399.220).

Informed Consent Participation was voluntary and written informed consent obtained in all cases.

Conflict of Interest The authors declare no competing interests.

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