Heavy Metals (Lead and Cadmium) in some Medicinal Herbal Products in Iranian Market

Zahra Mousavi[*1], *Parisa Ziarati*[2], *Mahdieh Esmaeli Dehaghi*[1], *Mahnaz Qomi*[2]

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ABSTRACT

Background: The use of herbal or medicinal plants in various forms has been popular for thousands of years. It is estimated that about 70–80% of the world's population relies on alternative medicine, mainly of herbal origin. However, due to the nature and sources of these plants, they are sometimes contaminated with toxic heavy metals, which pose serious health risks to consumers. Herbal formulations, especially those used in the treatment of diseases such as hypertension, diabetes, and weight loss may require long-term usage and the patient might be at risk of heavy metal poisoning. In this study, the levels of toxic heavy metals (Pb, Cd) were evaluated in 11 Iranian common herbal drugs for their health implications.

Methods: In this investigation, concentrations of lead and cadmium were quantitatively determined in Iranian herbal drugs sampled from pharmacies in Tehran, Iran, using atomic absorption spectrophotometry (wet digestion).

Results: The results indicated that lead and cadmium were present in all investigated herbal drugs. The concentrations of metals in drugs ranged from 0.19 to 1.75 µg/g for Cd and 9.61 to 52.74 µg/g for Pb.

Conclusion: The concentrations of lead and cadmium were higher than the maximum permissible daily levels in the majority of these herbal drugs, whereas the quantities of Pb and Cd were well below provisional tolerable weekly intake (PTWI). Daily total intake of these metals is considered in accord with the recommended daily intake of their corresponding formulations.

Keywords: Atomic Spectrophotometry, Cadmium, Heavy Metals, Herbal Medicine, Lead, Medicinal Plants.

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INTRODUCTION

The use of herbal or medicinal plants in various forms has been popular for thousands of years and despite significant developments in modern medicine, investigations of new drugs from natural sources are of great importance. Single herbs, polyherbal formulations, and standardized extracts are commonly used for various medicinal properties [1-5]. Poisonings associated with toxic metals in medicinal plants have been reported in Asia, Africa, Europe, and the United States [6-10]. A study in Brazil showed that samples of herbal medicines had cadmium of up to 0.74 µg/g and estimated lead intake through consumption of these herbs reached 440% of the tolerable intake [11]. The presence of heavy metals (Pb and Cd) was reported in various herbal products and even standard extracts in Iran, India, Pakistan, and China [12]. The presence of metal residues in the herbal plants is prevalent since they are easily contaminated during growth, development, and processing. After collection and transformation into drug form, heavy metals confined in plants finally enter the human body and may disturb normal functions of different organ systems [13]. WHO has emphasized the need for quality assurance of herbal products, including testing heavy metals [14]. The aim of this study was to determine the safety of some popular herbal formulations in Iranian market, as determined by heavy metals (Pb and Cd) residue.

1. Department of Pharmacology and Toxicology, Pharmaceutical Sciences Branch (IAUPS), Islamic Azad University, Tehran, Iran.
2. Department of Medicinal Chemistry, Pharmaceutical Sciences Branch (IAUPS), Islamic Azad University, Tehran, Iran.
*Corresponding Author: E-mail: moosavi.z@iaups.ac.ir

MATERIALS AND METHODS

Samples

Eleven different herbal drugs that are usually used in Iran were purchased from different pharmacies. Table1 shows the name of these drugs, part used in formulation, indications, recommended doses and origin of the sample analyses. The samples were kept at room temperature until analysis.

For heavy metals analysis, each sample was weighed and oven-dried at 60°C to a constant weight. Each oven-dried sample was ground in a mortar until it could pass through a 60 mesh sieve. The samples were stored in clean, dry, high density polyethylene bottles of 100 ml capacity with screw caps. All glassware and plastic containers used were washed with liquid soap, rinsed with water, soaked in 10% HNO_3 v/v for 24h, cleaned thoroughly with distilled water, and dried to ensure that no contamination occurs.

One gram of the powdered sample was weighed precisely on an electronic balance (Bosch D.7455). The samples were separately put in a 100 ml digestion flask and 5 ml of digestion mixture was added to each and heated on a hot plate in the fuming chamber for wet digestion with a digestion mixture comprising concentrated HNO_3 and HCl at the ratio of 6:1.

Table 1.Some common herbal formulations are used in Iran.

Herbal tablet Name	Botanical name In tablet form		Medicinal Properties	Max Dose (g/week)[a]	Origin of the sample
	Botanical name	Part used			
C-lax	*Cassia angustifolia* *Foeniculum vulgare*	leaves seed	laxative	10.15	Iran
Carvil	*Aplum graveolens* *Pimpinelin anisum* *Cuminum cyminum* *Rumex* acetosella	Leaves stems fruit fruit	weight loss	26.91	Iran
Garlet	*Allium sativum*	fruit	antihypertensive and lipid-lowering agents	8.40	Iran
Slim-quick	*Anethum graveolens* *Apium graveolens* *Green tea*	seed seed leaves	Appetite suppression Obesity weight loss	29.09	Iran
Galega	*Galega officinalis*	leaves	Anti-diabetic	30.53	Iran
Valiflore	*Passiflora incarnata* *Valeriana officinalis*	flower rhizome	Sedative hypnotic	26.50	Iran
Garcine	*Allium sativum*	fruit	anti-hypertensive , anti-hyperlipidemic, anti-thrombotic, anti-atherogenicity	14.89	Iran
Ginko	*Ginkgo biloba*	leaves	Enhance memory	16.76	Iran
Green teadin	*Camellia sinensis*	leaves	lowering cholesterol, weight loss, preventing diabetes and stroke	29.34	Iran
Aphrodit	*Tribulus terrestris* *Zingiber officinalis* *Crocus sativus* *Cinnamomum zeylanicum*	dried extract dried extract dried extract dried extract	in potency, premature ejaculation, sexual desire disorder and low sperm count	17.15	Iran
Anethum	*Anethum graveolens* *Cichorium intybus* *Fumaria parviflora* *Citrus aurantifolia*	Leaves, seed leaves leaves leaves	lipid-lowering agents	39.85	Iran

[a] In tablet form. Maximum daily dose reported by manufactures recommended, multiplied by 7.

The flasks were first heated slowly and then vigorously till a white residue was obtained. The residue was dissolved and mixed up to 10ml with 0.1N HNO_3 and NH_4I solution in a volumetric flask. Blanks and samples were also processed and analyzed in duplicates simultaneously. All the chemicals used were of analytical grade (AR).

Standardized international protocols were followed for preparation of the materials and analysis of heavy metals (Pb, Cd) contents. The samples were analyzed by a Flame Emission Spectrophotometer Model AA-6200 (Shimadzu, Japan) using an air-acetylene flame for heavy metals Pb and Cd, using at least four standard solutions for each metal. Coefficient of variations (%CV) in the determination of the heavy metals in all samples was less than 2.5%. All necessary precautions were taken into account to avoid any possible contamination of the samples as per the AOAC guidelines.

Calibration of Equipment

Standard solutions of heavy metals (1000 mg/L), cadmium (Cd), and lead (Pb) were procured from Merck. Solutions of varying concentrations were prepared for all the metals by diluting the standards.

RESULTS

Mean concentrations of cadmium and lead in the herbal drugs are presented in Table 2.

Cadmium was found in all of the herbal drugs, and its concentration ranged from 0.19µg/g in Anethum to 1.75µg/g in Galega. In the case of cadmium, seven products exceeded the maximum recommended limit of 0.3 µg Cd/g [14].

The levels of lead varied in the samples from 9.61µg/g (Ginko) to 52.74 µg/g with Garlet which had the highest concentrations. Ten products exceeded the maximum recommended limit of 10 µg Pb/g [14].

Weekly cadmium and lead intake were estimated for each drug based on the daily value recommended by the manufacturer. Weekly metal reception through consumption of these herbal drugs was calculated by multiplying the maximum recommended dose of each product by the mean levels of the metals found in the herbal formulation.

Tables 3 and 4 display the estimated daily and weekly lead and cadmium ingestion for these herbal drugs based on maximum recommended doses for adults.

The results showed that the maximum intake of the metals reached 53.43µg/week of cadmium and 576.41µg/week of lead in Galega (Tables 3, 4) due to its high daily recommended dose. Also, high intakes of lead, up to 574.24 µg/week, were found for Slim-quick (Table 3).

Table 2. Mean concentration (µg/g) of cadmium and lead in herbal formulations.

Herbal formulation (samples analysis)	Number of samples	Cd		Pb	
		Mean Cons. (µg/g) ± SD	limit(µg/g)	Mean Cons. (µg/g) ± SD	limit(µg/g)
C-lax	13	**1.3011**±0.0015	0.3	**19.915**±0.001	10
Carvil	12	**0.4533**±0.0002	0.3	**12.681**±0.001	10
Garlet	13	**0.3038**±0.0001	0.3	**52.741**±0.003	10
Slim-quick	14	0.2775±0.0003	0.3	**19.735**±0.001	10
Galega	13	**1.7531**±0.0031	0.3	**18.875**±0.001	10
Valiflore	12	**0.6871**±0.0002	0.3	**15.809**±0.001	10
Garcine	12	**1.2533**±0.0045	0.3	**16.586**±0.001	10
Ginko	12	0.2062±0.0002	0.3	9.693±0.001	10
Green teadin	13	**0.4038**±0.0028	0.3	**14.787**±0.001	10
Aphrodit	12	0.2373±0.0008	0.3	**16.826**±0.001	10
Anethum	12	0.1916±0.0007	0.3	**11.024**±0.001	10

Table 3. Possible intake of lead through the consumption of the maximum recommended dose of the herbal formulation.

Herbal tablet	intake daily [a] (µg/day)		MRL (µg/day)	Max Intake, (µg/week)	PTWI	
	Min	Max			(µg/kg)	(µg/person)
C-lax	28.18	56.36	75	202.19	25	1500
Carvil	32.50	**97.49**	75	341.22	25	1500
Garlet	63.28	**126.56**	75	443.02	25	1500
Slim-quick	82.01	**164.02**	75	574.24	25	1500
Galega	82.32	**164.64**	75	576.41	25	1500
Valiflore	26.60	**119.71**	75	418.97	25	1500
Garcine	70.32	70.33	75	247.03	25	1500
Ginko	23.02	46.04	75	161.06	25	1500
Green teadin	61.99	**123.98**	75	433.94	25	1500
Aphrodit	53.59	53.59	75	187.32	25	1500
Anethum	83.67	**125.51**	75	439.15	25	1500

[a] Calculated by multiplying the residue level (Table 2) by the dose of herbal formulation.
MRL=minimum risk level
PTWI= Provisional Tolerable Weekly Intake

Table 4. Possible intake of cadmium through the consumption of the maximum recommended dose of the herbal formulation.

Herbal tablet	intake daily [a] (µg/day)		MRL (µg/day)	Max Intake, (µg/week)	PTWI	
	Min	Max			(µg/kg)	(µg/person)
C-lax	1.84	3.68	14	13.20	7	420
Carvil	1.16	3.48	14	12.11	7	420
Garlet	0.36	0.73	14	2.52	7	420
Slim-quick	1.15	2.31	14	8.15	7	420
Galega	7.65	**15.29**	14	53.43	7	420
Valiflore	1.16	5.20	14	18.29	7	420
Garcine	5.31	5.31	14	18.61	7	420
Ginko	0.49	0.99	14	3.52	7	420
Green teadin	2.93	5.86	14	11.74	7	420
Aphrodit	0.76	0.76	14	2.67	7	420
Anethum	1.45	2.18	14	7.57	7	420

[a] Calculated by multiplying the residue level (Table 2) by the dose of herbal formulation.
MRL=minimum risk level
PTWI= Provisional Tolerable Weekly Intake

DISCUSSION

The overall results clearly indicated that cadmium and lead are present in some Iranian herbal drugs. Lead was detected in all samples and 10 out of 11 (about 91%) analyzed samples exceeded the maximum recommended limit of 10 µg Pb/g [14]. The contents of lead were higher than the maximum permissible daily levels in the majority of these herbal drugs. Weekly lead reception by consuming the maximum recommended therapeutic dose was estimated less than the WHO Provisional Tolerable Weekly Intake (PTWI) of 25 µg/kg bodyweight or 1500 µg/person, for herbal formulations [15]. The consumption of Galega and Slim-quick samples containing 18.9, 19.74µg/g lead would contribute with up to 38.4%, 38.3% of PTWI, respectively (Table 3). The maximum intake for the other analyzed samples reached 21% of the toxicological parameter.

Lead is the most recognized toxic environmental pollutant, and in many countries the intake from the diet can approach or exceed the PTWI [16]. Anthropogenic processes and increased industrialization involving the application of

synthetic fertilizers and persistence of lead in the environment require constant monitoring of all sources of human exposure, including medicinal herbs. Lead reacts or complexes with many biomolecules and adversely affects the reproductive, neurological, gastrointestinal, immune, renal, cardiovascular, hematological, and musculoskeletal systems as well as developmental processes.

The results of this study indicated that cadmium was present in all samples and about 64% of the herbal drugs contained cadmium levels above 0.3µg/g, which is a point to be concerned about.

The estimated maximum weekly intake of cadmium after consumption of the maximum recommended therapeutic dose of the herbal drugs reaches up to 12.7% (in Galega) of the PTWI of 7µg/kg body weight or 420µg/person [18]. Human exposure to cadmium from the diet and drinking water can reach up to 60% of PTWI in some regions of the world and the possible contribution from medicinal herbs might be significant [16-18]. For instance, renal dysfunction is expected in sensitive population groups at cadmium exposure levels of half of the present PTWI [19]. Cadmium is a non-essential trace element with uncertain direct functions in humans that its intoxication can affect cardiovascular, gastrointestinal, neurological, renal, and respiratory systems [20].

Heavy metals have been found in herbal medicines from Malaysia, Brazil, Africa, Poland, India, and Pakistan [11, 21-24]. Caldas and Machado (2004) reported that some medicinal herbs in Brazil had cadmium and lead concentrations exceeding the maximum recommended limit by WHO [11]. Higher concentrations of toxic heavy metals, such as As, Pb, Cd and Hg, exceeding the proposed Ph. Eur. Limits (lead: 5mg/kg, cadmium: 0.5mg/kg) have been reported in some Chinese herbal medicinal plants [25-27].

There are a number of factors contributing to heavy metal contamination in herbal medicinal plants of agricultural soils, including fertilizers, pesticides, atmospheric deposition from town wastes, industrial emissions, and metal production plants [28,29]. On the other hand, it was confirmed that heavy metals contents varied depending on the country of origin, environmental pollution levels, plant part, and processing methods [30-32].

CONCLUSION

The contamination of medicinal herbs by toxic heavy metals might result in serious safety issues due to the increasing popularity of herbal remedies in the world. Therefore, it is critical to analyze heavy metals in herbal medicine in order to ensure that their levels do not exceed the required limits established by regulations. Like conventional drugs, herbal products should be subjected to adequate quality control requirements, such as those recommended by WHO, to ensure their efficacy, potency, and safety. This study demonstrated that in some Iranian herbal medicines Cd and Pb content is above maximum permissible limits in herbal medicines and products, although the weekly quantities of Cd and Pb intake were below the acceptable intake recommended by global standards. Herbal medicines are not the only source of heavy metals and the combined effect of these drugs and other sources can exceed the recommended weekly doses. According to the Agency for Toxic Substances and Disease Registry, a division of the U.S. Public Health Service, the major source of lead in the general population food is through fruits, vegetables, and grains [33]. Therefore, certain groups of patients, such as the elderly with cardiovascular problems and renal deficiency who might consume these herbal products for long periods, should be cautious as they are more susceptible to toxicities.

Based on the results, it is strongly recommend that authorities should enforce regulations for pre-marketing safety studies on herbal products in order to protect the health of the public.

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