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Potential Health Risk of Herbal Distillates and Decoctions Consumption in Shiraz, Iran

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Abstract Concentration of 26 elements in 16 different herbal distillates and 5 herbal decoctions, were determined using inductively coupled plasma-mass spectrometry (ICP-MS). The elemental content of five raw herbal materials used for making decoctions and seven distilled and boiled residues were also evaluated by inductively coupled plasma optical emission spectrometry (ICP-OES). The results indicated that herbal products display a wide range of elemental concentrations. Compared with world health regulations, the concentrations of the elements in herbal distillates and decoctions did not exceed the recommended limits. The analysis of herbal extracts did not show a significant transfer of toxic elements during decoction preparation. Comparison of elemental content among fresh herbal material and herbal distillate and decoction of the same herb showed that, besides the elemental abundance of herbal organs, the ionic potential of elements also play an important role in elemental content of herbal products. Based on the results of the research, it seems that most health benefits attributed to herbal products (especially herbal distillates) are more related to their organic compounds rather than elemental composition. Calculated hazard quotient (HQ) and hazard index (HI) were used to evaluate the noncarcinogenic health risk from individual and combined metals via daily consumption of 100 ml of herbal distillates and 250 ml of herbal decoctions. Both HQs and HI through consumption of herbal distillates and herbal decoctions (except *Valerian*) were below 1. Apparently, daily consumption of herbal distillates and decoctions at the indicated doses poses no significant health risk to a normal adult.

Keywords Herbal distillates · Herbal decoctions · Elemental content · Potential health risk · Dietary intake

Introduction

Since ancient times, humans have explored their environment for plants that could be used to cover all their basic needs: food, shelter, fuel, and health [1]. Phytotherapy is a famous medical modality that uses some plants to treat humans. Although the root of phytotherapy lies in the past, the practice is still meaningful and relevant [2]. In recent decades, the use of medicinal herbs and herbal decoctions increased significantly even in the industrialized countries due to their availability, acceptability, and minimal side effects [3, 4]. Herbal drug preparations mostly include subjecting the plants to treatments, such as extraction, distillation, fractionation, purification, concentration, or fermentation [1, 5].

It is well known that high consumption of herbal medicines with generally high content of heavy metals pose a serious health hazard due to their toxic, carcinogenic, and mutagenic effects [5]. The concentrations of essential and nonessential elements in herbal products depends on many factors, i.e., plant species, soil condition, geographical origin, harvesting time, the applied extraction technique, preparation method, instrument contamination, and storage [3, 4].

The production of Herbal distillates (also known by other names such as floral water, hydrosol, hydrolate, herbal water, and essential water) is currently going on in many countries. In major producing countries such as Iran, Turkey, and Egypt, selected plant organs (leaf, petal, stamen, seed, fruit, and root)

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are distilled in large closed pots. In Iran, herbal distillates are produced using both Industrial and traditional method. In the traditional method, the distillation pots are usually made of copper, while the collecting vessels and condensation pipes are made of galvanized steel. In the industrial method, most equipment and vessels are made of stainless steel. However, in both methods, soft plant organs such as leaves and petals are directly loaded into the distilling pot, but hard parts such as cumin seed or ginger root, must first be ground. Within the pot, the soft or powdered organs are mixed with water and heated to boiling point. The resulting vapor is then condensate and transferred to the collecting container through pipes. Daily consumption of herbal distillates by local residents is normally less than one teacup (100 ml).

Herbal decoctions are generally prepared from dried or fresh plant organs, i.e., flowers, leaves, seeds, and roots [3]. The usual practice for preparing herbal decoctions in Iran is to add water and boil for few minutes. Then let it steep for 15–20 min. Consumption of herbal decoctions is normally one teacup (125 ml) two or three times a day.

A large number of Shiraz residents (especially the old generation) consume herbal distillates and decoctions to regain their own well-being. Thus, health hazard assessment of these food supplements, as a major exposure pathway, seems necessary. The main purpose of this research is the determination of essential and nonessential elements in 16 most used herbal distillates (prepared by traditional methods) and 5 most consumed decoctions in Shiraz city and to estimate the potential health risks.

Materials and Methods

Sixteen specimens of the most commonly used herbal distillates were purchased from two main distribution centers in Shiraz, Iran. The samples were originally produced in Meymand city (121 km south of Shiraz), which is a major center for herbal distillates production. All samples were collected in 60 ml sterile glass bottles that were previously washed and dried in oven at 180 °C.

Five specimens of the most commonly used herbal decoctions were also purchased and prepared the same way that local residents prepare herbal decoctions, which is using about 4.0 g of dried plant parts (flowers, leaves, and roots) and 250 ml of water in clean, dry stainless steel teapot and bringing to a boil. The mixture boiled for 15 min, and then left to cool at room temperature for another 10 to 15 min. The supernatant was then filtered using 45 μm syringe filters.

In order to determine heavy metals content in herbal residues used for making herbal distillates and herbal decoctions, the residues were dried at room temperature and then ground. 2 g of each sample was used for analysis.

The concentration of essential and nonessential elements in herbal distillates and herbal decoctions samples were determined using inductively coupled plasma-mass spectrometry (ICP-MS). The residues were analyzed using inductively coupled plasma optical emission spectrometry (ICP-OES). In order to vouch the reliability of the results, appropriate quality assurance procedures and precautions were performed. QA/QC included reagent blanks and analytical duplicates and analysis of the standard reference material (GBW 07604-poplar leaves, GBW 08505-tea, GBW 07605- tea). One-way analysis of variance (ANOVA) was carried out, and significance level was considered at P value ≤0.05. All data were analyzed using SPSS statistics v.21 and Excel 2013 software for Windows.

The characteristics of plants used in this study and the claimed medicinal/health-promoting effects of their distillates and decoctions are presented in Tables 1 and 2.

Risk Assessment

Potential health risks of heavy metals in herbal products can be assessed by the same methods used for assessing carcinogenic or noncarcinogenic risks. Hazard quotient (HQ) and hazard index (HI) are introduced by US Environmental Protection Agency for noncancer risk assessment [3, 6–9].

$$\mathrm{HQ} = \frac{\mathrm{ADD}}{\mathrm{RFD}}$$

$$\mathrm{ADD} = \frac{C \times \mathrm{IR}}{\mathrm{BW}}$$

$$\mathrm{HI} = \sum \mathrm{HQ} = \mathrm{HQ}_1 + \mathrm{HQ}_2 + \cdots + \mathrm{HQ}_n$$

Where, ADD is the average daily intake of metals (μg/kg-day), RFD is the daily intake reference dose (μg/kg-day), C is the mean concentration of metals in the herbal products (μg/g), IR is the average consumption rate of herbal products (kg/person-day), and BW is the body weight (kg). The RFD values are shown in Tables 3 and 4.

Results and Discussion

Herbal Distillates

The concentration of essential and nonessential elements in the analyzed herbal distillates is summarized in Tables 3 and 4, respectively. Measured concentrations showed a wide variability due to differences in botanical structure, soil composition in which the plants are cultivated, irrigation water, distillation equipment, and containers. The concentration of Cr, Mn, P, Sr, and V were below detection levels in all analyzed samples. The concentration of toxic elements in the herbal distillates were well below food and agriculture organization

Table 1 Characteristics of plants used for extracting herbal distillates

Common name	Scientific name	Used organ	Claimed therapeutic property
Rose	*Rosa damascena*	Flower	Mild sedative, skin treatments
Peppermint	*Mentha piperita*	Leaves	Improved functional dyspepsia (upset stomach and indigestion), skin irritation
Dog Rose	*Rosa canina*	Flower	Carminative, skin care
Orange blossom	*Citrus sinensis*	Flower	Invigorating for the skin, relaxing effect on mind and body
Common nettle	*Urtica dioica*	Seed and leaves	Treatment of kidneys and urinary tract, antidiabetic
Pussy willow	*Salix aegyptiaca*	Flower	Mild sedative, treating skin
Starflower	*Borago officinalis*	Flower	Mild sedative
Chicory	*Cichorium intybus* L	Flower	Treatment of liver and gallbladder disorder, curing constipation
Fumitory	*Fumaria officinalis*	Shoots	Bile disorders, eye irritation
Dill	*Anethum graveolens dhi*	Stem and leaves	Carminative
Fenugreek	*Trigonella foenum-graecum*	Shoots	Digestive problems and antidiabetic
Camelthorn	*Alhagi maurorum*	Shoots	Blood purifier, kidney detersive
Crataegus	*Hawthorn*	Fruit	Treating cardiovascular diseases and skin care
Sycamore	*Platanus orientalis*	Leaves	Improving blood circulation to brains and heart
Date palm flower	*Phoenix dactylifera*	Flower	Sedative, antirheumatic
Herbal mixture (different herbs)	–	–	Sedative, used for upset stomach

of the United Nations/world Health Organization (FAO/WHO) provisional tolerable daily intake, American Herbal Products Association (AHPA), minimum risk level (MRL) from the US Agency for Toxic Substances and Disease (ATSDR), and WHO permission limit for finished herbal products in most samples (Tables 3 and 4) [10–15].

Metals such as Co, Ni, Fe, Mn, Cu, Cr, and Zn are generally categorized as essential element, and play an important role in biological systems. As the difference between the essentiality and toxicity ranges is very narrow for heavy metal ions, essential metals can also produce toxic effects if the metal intake is high; whereas nonessential elements such as Cd, Pb, As, Al, and Rb are toxic even at very low concentrations for human health [3, 16, 17].

High zinc and copper content in herbal distillates prepared by the traditional method is probably the result of copper pots and galvanized pipes used in the distillation process. However, considering the Zn and Cu deficiency in the developing countries, where people's diet rely more on vegetables [18], the consumption of herbal distillates may provide the needed Zn and Cu, especially for those living in the developing countries and also for vegetarians if taken at recommended levels.

Rose water displayed the highest Cu (243. 8 μg/kg) and Fe (600 μg/kg) contents. Other determined elemental concentrations in *Rose water* include: Se (25.4 μg/kg), Ca (1070 μg/kg), Na (950 μg/kg), Al (0.04 μg/kg), and Si (1.07 μg/kg). *Crataegus* distillate had the highest level of Zn (11,980 μg/kg), Co (1.3 μg/kg), Rb (15.4 μg/kg), and U (1.1 μg/kg). *Pussy willow* distillate displayed the highest molybdenum (8.3 μg/kg) and bismuth (0.8 μg/kg) contents. The highest level of As (6.5 μg/kg) and Sn (7.7 μg/kg) had been shown in *Starflower* distillate. *Date palm flower* distillate revealed the highest Pb (19.9 μg/kg) and Ni contents (21.1 μg/kg). Finally, the highest contents of Cd, K, and Mg were seen in *Sycamore*, *Fenugreek*, and the herbal mixture, respectively.

Calcium is an important element in bone and tooth development, regulating blood pressure and enzyme regulation [4]. Herbal distillates such as *Rose water* and *Orange blossom* distillate with high Ca content could be profitable for those who cannot use animal-based Ca sources. Relatively high

Table 2 characteristics of plants used in preparing herbal decoctions

Common name	Scientific name	Parts used	Claimed therapeutic property
Starflower	*Borago officinalis*	Flower	Mild sedative
Lavender	*Lavandula officinalis*	Flower	Analgesic, antimicrobial
Chamomile	*Matricaria chamomilla*	Flower	Treatment of insomnia and colds
Lemon verbena	*Lippa citrodora*	Leaves	Digestive disorders
Valerian	*Valeriana officinalis*	Rhizome and root	Sleep disorders and psychological stress

Table 3 Concentration of essential elements in the analyzed herbal distillates and regulatory limit values (μg/kg except where noted)

n=16	Cr	Cu	Mn	Mo	Fe	Co	Se	Zn	K	Mg	Ca	P	Na
Pussy willow distillate	<50	29.4	<100	8.3	100	0.4	2.1	4170	310	<100	<100	<50	690
Rose water	<50	243.8	<100	6.7	600	0.5	25.4	4100	360	110	1070	<50	950
Peppermint distillate	<50	18.9	<100	5.1	180	0.5	14.2	4600	460	<100	<100	<50	620
Chicory distillate	<50	67	<100	3.8	<100	0.4	13.9	2990	350	<100	<100	<50	810
Dog rose distillate	<50	34.6	<100	3.1	<100	0.5	1.2	3890	310	<100	<100	<50	740
Orange blossom distillate	<50	84.7	<100	2.4	<100	0.4	17.4	3120	370	<100	250	<50	710
Fumitory distillate	<50	41.5	<100	2.1	160	0.4	<0.5	3580	310	<100	170	<50	740
Starflower distillate	<50	12.6	<100	1.7	<100	0.5	12.9	7590	320	<100	<100	<50	720
Dill distillate	<50	71.9	<100	1.5	<100	0.5	9	2220	300	<100	<100	<50	670
Date palm flower distillate	<50	31.4	<100	2.7	120	1.2	<0.5	5250	310	<100	<100	<50	730
Crataegus distillate	<50	16.8	<100	2.7	110	1.3	0.9	11,980	300	<100	<100	<50	620
Sycamore distillate	<50	76.3	<100	1.6	<100	0.6	<0.5	4660	370	<100	130	<50	870
Camel thorn distillate	<50	31.2	<100	1.4	<100	0.5	<0.5	3930	290	<100	<100	<50	690
Common nettle distillate	<50	112.7	<100	1	<100	0.5	<0.5	250	300	<100	<100	<50	650
Fenugreek distillate	<50	23.6	<100	1.4	<100	0.6	<0.5	<100	510	110	<100	<50	890
Mixture of different herbs distillate	<50	124	<100	1.6	<100	0.5	8.5	1110	360	130	280	<50	680
Minimum value	–	12.6	–	1	100	0.4	0.9	250	290	110	130	–	620
Maximum value	–	243.8	–	8.3	600	1.3	25.4	11,980	510	130	1070	–	950
Mean value	–	63.7	–	2.9	211.7	0.6	10.5	4229.3	345.6	116.7	380	–	736.2
Standard deviation	–	58.9	–	2.1	192.7	0.3	7.9	2748.3	61.5	11.5	390.4	–	96.6
RfD[a] (μg/kg-day)	3	40	5	5	700	60	5	300	–	–	–	0.02[d]	–
Joint FAO/WHO[b] Expert Committee on Food Additives (JECFA) (mg/kg-bwt)	15	50	–	–	–	–	–	–	–	–	–	–	–
AHPA[c]	–	–	–	–	–	–	–	–	–	–	–	–	–
US Agency for Toxic Substances and Disease (ATSDR) (μg/kg-day)	50	10	–	–	–	10	5	300	–	–	–	0.2	–
WHO permission limit (finished herbal products)	20	73	–	–	–	–	–	700	–	–	–	–	–

[a] Oral reference dose

[b] Food and Agriculture Organization of the United Nations/World Health Organization Provisional tolerable daily intake

[c] American Herbal Products Association

[d] White phosphorus

concentration of K, Cu, Rb, and Mg in *Common nettle* and *Fenugreek* distillates correlates with the metal content of other herbal distillates with the reputation of beneficially influencing glucose levels in diabetes [4, 19, 20]. The reputation of *Crataegus* distillate, *Peppermint* distillate, *Pussy willow* distillate, and *Rose water* in treating skin disease and upset stomach is probably due to the high zinc content. Zn is known to play an important role in treating skin irritation and mitigating ulcer [4]. Cancer and associated mortality decrease in humans with consumption of selenium (Se) is already reported in the literature [21–23]. The result of this study indicated that consumption of only 100 ml/day of *Rose water* and *Orange blossom* distillate may provide 5 and 4 % of recommended Se requirement (55 μg/day), respectively. So, these two herbal distillates could also be considered anticancer due to relatively high Se content.

Overall, considering the proven Zn, Cu, and Fe deficiency in Shiraz [24–27], *Rose water* with high concentration of essential elements such as Cu, Fe, Se, K, Mg, Na, and Zn seems to be more beneficial for health among the investigated herbal distillates. On the other hand, considering the fact that Ni content of Shiraz soils are high [28], *Date palm flower* distillate with high nonessential and toxic element contents such as Pb and Ni, if not harmful should be considered a non beneficial herbal distillates.

Herbal Decoctions

The concentration of essential and nonessential elements in the analyzed herbal decoctions is summarized in Tables 5 and 6, respectively. It can be seen that all analyzed herbal decoctions contain macroelements in the range of milligrams

Table 4 Concentration of nonessential elements in analyzed herbal distillates and regulatory limit values (μg/kg except where noted)

n=16	Al	As	Rb	Sr	Cd	Sn	Pb	Ni	Si	V	Ag	Bi	U
Pussy willow distillate	0.02	<0.5	10.2	<0.05	<0.05	3.6	<1.0	<1.0	0.1	<1.0	0.1	0.8	<1.0
Rosewater	0.04	<0.5	5.9	<0.05	<0.05	3.5	2.5	8	1.07	<1.0	0.1	0.7	<1.0
Peppermint distillate	0.01	<0.5	7.1	<0.05	0.1	3.2	<1.0	<1.0	0.1	<1.0	0.1	0.7	<1.0
Chicory distillate	0.01	<0.5	6.1	<0.05	<0.05	2.8	<1.0	<1.0	0.11	<1.0	0.1	0.7	<1.0
Dog rose distillate	<0.01	3.5	4.3	<0.05	<0.05	2.8	<1.0	<1.0	<0.1	<1.0	0.1	0.7	<1.0
Orange blossom distillate	0.02	4.8	5.8	<0.05	0.1	2.8	<1.0	<1.0	<0.1	<1.0	0.1	0.7	<1.0
Fumitory distillate	0.01	3.9	4.9	<0.05	0.1	2.5	<1.0	<1.0	0.17	<1.0	0.09	0.6	<1.0
Starflower distillate	0.01	6.5	5.2	<0.05	0.2	7.7	<1.0	<1.0	0.26	<1.0	0.1	0.7	<1.0
Dill distillate	0.01	3.2	4.8	<0.05	<0.05	2.5	<1.0	<1.0	0.36	<1.0	0.09	0.6	<1.0
Date palm flower distillate	0.01	2.5	5.7	<0.05	<0.05	3	19.9	21.1	0.47	<1.0	0.1	0.7	<1.0
Crataegus distillate	0.03	3.4	15.4	<0.05	<0.05	2.8	<1.0	<1.0	0.13	<1.0	0.1	0.6	1.1
Sycamore distillate	0.01	2.9	13.6	<0.05	1.5	2.7	<1.0	<1.0	<0.1	<1.0	0.1	0.6	<1.0
Camelthorn distillate	0.01	3.9	7.3	<0.05	<0.05	2.6	<1.0	<1.0	<0.1	<1.0	0.1	0.6	<1.0
Common nettle distillate	0.01	<0.5	10.7	<0.05	0.3	2.5	<1.0	<1.0	<0.1	<1.0	0.09	0.6	<1.0
Fenugreek distillate	0.01	4.4	6.8	<0.05	<0.05	2.4	<1.0	<1.0	<0.1	<1.0	0.09	0.7	<1.0
Mixture of different herbs distillate	<0.01	5.6	10.3	<0.05	<0.05	2.7	<1.0	<1.0	<0.1	<1.0	0.1	0.7	<1.0
Minimum value	–	–	–	–	–	–	–	–	–	–	–	–	–
Maximum value	0.04	6.5	15.4	–	1.5	7.7	19.9	21.1	1.1	–	0.1	0.8	1.1
Mean value	0.02	4.1	7.8	–	0.4	3.1	11.2	14.5	0.3	–	0.1	0.7	1.1
Standard deviation	0.01	2.2	3.3	–	0.4	1.3	4.9	5.5	0.3	–	0.004	0.6	0.3
RfD[a] (μg/kg-day)	1000	0.3	–	600	0.5	–	3.57[d]	20	–	7	5	500	3
Joint FAO/WHO[b] Expert Committee on Food Additives (JECFA)	–	15	–	–	7	–	25	–	–	–	–	–	–
AHPA[c]	–	10	–	–	4.1	–	6	–	–	–	–	–	–
US Agency for Toxic Substances and Disease (ATSDR) (μg/kg-day)	1000	0.3	–	2000	0.1	–	–	–	–	10	–	–	2
WHO permission limit (finished herbal products)	–	10	–	–	6	–	20	–	–	–	–	–	–

[a] Oral reference dose

[b] Food and Agriculture Organization of the United Nations/World Health Organization Provisional tolerable daily intake

[c] American Herbal Products Association

[d] The RFD for Pb was not available in USEPA guidelines; reference in this case is JECFA [3]

per kilogram and microelements in the range of microgram per kilogram. The elemental concentrations vary widely, and compared with herbal distillates, all elements except Zn and Cu displayed higher concentrations. Generally speaking, elements known to be essential for good health, have five general physiological role i. e., Ca, P, and Mg play important roles in bone and membrane structure; Na and K are essential for water and electrolyte balance; Zn, Cu, Se, Mg, and Mo are important in the metabolism of cholesterol and cardiovascular health problems. Cr and Mn in herbal decoctions are known to have some therapeutic properties against diabetic and cardiovascular diseases [29, 30].

The lowest K (3.4 mg kg^{-1}), P (0.01 mg kg^{-1}), and Mg (37.9 mg kg^{-1}) contents occur in *Lemon verbena*, and the highest occurs in *Chamomile*, being 1130, 44.2, and 114.7 mg kg^{-1}, respectively. Ca content varied between 79.2 mg kg^{-1} (*Valerian*) and 200.7 mg kg^{-1} (*Lavender*), while Na ranged from 107.3 mg kg^{-1} (*Starflower*) to 289.5 mg kg^{-1} (*Chamomile*).

Concentration of microelements in herbal decoction revealed that decoctions are generally rich in Mn, Zn, Fe, Cu, Sr, Ni, and Rb. Presence of Fe, Mn, Cu, and Zn in these herbal products makes them useful nutritional supplements to human health, especially for vegetarians and residents of Shiraz, where a deficiency of these elements is already proven [18, 24–27]. On the other hand, the concentrations of As, Pb, and Cd in some samples exceeded the WHO permissible limit for finished herbal products [13]. Hence, the best benefit for human health lies in obtaining the correct amount of supplementation in the right form at the right time.

Valerian had the highest concentration of Fe and Mn (400 and 1200 μg/kg, respectively), while *Starflower* displayed the highest Zn concentration (930 μg/kg), and *Chamomile* the highest Cu concentration (144.6 μg/kg).

Table 5 Concentration of essential elements in herbal decoctions and regulatory limit values (in μg/kg except where noted)

n=5	Cr	Cu	Mn	Mo	Fe	Co	Se	Zn	K (mg/kg).	Mg (mg/kg).	Ca (mg/kg).	P (mg/kg).	Na (mg/kg).
Starflower	<50	45	<100	5.5	120	3	4.8	930	734	47	88	19.29	107.3
Chamomile	<50	144.6	770	11	71.42	8.1	<0.5	900	1130	114.7	158.5	44.2	289.5
Lavender	<50	47.1	500	1.2	200	3.3	0.1	350	569.9	91.6	200.7	20.3	164.4
Lemon verbena	<50	46.4	<100	15.2	<10	<1	<0.1	509	3.4	37.9	97.1	<0.01	110.5
Valerian	<50	34.6	1200	2.9	400	3.8	<0.1	80.1	99.4	42.5	79.2	4.8	136.7
Minimum value	–	34.6	–	1.2	–	–	–	80.1	3.4	37.9	79.2	–	107.3
Maximum value	–	144.6	1200	15.2	400	8.1	4.8	930.0	1130.0	114.7	200.7	44.2	289.5
Mean value	–	63.5	823.3	7.2	197.9	4.6	2.5	553.8	507.3	66.7	124.7	22.1	161.7
Standard deviation	–	45.6	353	5.8	144.8	2.4	3.3	363.8	464.6	34.4	52.7	16.3	75.1
RfD[a] (μg/kg-day)	3	40	5	5	700	60	5	300				0.02[e]	
US RDA[b] (μg/day)	50–100	1500–3000	2000–5000	–	10000–18000	–	50–100	15000	–	–	–	–	–
Joint FAO/WHO[c] Expert Committee on Food Additives (JECFA) (mg/kg-bwt)	15	50	–	–	–	–	–	–	–	–	–	–	–
AHPA[d]	–	–	–	–	–	–	–	–	–	–	–	–	–
US Agency for toxic substances and Disease (ATSDR) (μg/kg-day)	50	10	–	–	–	10	5	300	–	–	–	0.2	–
WHO permission limit (finished herbal products)	20	73	–	–	–	–	–	700	–	–	–	–	–

[a] Oral refrence dose

[b] Recommended daily dietary allowance for metals in herbal drugs

[c] Food and Agriculture Organization of the United Nations/ World Health Organization provisional tolerable weekly intake, b wt. body weight

[d] American Herbal Products Association

[e] White phosphorus

Table 6 Concentration of non-essential elements in herbal decoctions and regulatory limit values (in μg/kg except where noted)

n=5	Al	As	Rb	Sr	Cd	Sn	Pb	Ni	Si	V	Ag	Bi	U
Starflower	260	4.4	697.9	1260	0.2	3.5	<1.0	27.4	18.42	2.5	0.09	0.9	<1.0
Chamomile	380	1.6	582.9	2580	0.9	2.9	<1.0	87.9	10.52	1.3	0.1	0.8	<1.0
Lavender	500	11.9	511.6	1048	<0.05	1.4	9.8	23.4	15.3	3.5	<0.05	<0.1	<1.0
Lemon verbena	<10	5.6	154.5	3943	0.07	2.2	4	35.5	9.4	3.2	<0.05	<0.1	<1.0
Valerian	<10	12.1	457.5	660	<0.05	2.2	5.9	22.3	12.9	1.1	<0.05	<0.1	<1.0
Minimum value	–	1.6	154.5	660	–	1.4	–	22.3	9.4	1.1	–	–	–
Maximum value	500	12.1	697.9	3943	0.9	3.5	9.8	87.9	18.4	3.5	0.1	0.9	–
Mean value	380	7.1	480.9	1898.2	0.4	2.5	6.6	39.3	13.3	2.3	0.1	0.8	–
Standard deviation	120	4.7	203.4	1351.8	0.5	0.8	2.9	27.7	3.6	1.1	0.01	0.07	–
RfD[a] (μg/kg-day)	1000	0.3	–	600	0.5	–	3.57[e]	20	–	7	5	500	3
US RDA[b] (μg/day)	–	150	–	–	70	–	250	130-400	–	0.1–0.4	–	–	–
Joint FAO/WHO[c] Expert Committee on Food Additives (JECFA) (mg/kg-bwt)	–	15	–	–	7	–	25	–	–	–	–	–	–
AHPA[d]	–	10	–	–	4.1	–	6	–	–	–	–	–	–
US Agency for toxic substances and Disease (ATSDR) (μg/kg-day)	1000	0.3	–	2000	0.1	–	–	–	–	10	–	–	2
WHO permission limit (finished herbal products)	–	10	–	–	6	–	20	–	–	–	–	–	–

[a] Oral reference dose

[b] Recommended daily dietary allowance for metals in herbal drugs

[c] Food and Agriculture Organization of the United Nations/ World Health Organization provisional tolerable weekly intake, b wt. body weight

[d] American Herbal Products Association

[e] The RFD for Pb was not available in USEPA guidelines, refrence in this case is JECFA [3]

The concentration of Cr and U were below the detection limits in all samples. On the contrary, As, Rb, Sr, Sn, Ni, V, and Co were detected in the majority of the samples (Tables 5 and 6). The high concentrations of Al, Pb, and V occur in *Lavender* (500, 9.8, and 3.5 μg/kg, respectively). The highest concentration of arsenic, as a toxic element occurs in *Valerian* (12.1 μg/kg). *Chamomile* and *Valerian* contained the highest (87.9 μg/kg) and lowest (22.3 μg/kg) concentrations of Ni, respectively. Soil condition, ambient pollution, species, and irrigation water play significant roles in elemental composition of herbal decoctions [18].

Elemental concentrations of herbal raw materials used in making herbal decoctions are presented in Tables 7 and 8. In order to compare elemental concentrations in herbal raw materials and herbal extracts, the extraction ratio was calculated (%). Extraction ratio (ER) is defined as:

$$\mathrm{ER}_a = \frac{C_{\mathrm{extract}}}{C_{\mathrm{plant}}} \times 100$$

Where, a is the specific element, C_{extract} is concentration of a in herbal decoctions, and C_{plant} is concentration of a in herbal raw materials [31]. Figure 1 shows the extraction ratios.

Table 7 Concentration of essential elements in raw herbal materials used for making herbal decoction (mg/kg)

n=5	Cr	Cu	Mn	Mo	Fe	Co	Se	Zn	K	Mg	Ca.	P	Na
Starflower	39	10	12	1.1	1295.5	1.9	<0.5	36	22,905	2008	9368	2601	517
Chamomile	15	25	101	1.9	420.3	2	<0.5	71	39,936	5599	12,863	5543	9584
Lavender	10	13	21	0.6	1153.3	2	<0.5	33	18,731	3030	13,061	2065	583
Lemon verbena	9	15	80	2.8	578.9	1.7	<0.5	31	13,564	11,470	24,344	2238	297
Valerian	28	14	364	1.2	5605.2	3.4	<0.5	54	6516	3310	10,630	667	1456
Minimum value	9	10	12	0.6	420.3	1.7	–	31	6516	2008	9368	667	297
Maximum value	39	25	364	2.8	5605.2	3.4	–	71	39,936	11,470	24,344	5543	9584
Mean value	20.2	15.4	115.6	1.52	1810.6	2.2	–	45	20,330.4	5083.4	14,053.2	2622.8	2487.4
Standard deviation	12.9	5.7	143.9	0.8	2153.3	0.7	–	17.2	12,551.8	3803.7	5957.6	1789.7	3991.6

Table 8 Concentration of nonessential elements in raw herbal materials used for making herbal decoction (mg/kg)

n=5	Al	As	Rb	Sr	Cd	Sn	Pb	Ni	V	Ag	Bi	U
Starflower	1212	<0.5	15	39.1	<0.1	1.7	8	1	6	0.4	<0.1	<0.5
Chamomile	508	1.2	15	2580	<0.1	1.6	7	2	5	0.4	0.8	<0.05
Lavender	1618	2.1	10	16.9	<0.1	1.6	11	1	6	0.4	<0.1	0.5
Lemon verbena	631	1.4	3	904	<0.1	1.6	7	1	5	0.3	<0.1	<0.5
Valerian	9467	1.9	26	68.4	<0.1	2.1	11	7	14	0.4	0.1	0.8
Minimum value	508	–	3	16.9	–	1.6	7	1	5	0.3	–	–
Maximum value	9467	2.1	26	2580	–	2.1	11	7	14	0.4	0.8	0.8
Mean value	2687.2	1.6	13.8	721.7	–	1.7	8.8	2.4	7.2	0.4	0.5	0.7
Standard deviation	3816.4	0.4	8.4	1104.1	–	0.2	2.1	2.6	3.8	0.04	0.5	0.2

The ER varied from 0.01 to 37.21 %. As shown in Fig. 1, for all elements except "Na" ER is below 10 % and shows low extraction ratio [31]. The ER depends on plant species, plant organs used for making decoctions and geochemical behavior of elements.

Comparison of elemental content of *Starflower* raw material with its distillate and decoction is illustrated in Fig. 2. The general decreasing order of most elements is: raw *Starflower*> *Starflower* decoction>*Starflower* distillate. Based on Fig. 3 (ionic charge vs. ionic radius), Sn^{+4}, Se^{+4}, As^{+3}, As^{+5}, and Be^{+2} plot in the middle zone, where cations have sufficient density of charge to bind strongly to O^{2-} and form insoluble stable oxides/hydroxides [32]. As already mentioned, high zinc content in herbal distillates probably comes from galvanized pipes of the distillation line. Hence, it displayed lower concentration of these five elements in decoctions than in distillates.

Herbal Residues

Rhizome, leaf, and flowers of seven plant species used for making herbal distillates and herbal decoctions were analyzed. Variable concentrations of essential, nonessential, and toxic elements were determined (Tables 9 and 10, respectively). Although the analyzed elements displayed a wide range of

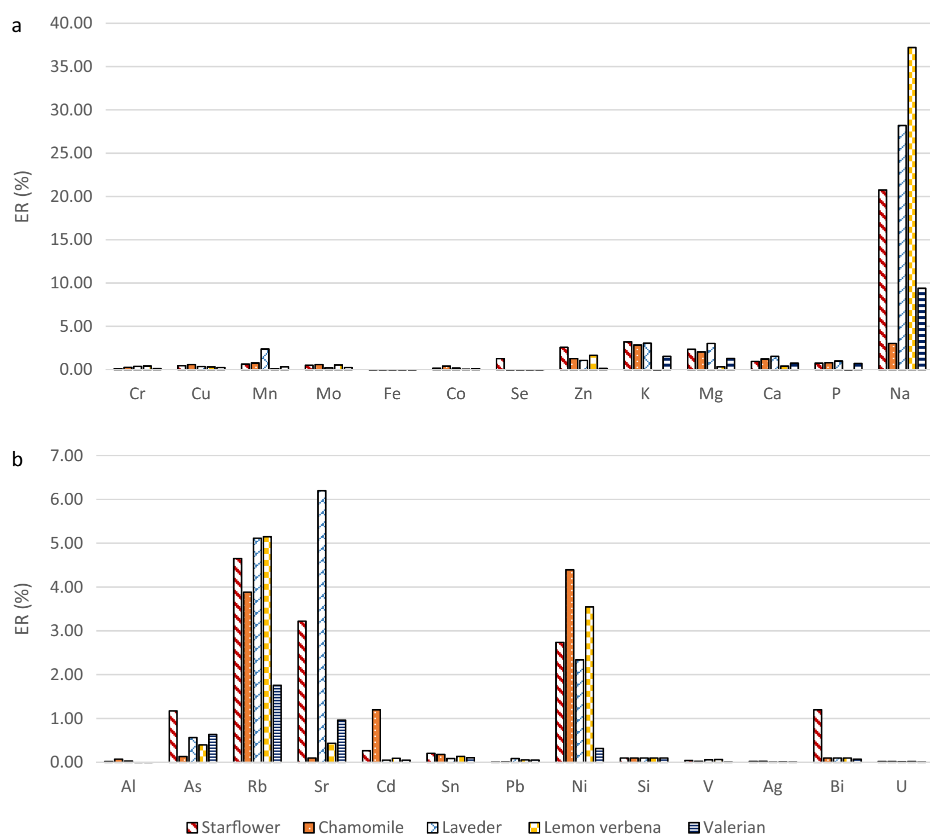
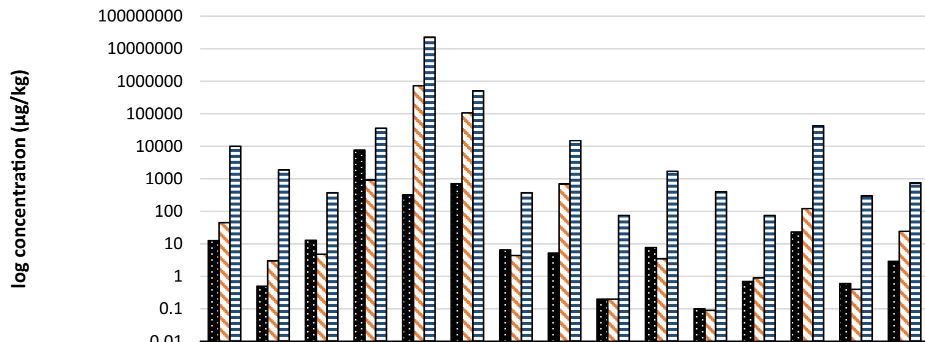


Fig. 1 Extraction ratio of **a** essential and **b** nonessential elements

Fig. 2 Elemental content of *Starflower* raw material and its distillate/decoction



	Cu	Co	Se	Zn	K	Na	As	Rb	Cd	Sn	Ag	Bi	Ba	Be	Li
Starflower distillate	12.6	0.5	12.9	7590	320	720	6.5	5.2	0.2	7.7	0.1	0.7	23	0.6	2.9
Starflower decoction	45	3	4.8	930	7E+05	1E+05	4.4	697.9	0.2	3.5	0.09	0.9	122.1	0.4	24.3
Raw Starflower	10000	1900	375	36000	2E+07	5E+05	375	15000	75	1700	400	75	43000	300	750

Extracted elements of Starflower distillate (%)	0.1	0.03	3.4	21	0.00 1	0.2	1.7	0.1	0.3	0.4	0.03	0.9	0.1	0.2	0.3
Extracted elements of Starflower decoction (%)	0.4	0.16	1.3	2.6	3.20	21	1.7	4.6	0.3	0.2	0.02	1.2	0.3	0.1	3.2

concentration, all were significantly higher than corresponding concentration in herbal distillates and herbal decoctions, reflecting the low extraction ratio from raw herbal materials.

In order to identify the similarities in elemental contents of herbal residues, hierarchical cluster analysis (HCA) of herbal residues using furthest neighbor method for calculating cluster distances and applying Euclidean distance as a measure of between plant samples was carried out. Figure 4 shows the results as a dendrogram. All samples were classified according to elemental concentration in to three groups. Group 1, *Rose* and *Lavender*; group 2, *Fumitory* and *Chicory*; group 3, *Lemon verbena*, *Date palm flower*, and *Dill*. Okem et al. [33] believe that similarity of elemental concentrations in herbal extracts is either the result of using the same plant organs or similar accumulation routs [33]. As shown in Fig. 4, classification is more based on the plant organs from which the herbal products were prepared than the preparation methods. Cluster 1 relates to distillates and decoctions prepared from flowers. Cluster 3 contains herbal residues from the leaves and flowers of the medicinal plants. While, cluster 2 does not relate to any specific plant organs. Based on HCA, and Tables 9 and 10, plant samples in group 1 have displayed high levels of heavy metals, while group 3 plants did not display high metal content.

Risk Assessment

Important factors involved in the absorption of elements from ingested food include elemental concentrations, amount and types of the food consumed, and the pH of the food [3]. The WHO recommended limits for As, Cd, Cr, and Pb in processed herbal products are 10, 6, 20, and 20 µm/kg,

Fig. 3 Ionic potential of the studied elements

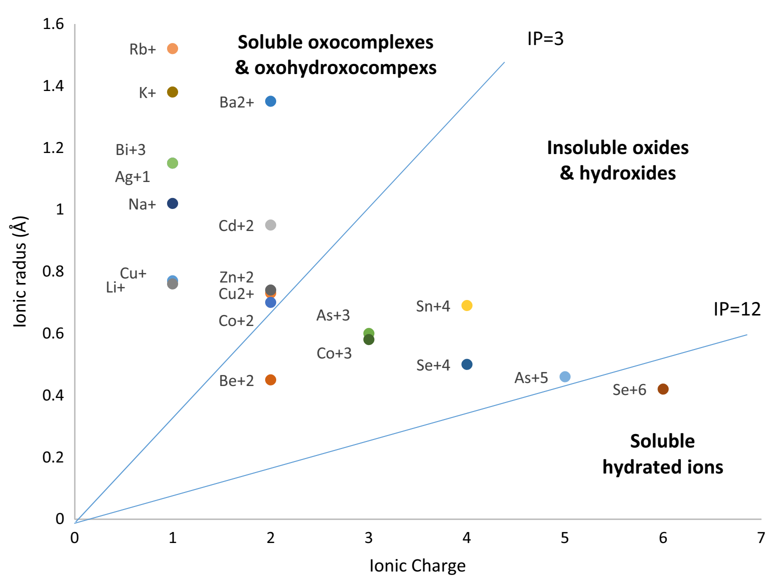


Table 9 Concentration of essential elements in herbal residues (mg/kg)

n=7	Cr	Cu	Mn	Mo	Fe	Co	Se	Zn	K	Mg	Ca	P	Na
Dill	4	49	22	0.5	608	1.1	<0.5	9	27,521	4468	10,898	1519	11,132
Rose	6	124	57	1.1	695	1.2	<0.5	24	11,495	3517	15,214	1536	2769
Fumitory	7	57	14	2.3	573	1.2	<0.5	17	11,992	5242	30,094	1588	2537
Chicory	8	22	118	2.4	516	1.2	<0.5	34	2313	7939	29,234	2431	462
Lemon verbena	5	48	13	0.4	363	1.1	<0.5	9	3775	2250	9963	258	2002
Date palm flower	8	58	15	0.5	418	1	<0.5	11	9916	1729	3561	693	1015
Lavender	11	35	32	0.7	1006	1.3	<0.5	36	8018	2771	22,249	1600	1603
Minimum value	4	22	13	0.4	363	1	–	9	2313	1729	3561	258	462
Maximum value	11	124	118	2.4	1006	1.3	–	36	27,521	7939	30,094	2431	11,132
Mean value	7	56.1	38.7	1.1	597	1.2	–	20	10,718.6	3988	17,316.1	1375	3074.3
Standard deviation	2.3	32.5	38.2	0.7	212.5	0.1	–	11.6	8280	2130.7	10,153.2	703.6	3644.3

respectively. Also, United Nations Food and Agriculture Organization (FAO) and WHO provisional tolerable weekly intake of As, Pb, and Cd is 15, 25, and 7 μm/kg per body weight, respectively (Tables 3, 4, 5, and 6) [10–13, 34]. No permissible limits for all metals in medicinal plants are set by WHO. The reason is the essentiality of many of these metals as dietary micronutrients for humans [34]. The low concentration of the potentially toxic elements in the analyzed herbal distillates (except date palm flower distillate) indicates that their daily consumption as dietary supplement poses no threat to human health. However, Pb, Cd, and As concentration in herbal decoctions is a different matter and exceeds WHO permissible limits in some samples. Hence, their long-term consumption may cause serious problems for human health. Possible health threats of herbal distillates and decoctions are presented in Tables 11 and 12, respectively. As a rule, HQ and HI greater than 1, needs consideration [3]. Daily intake of herbal distillates and decoctions for a 70-kg individual is assumed to be approximately 100 and 250 ml, respectively.

As shown in Tables 11 and 12, HQs and HI for all measured elements in every herbal distillates and herbal decoctions (except *Valerian*) are well below 1, meaning that daily intake of metals through consumption of herbal distillates does not pose a significant potential health hazard for a normal adult. Nevertheless, HI for *Valerian* is between 1 and 5 which is of a concern [35].

Conclusion

In this research, the elemental concentrations of herbal distillates and decoctions consumed by Shiraz residents were measured to determine their potential health risk. The results indicated that different herbal products and distillate/decoction residues display a wide variety of elemental concentrations. Comparison of elemental content between raw herbal material and herbal distillate/decoction of the same species indicated that there is no direct correlation between concentration of elements in plant organs and its products. The reason is apparently the fact that elemental concentration of herbal products apart from abundance in raw herbal materials, also depends on the ionic potential of each element, preparation

Table 10 Concentration of nonessential elements in herbal residues (mg/kg)

n=7	Al	As	Rb	Sr	Cd	Sn	Pb	Ni	Th	V	Ag	Bi	U
Dill	311	<0.1	5	439.7	0.3	7.8	12	1	0.71	4	0.1	<0.1	<0.5
Rose	750	<0.1	6	212.3	0.3	8	8	2	0.76	5	<0.1	<0.1	0.5
Fumitory	627	0.3	4	777.4	0.5	7.9	10	3	0.73	5	0.2	<0.1	<0.5
Chicory	503	0.8	1	1042	0.3	6.8	10	4	0.72	5	<0.1	<0.1	<0.5
Lemon verbena	277	<0.1	1	210.2	0.4	7.2	16	1	0.77	4	<0.1	<0.1	<0.5
Date palm flower	256	<0.1	4	71.1	0.2	7.2	12	1	0.7	4	0.1	<0.1	<0.5
Lavender	1119	<0.1	4	81.7	0.3	7.9	30	2	0.81	5	<0.1	<0.1	0.1
Minimum value	256	–	1	71.1	0.2	6.8	8	1	0.7	4	–	–	–
Maximum value	1119	0.8	6	1042	0.5	8	30	4	0.81	5	0.2	–	0.5
Mean value	549	0.6	3.6	404.9	0.32	7.5	14	2	0.7	4.6	0.1	–	0.3
Standard deviation	313.6	0.3	1.9	373.4	0.1	0.5	7.5	1.2	0.04	0.5	0.06	–	0.28

Fig. 4 Dendrogram of herbal residues used for making herbal distillates and decoctions

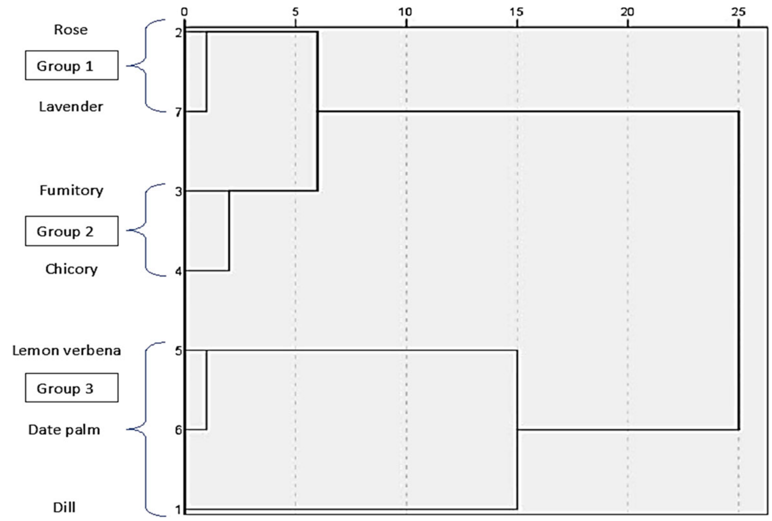


Table 11 HQ and HI for the analyzed herbal distillates

n=16	HQ											HI
	Al	As	Cd	Cr	Pb	Ni	Ag	Bi	Cu	Se	Zn	
Pussy willow	2.9E−08	1.7E−03	1.0E−04	1.7E−02	2.8E−04	5.1E−05	2.E−05	2.3E−06	1.1E−03	6.0E−04	2.0E−02	4.0E−02
Rose	5.7E−08	1.7E−03	1.0E−04	1.7E−02	1.0E−03	5.7E−04	2.E−05	2.0E−06	8.7E−03	7.3E−03	2.0E−02	5.6E−02
Peppermint	1.4E−08	1.7E−03	2.E−04	1.7E−02	2.8E−04	5.1E−05	2.E−05	2.0E−06	6.8E−04	4.1E−03	2.2E−02	4.6E−02
Chicory	1.4E−08	1.7E−03	1.0E−04	1.7E−02	2.8E−04	5.1E−05	2.E−05	2.0E−06	2.4E−03	4.0E−03	1.4E−02	4.0E−02
Dog rose	1.0E−08	7.6E−03	1.0E−04	1.7E−02	2.8E−04	5.1E−05	2.E−05	2.0E−06	1.2E−03	3.4E−04	1.E−02	4.5E−02
Orange blossom	2.E−08	2.3E−02	2.E−04	1.7E−02	2.8E−04	5.1E−05	2.E−05	2.0E−06	3.0E−03	5.0E−03	1.5E−02	6.3E−02
Fumitory	1.4E−08	1.E−02	2.E−04	1.7E−02	2.8E−04	5.1E−05	2.6E−05	1.7E−06	1.5E−03	1.0E−04	1.7E−02	5.5E−02
Starflower	1.4E−08	3.1E−02	5.7E−04	1.7E−02	2.8E−04	5.1E−05	2.E−05	2.0E−06	4.5E−04	3.7E−03	3.6E−02	8.E−02
Dill	1.4E−08	1.5E−02	1.0E−04	1.7E−02	2.8E−04	5.1E−05	2.6E−05	1.7E−06	2.6E−03	2.6E−03	1.1E−02	4.8E−02
Date palm flower	1.4E−08	1.2E−02	1.0E−04	1.7E−02	8.0E−03	1.5E−03	2.E−05	2.0E−06	1.1E−03	1.0E−04	2.5E−02	6.5E−02
Crataegus	4.3E−08	1.6E−02	1.0E−04	1.7E−02	2.8E−04	5.1E−05	2.E−05	1.7E−06	6.0E−04	2.6E−04	5.7E−02	9.1E−02
Platanus	1.4E−08	1.4E−02	4.3E−03	1.7E−02	2.8E−04	5.1E−05	2.E−05	1.7E−06	2.7E−03	1.0E−04	2.2E−02	6.0E−02
Camelthorn	1.4E−08	1.E−02	1.0E−04	1.7E−02	2.8E−04	5.1E−05	2.E−05	1.7E−06	1.1E−03	1.0E−04	1.E−02	5.6E−02
Common nettle	1.4E−08	1.7E−03	8.6E−04	1.7E−02	2.8E−04	5.1E−05	2.6E−05	1.7E−06	4.0E−03	1.0E−04	1.2E−03	2.5E−02
Fenugreek	1.4E−08	2.1E−02	1.0E−04	1.7E−02	2.8E−04	5.1E−05	2.6E−05	2.0E−06	8.4E−04	1.0E−04	3.4E−04	4.0E−02
Mixture of different herbs	1.0E−08	2.7E−02	1.0E−04	1.7E−02	2.8E−04	5.1E−05	2.E−05	2.0E−06	4.4E−03	2.4E−03	5.3E−03	5.6E−02

Table 12 HQ and HI for the analyzed herbal decoctions

n=5	HQ											HI
	Al	As	Mn	Mo	Pb	Ni	Sr	Cu	Cd	Zn	V	
Starflower	0.0009	0.0524	0.0510	0.0039	0.0007	0.0049	0.0075	0.0040	0.0014	0.0111	0.0013	0.139
Chamomile	0.0014	0.0190	0.5500	0.0079	0.0007	0.0157	0.0154	0.0129	0.0064	0.0107	0.0007	0.641
Lavender	0.0018	0.1417	0.3571	0.0009	0.0098	0.0042	0.0062	0.0042	0.0003	0.0042	0.0018	0.532
Lemon verbena	0.0000	0.0667	0.0510	0.0109	0.0040	0.0063	0.0235	0.0041	0.0005	0.0061	0.0016	0.175
Valerian	0.0000	0.1440	0.8571	0.0021	0.0059	0.0040	0.0039	0.0031	0.0003	0.0010	0.0006	1.022

method, and contamination from preparing instruments and storage containers. Considering the low elemental concentration of herbal products (especially herbal distillates), it seems that most attributed health benefits are apparently more related to organic compounds rather than elemental concentrations. Finally, although phytotherapy may provide essential elements for people especially in the developing countries, but adequate precautions (e.g. controlling type and dose of consumption) seems necessary to avoid metal toxicity.

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