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RESEARCH ARTICLE

Quantitative Analysis of Toxic Elements by ICP-MS in Herbal Tablets

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Abstract

Heavy metals are naturally occurring elements that have high atomic weight and density greater than that of water. Their multiple applications in domestic, agricultural and medical products have led to their wide distribution in the environment, raising concerns over their potential effects on human health. Their toxicity depends on several factors including the dose, route of exposure as well as the age, gender, genetics and nutritional status of exposed individuals. Because of their high degree of toxicity, mercury, cadmium, lead, and arsenic rank among the top priority of hazardous metals that are of public health significance. Use of herbal medicines is growing worldwide because of their minimal side effects. Herbal medicines required standardization, with implementation and constant review of technical standards of production and effective quality control methods. It is necessary to promote this study in the view of the importance of herbal medicines. From this angle, the present submission of toxic elemental determination will lead to further clinical studies. These metals can bind to vital cellular components such as structural proteins, enzymes and nucleic acid and interfere with their functions. In human, these metal can cause severe physiological and health effects. Hence, it was thought utmost necessary to study these health effects, some important herbal medicines are scanned for the analysis of toxic elements, like Hg (Mercury), Cd (Cadmium), Pb (lead), As (Arsenic) etc. and these metals are determined quantitatively by using modern technique like ICP-MS, it should be incorporated in routine quality control parameters.

Keywords: Quantitative analysis, ICP-MS, herbal tablets, elemental analysis, toxic elements, heavy metals.

Introduction

Many synthetic drugs are derived from herbal preparations e.g. Aspirin (acetyl salicylic acid) and Reserpine (Sarpagandha). Due to increase in population, most of the people use herbal products which are now available in different forms like tablets, elixirs and powders (Lozak *et al.,* 2012). Contamination or adulteration of herbal products with heavy metals such as lead, mercury, cadmium, arsenic, etc. is of major concern. However, some herbal products do contain heavy metals as essential ingredients. The poor quality control of these products causes health hazard as some products may present unusually high concentrations of toxic metals that could lead to fatality if consumed (Anim *et al.,* 2012). Therefore, it is thought necessary to study the levels of toxic elements being consumed by patient per tablet so that their repercussions can be evaluated. Ayurveda is based on the hypothesis that everything in the universe is composed of five basic elements viz. space, air, energy, liquid and solid (Panchamahabuta). They exists in the human body in combined form like vata (space and air), pitta (energy and liquid) and kapha (liquid and solid), vata, pitta and kapha together are called three pillars of life. In the preparation of herbal medicines, various parts of the plant like root, leave, bark, seed, flower, fruit and stem are used as a raw material, single or in combination. After passing through many processes, they are converted into finished herbal products. But patients are not aware about their contents and standards. World Health Organization gives some guidelines (2007) for the preparation of herbal medicines and listed some methods for the standardization of herbal medicines (WHO, 2011) and also give maximum permissible limit of heavy metal (Merck index, 1989) and quality controlled norms. It is important to follow the quality control norms to standardize the herbal medicines. Herbal medicinal product should be entirely free from moulds or insects, including excreta, visible contaminant, microbial contaminants, bacteria, fungi and chemical residues. Animal matters such as insects and invisible microbial contaminants, which can produce toxins, are also among the potential contaminants of herbal medicines. Thin layer chromatography (TLC) is often needed to detect the contaminants. The main methods commonly used are Atomic Absorption Spectrophotometry (AAS), Inductively Coupled Plasma (ICP) and Neutron Activation Analysis (NAA) for the quantitative analysis of toxic metals. Samples of herbal material are extracted by a standard procedure, impurities are removed by partition and/or adsorption and individual pesticides are measured by GC, MS or GC/MS.

Table 1. Tablet name with the company name and plants as per label.

Code	Brand and company name	Product name	Plants as per label*
A	Baidyanath (Mfg. Lic. No. ND/AYU/4)	Sarpagandha	Sarpagandha powder
B	Safe life (Mfg. Lic. No. NKD/AYU 82)	Cardiol vati	Suthi, Arjun ghan, Punarnava, Bringrajn, Abhrak bhasma, shuddha shiljit, Amalki ghan, Guduch ghan, Gokshur ghan, Akik pisti.
C	Safe life (Mfg. Lic. No. NKD/AYU 82)	Hemiplus vati	Amalaki, Haritaki, Bibhitaki, Sunthi, Pipali, marich, Vidang, Suvarna makshik bhasma, kasis bhasma.
D	Safe life (Mfg. Lic. No. NKD/AYU 82)	Medomine vati	Pipali, Marich, Amalki ghan, Haritaki ghan, Bibhitaki ghan, Trmad churn, Loha bhasma, Shuddha shilajit, Kitatika, Guduchi, Gugul, Sunthi.
E	Safe life (Mfg. Lic. No. NKD/AYU 82)	Arthowin vati	Rasna mool, Sunthi, Gokshur, Erand mool, Ashwagandha, Guggul, Guduchi.
F	Peekay pharma (Mfg. Lic. No. 25D/10/88)	B.P.C capsule	Sarpgandha, Lahasun, Arjun chhal Ex, Guggul Ashwag Jatamansi, Naandha, Isabgol, Brahmi, Jatamansi, Nagarmotha, Shankpushi, Kapoor kachri, Badi ilaichi.

*Data collected from the labelled contain with the tablets.

Table 2. Sample weight and dilution.

Samples	Weight (g)	Dilution
Sarpagandha	0.37287	100 mL in 1% HNO_3
Cardiol vati	0.45548	100 mL in 1% HNO_3
Hemiplus vati	0.2527	100 mL in 1% HNO_3
Medomin vati	0.47809	100 mL in 1% HNO_3
Arthowin vati	0.41698	100 mL in 1% HNO_3
B.P.C capsule	0.11798	100 mL in 1% HNO_3

Some simple procedures namely TLC, HPLC, GC, quantitative TLC (QTLC) and high-performance TLC (HPTLC) can determine the homogeneity of a plant extract. Over-pressured layer chromatography (OPLC), infrared and UV-VIS spectrometry, MS, GC, liquid chromatography (LC) used alone, or in combinations such as GC/MS, LC/MS and nuclear magnetic resonance (NMR), electrophoretic techniques, especially by hyphenated chromatography are powerful tools often used for standardization and to control the quality of both the raw material and the finished product. Validation investigations must include studies on specificity, linearity, accuracy, precision, range, detection and quantitative limits, depending on whether the analytical method used is qualitative or quantitative. TLC and HPLC are the main analytical techniques commonly used in cases when active ingredients are not known or too complex. Quality control for efficacy and safety of herbal products is of utmost importance. The assurance of the safety of herbal drug requires monitoring of the quality of the finished product as well as the quality of the consumer information on the herbal products. It is important that consumers are made aware of interactions herbs might have with other drugs they are taking. Unfortunately this information is not available with herbal medicines (Palambo, 2006). Standardized herbal medicines maintained the quality and containing well defined constituents are required for reliable maximum beneficial therapeutic effects.

Most of the herbal medicinal products are not labeled appropriately in their elemental contents. Keeping the above points in view, the determination of various metals in the herbal medicines was done by ICP-MS method which has high degree of sensitivity and specificity.

Materials and methods

Chemicals: Yttrium as internal standard, deionized water solution of 0.5% nitric acid and 2 ppm gold (Thermo- fisher ICP-MS icap model).

Sampling: In the present study, the marketed herbal tablets Sarpagandha, Cardiol vati, Hemiplus vati, Medomine vati, Arthowin vati and B.P.C capsules are selected for the analysis. The brand names of the products, license number and the plants used as per company's label are included (Table 1).

Experimental design: Code numbers namely A to F was assigned for Sarpagandha, Cardiol vati, Hemiplus vati, Medomine vati, Arthowin vati and B.P.C capsules. By taking the weight of each tablet on digital balance, each tablet sample was gently ground to fine powder using mortar and pestle and packed in butter paper until analysis. The dilution is given in Table 2 and the general analytical conditions are shown in Table 3. Quantitative multi-elemental analysis by inductively coupled plasma (ICP) [Icap-Q] mass spectrometry depends on complete digestion of solid samples.

Table 3. General analytical conditions.

Parameter	Value
Spray chamber temperature	2.7
Cool flow	14
Sampling depth	5
Plasma power	1550
Auxiliary flow	0.8
Nebulizer flow	1.0079
Spray chamber temperature	2.7
Peristaltic pump speed	25

Table 4. Multi-Elemental standards and mercury analysis.

Concentration	Yttrium (1 ppm)	MES	MES + Hg (20 ppb)	Final volume (mL)
Std .05 ppb	750 µL	-	75 µL	30
Std 0.5 ppb	750 µL	-	750 µL	30
Std 1.0 ppb	750 µL	-	1500 µL	30
Std 2.0 ppb	750 µL	-	3000 µL	30
Std 5.0 ppb	750 µL	150 µL	-	30
Std 20 ppb	750 µL	600 µL	-	30
Std 50 ppb	750 µL	1500 µL	-	30
Std 100 ppb	750 µL	3000 µL	-	30
Std 200 ppb	750 µL	6000 µL	-	30

Table 5. Accuracy of toxic elemental concentration in ppm by ICP-MS.

Samples	Elements in ppm			
	Hg	Cd	Pb	As
Sarpagandha	ND	0.0003	0.00645	0.00068
Cardiol vati	ND	0.00015	0.01261	0.00081
Hemiplus vati	ND	0.00028	0.02499	0.00298
Medomin vati	ND	0.0002	0.01412	0.00062
Arthowin vati	ND	0.00031	1.001	0.00056
B.P.C capsule	ND	0.00055	0.05478	0.00074

ND: Not detected.

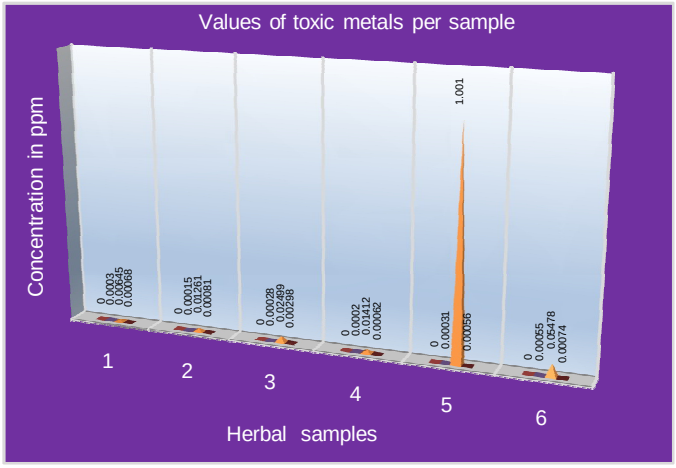
However, fast and thorough sample digestion is a challenging analytical task in modern multi-elemental analysis. To determine each toxic metal concentrations, 0.125 mL internal standard and 4.675 mL of diluent was added in to 0.2 mL sample solution. Deionzed water solution of 0.5% nitric acid and 2 ppm gold was used as a diluent. Multi-elemental standards and mercury analysis is given in detail in Table 4.

Statistical analysis: The obtained values were properly validated with standard deviation, standard error and coefficient variance. In addition to normal validation parameters, average weight equal to each tablet is analyzed from the crushed powder (3/4/5/6 tablets) as additional validation.

Results and discussion

Toxic elements namely Hg, Cd, Pb and As are of great importance for life in micro quantities and these metallic elements are considered as systemic toxicants that are known to induce multiple organ damage, even at lower levels of exposure. Figure 1 indicates the graphical representation of each toxic element per sample. X-Axis indicates the sample number 1 to 6 and Y-axis indicate the detected values of toxic elements per sample in ppm.

Fig. 1. Graphical representation of toxic elements in each sample.



As shown in Fig. 1, samples Sarpagandha (1), Cardiol vati (2), Hemiplus vati (3), Medomine vati (4), Arthowin vati (5) and B.P.C capsules (6), detected the highest value of Pb-0.00645 ppm, 0.01261 ppm, 0.02499 ppm, 0.01412 ppm, 1.001 ppm and 0.05478 ppm respectively, second highest toxic element was As, Hg was not detected in all samples.

Table 6. LD50 of the elements (The Merck Index, 1989).

Elements	Compounds	LD 50
Mercury	Mercumatilin sodium Mersalyl	238 mg/kg orally in rats 17.7 mg/kg iv in rats
Cadmium	Cadmium chloride	88 mg/kg orally in rat
Lead	Lead acetate	200 mg /kg ip in rat
Arsenic	Arsenic acid	6 mg/kg iv in rabbit

Table 7. JECFA (and EU as indicated) heavy metal limits.

Element	Stated Limit (PTWI–Weekly)	Calculated daily limit (Adult, 70 kg)	EU status
Mercury	1.6 µg methylmercury/kg bw	16 µg	Adopted 2/4/2004
Cadmium	7 µg cadmium/kg bw	70 µg	Endorsed 6/2/1995
Lead	25 µg lead/kg bw	250 µg	Endorsed 6/19/1992
Arsenic	15 µg inorganic arsenic/kg bw	150 µg	No information found

The detected level of toxic elemental concentration in selected samples by ICP-MS is given in Table 5. Recently published FDA regulations hold supplement manufacturers or distributors responsible for the content of the dietary supplement which should only contain what they are labeled and not any harmful or undesirable substances, including pesticides and heavy metals (Bharathi *et al.,* 2010). However, it should be made mandatory to include concentration of all elements present in the herbal preparations. Lead, Cadmium, Arsenic and Mercury are considered as toxic elements, therefore, their daily involuntary intake via herbal supplements has been regulated.

Estimated exposures/intakes of As, Cd, Hg and Pb were assessed with respect to safe/tolerable exposure levels described by various national and public health organizations (Bharathi *et al.,* 2010).

Sarpagandha: In Sarpagandha sample, most abundant element was Pb-0.00645 ppm, whereas, Cd was found in lowest concentration (0.0003 ppm) and Hg was not detected.

Cardiol vati: In Cardiol vati sample, most abundant element was Pb-0.01261 ppm, whereas, Cd was found in lowest concentration (0.00015 ppm) and Hg was not detected.

Hemiplus vati: In Hemiplus vati sample, most abundant element was Pb-0.02499 ppm whereas, Cd was found in lowest concentration (0.00028 ppm) and Hg was not detected.

Medomine vati: In Medomine vati sample, most abundant element was Pb-0.01412 ppm whereas, Cd was found in lowest concentration (0.0002 ppm) and Hg was not detected.

Arthowin vati: In Arthowin vati sample, most abundant element was Pb-1.001 ppm whereas, Cd was found in lowest concentration (0.00031 ppm) and Hg was not detected.

BPC capsules: In BPC capsule samples, most abundant element was Pb-0.05478 ppm whereas, Cd was found in lowest concentration (0.00055 ppm) and Hg was not detected.

Conclusion

Results obtained from ICP-MS analysis of tablet samples detected the accurate values of toxic elements concentration in ppm. All these values of toxic elements showed less toxicity in herbal medicines and detected below LD50 (Table 6) and Joint FAO/WHO Expert Committee on Food Additives (JECFA) values for heavy metal limits is shown in Table 7, these shows the herbal medicines are very safe for human consumption. The content of the toxic elements is not indicated on their label. Elemental analysis by ICP-MS is a recent technique which gives more accurate concentration of toxic elements contain in the samples which is not previously reported by researchers. Determination of metals is done by atomic absorption spectrophotometer in bhasma only, not in tablets. The concentration of the toxic elements is found below the hazardous levels. The tablets studied did not show concentration hazardous to humans.

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