DETERMINATION OF HERBAL PRODUCT CARDIOL VATI BY ICP-MS VALIDATION AND APPLICATION

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ABSTRACT

Popularity 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 results of both individual and social field. Ayurveda names three elemental substances, called Vata, Pitta and Kapha, and states that a balance results in health, while imbalance results in disease. Plant-based treatments in Ayurveda derived from roots, leaves, fruits, bark, seeds.

The origins of Ayurveda have been traced back to around 5,000 BC. Fe (Iron) is an important and essential element in human being and plays a vital role in the formation of hemoglobin, oxygen and electron transfer in human body. Cu and Cd also having importance for human being as an essential trace elements. In human, these metal can cause severe physiological and health effects. Hence in present study, herbal medicine samples of Cardiol vati is scanned for the validation and application. Herbal medicines contain many Toxic, Essential, Trace metals. Minerals, Alkaloids, Steroids and organic compounds, besides that it also contain enzymes, proteins, alkaloids. For the present study Cardiol Vati was scanned and detect the heavy metals like Cd (Cadmium), Fe (Iron), Cu (Copper) etc. was scanned and these metals are evaluated and validated quantitatively and statistically by using ICP-MS, which can be incorporated in routine quality control parameters.

KEYWORDS: ICP-MS, herbal tablets, Cardiol Vati, elemental analysis, validation, Herbal quality controlled.
INTRODUCTION
Ayurveda derived from Ayur means life and Veda means science, it means science of life and health practiced by ancient Aryans which is based on Atharvaveda, one of the oldest scriptures of hindus. World health Organization states that around 85-95% of the world population uses traditional herbal medicines. Due to increase in population most of the people use herbal products which are now available in different forms like tablets, elixirs and powders. Therefore, it is necessary to think about their study the contamination of essential elements, trace elements, Toxic elements, Minerals and the methods of collection raw materials, quality of raw material, method of preparation, standardization and validation. According to the Ayurveda the entire universe is composed of the basic elements known as Panchmahabhuta include akash, vayu, teja, jal, and prithvi,[1] Panchamahabhuta is in balance with each other it is called as healthy condition and imbalance called unhealthy. In the preparation of herbal medicines or herbal tablets various parts of plants like roots, leaves, barks, seeds, flowers, fruits, stems are used as a raw material. After passing through many processes they are converted into finished herbal product. But patients are not aware about their content, standards and validation. World health Organization gives some guidelines,[2] for the preparation of herbal medicines and listed some methods for the standardization of herbal medicines[3] and also give maximum permissible limit of heavy metal[4] and quality controlled norms. It is important to follows the quality control norms to standardize the herbal medicines. Varies instrumental methods like HPLC-high–performance chromatographic techniques[5], GC-gas chromatography[6], XRPD-Ray diffraction[7], electrophoresis and TLC -thin layer chromatography[8] Standardized herbal medicines maintained the quality and containing well defined constituents are required for reliable beneficial therapeutic effects. Keeping above points in view study the various heavy metals in the herbal medicines were done by ICP-MS methods which has high degree of sensitivity and specificity.

MATERIALS AND METHODS
Chemicals
Yttrium as internal standard, de-ionized 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 Cardiol vati, was selected for the analysis. The brand names of the medicines, license number and the plants used as per company’s label are included (Table 1).

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

<table>
<thead>
<tr>
<th>Sr. No</th>
<th>Brand and Company Name</th>
<th>Medicines Name</th>
<th>Plants as per label *</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Safe life (Mfg. Lic.No-NKD/AYU 82)</td>
<td>Cardiol Vati</td>
<td>Suthi, Arjun ghan, Punarnava, Bringrajn, Abhrak bhasma, shuddha shiljit, Amalki ghan, Guduch ghan, Gokshur ghan, Akik pisti,</td>
</tr>
</tbody>
</table>

*Data as per container labelled.

Experimental design

METHODS

Samples

Cardiol vati, taking five tablets code number was given A, B, C, D and E. By taking the weight of each tablet on digital balance. Tablet of each sample is gently ground to fine powder using mortar and pestle and packed in butter paper until analysis. Quantitative multi-elemental analysis by inductively coupled plasma (ICP) Icap-Q spectrometry depends on a complete digestion of solid samples. However, fast and thorough sample digestion is a challenging analytical task in modern multi-elemental analysis. To determine each heavy metal concentration, 0.125 mL internal standard and 4.675 mL of diluent added in to 0.2 mL sample solution. De-ionized water solution of 0.5% nitric acid and 2 ppm gold was used as a diluent.

Instrument configuration

Thermo – fisher ICP-MS icap model was used for all measurements. The instrument was operated in a single collision cell mode with kinetic energy discrimination (KED), using pure He (Helium) as collision gas. The general analytical condition set for the ICP-MS are given in table number 2.

Table: 2. General analytical conditions

<table>
<thead>
<tr>
<th>Sr. No</th>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Spray Chamber Temperature</td>
<td>2.7</td>
</tr>
<tr>
<td>2</td>
<td>Cool Flow</td>
<td>14</td>
</tr>
<tr>
<td>3</td>
<td>Sampling Depth</td>
<td>5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Concentration</th>
<th>Yttrium 1 ppm</th>
<th>MES</th>
<th>MES + Hg (20 ppb)</th>
<th>Final Volume (mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Std .05 ppb</td>
<td>750 µL</td>
<td>-</td>
<td>75 µL</td>
<td>30</td>
</tr>
<tr>
<td>Std 2.0 ppb</td>
<td>750 µL</td>
<td>-</td>
<td>3000 µL</td>
<td>30</td>
</tr>
<tr>
<td>Std 5.0 ppb</td>
<td>750 µL</td>
<td>150 µL</td>
<td>-</td>
<td>30</td>
</tr>
<tr>
<td>Std 20 ppb</td>
<td>750 µL</td>
<td>600 µL</td>
<td>-</td>
<td>30</td>
</tr>
<tr>
<td>Std 50 ppb</td>
<td>750 µL</td>
<td>1500 µL</td>
<td>-</td>
<td>30</td>
</tr>
<tr>
<td>Std 100 ppb</td>
<td>750 µL</td>
<td>3000 µL</td>
<td>-</td>
<td>30</td>
</tr>
<tr>
<td>Std 200 ppb</td>
<td>750 µL</td>
<td>6000 µL</td>
<td>-</td>
<td>30</td>
</tr>
</tbody>
</table>

**Cadmium**

Cadmium and cadmium compounds are known human carcinogens. Smokers get exposed to significantly higher cadmium levels than non-smokers. Severe damage to the lungs may occur through breathing high levels of cadmium.

- ingesting very high levels severely irritates the stomach, leading to vomiting and diarrhea.
- Long-term exposure to lower levels leads to a build-up in the kidneys and possible kidney disease, lung damage, and fragile bones. Regulatory limits.

**Toxicity**

Their toxicity depends on several factors including the dose, route of exposure, and chemical species, as well as the age, gender, genetics, and nutritional status of exposed individuals. Because of their high degree of toxicity, cadmium, rank among the priority metals that are of public health significance. These metallic elements are considered systemic toxicants that are known to induce multiple organ damage, even at lower levels of exposure.

**Biological role**

**Iron**

Iron (Fe)-Iron plays an important role in living organism forming complex with molecular oxygen in hemoglobin and myoglobin and in varies biological processes.\(^9\)
Toxicity
High blood level of free ferrous iron react with peroxide to produced free radicals which are highly reactive and can damage DNA, Proteins, Lipids and other cellular compounds. Iron can damage cell in the heart, liver and other organs which can cause adverse effect includes coma, metabolic acidosis, shock, liver failure, long term organs damage and even death.\textsuperscript{[9]}

Levels in humans (Fe)
Human abundance by weight is 60000 ppb by weight and 6700 atoms by atoms.\textsuperscript{[9]}

RESULTS AND DISCUSSION
Diluted samples of Cardiol vati were used for the further analysis on ICP-MS Icap Q model. As a heavy metals Fe, Cu and Cr. are great importance for life. Detected accuracy of essential elemental concentration in selected samples by ICP-MS are given in Table 4.

Table: 4. Accuracy of elemental concentration per Tablet.

<table>
<thead>
<tr>
<th>Sr. No</th>
<th>Samples/ Tablet code</th>
<th>Elements in ppm</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Cd</td>
</tr>
<tr>
<td>1</td>
<td>A</td>
<td>0.000341443</td>
</tr>
<tr>
<td>2</td>
<td>B</td>
<td>0.00041</td>
</tr>
<tr>
<td>3</td>
<td>C</td>
<td>0.00045</td>
</tr>
<tr>
<td>4</td>
<td>D</td>
<td>0.00034999</td>
</tr>
<tr>
<td>5</td>
<td>E</td>
<td>0.00031635</td>
</tr>
</tbody>
</table>

Fig: 1. Cardiol Vati

Cardiol Vati- Application
Heart is the most important organ of the circulatory system which nourishes the whole body by supplying pure blood. Obviously abnormal heart function lead to serious problems. Heart is made up of muscle fibers. Any abnormality in the constitution of heart and the other factors like blood, mind and Oja give rise to diseases related to heart. Cardiol vati helps to reduce
cholesterol and triglyceride level in blood. It also tones the cardiac muscles and improves the function of heart. (Information collected from the leaflet provided with sample).

Fig: 2. Graphical representation of Elements present in different samples

Table: 5. LD 50 FROM MERCK INDEX - 11TH EDITION

<table>
<thead>
<tr>
<th>Sr. No</th>
<th>Elements</th>
<th>Compounds</th>
<th>LD50</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Cadmium</td>
<td>Cadmium chloride</td>
<td>88 mg/kg orally in rat</td>
</tr>
<tr>
<td>2</td>
<td>Iron</td>
<td>Iron pentacarbonyl</td>
<td>02.19 mg/l in mice, 0.91 mg/l in rat</td>
</tr>
<tr>
<td>3</td>
<td>Copper</td>
<td>Cupric acetate</td>
<td>0.71 g/kg orally in rat</td>
</tr>
</tbody>
</table>

Table: 6. Standard deviation, Coefficient variance and standard errors in Cardiol Vati

<table>
<thead>
<tr>
<th>Sr. No</th>
<th>Observations</th>
<th>Concentration of Elements in ppm</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Cd</td>
<td>Fe</td>
<td>Cu</td>
</tr>
<tr>
<td>1</td>
<td>1</td>
<td>0.000341443</td>
<td>2.54366</td>
<td>0.046184</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>0.00041</td>
<td>2.57465</td>
<td>0.051762</td>
</tr>
<tr>
<td>3</td>
<td>3</td>
<td>0.00045</td>
<td>2.51323</td>
<td>0.04823</td>
</tr>
<tr>
<td>4</td>
<td>4</td>
<td>0.00034999</td>
<td>2.51585</td>
<td>0.05045</td>
</tr>
<tr>
<td>5</td>
<td>5</td>
<td>0.00031635</td>
<td>2.56122</td>
<td>0.05975</td>
</tr>
<tr>
<td>6</td>
<td>SD</td>
<td>±5.47723E-05</td>
<td>±0.027153895</td>
<td>±0.005194555</td>
</tr>
<tr>
<td>7</td>
<td>CV</td>
<td>0.146623698</td>
<td>0.010683267</td>
<td>0.101307354</td>
</tr>
<tr>
<td>8</td>
<td>SE</td>
<td>±2.44949E-05</td>
<td>±0.012143591</td>
<td>±0.002323076</td>
</tr>
</tbody>
</table>

Table: 7. Calibration correlation coefficient R and BEC (ppb) data.

<table>
<thead>
<tr>
<th>Sr. No</th>
<th>Isotope</th>
<th>R</th>
<th>BEC (ppb)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>¹¹¹Cd</td>
<td>0.993</td>
<td>0.037</td>
</tr>
<tr>
<td>2</td>
<td>⁵⁷Fe</td>
<td>0.996</td>
<td>-0.829</td>
</tr>
<tr>
<td>3</td>
<td>⁶⁵Cu</td>
<td>0.994</td>
<td>0.534</td>
</tr>
</tbody>
</table>

Toxic elements namely Cd, Fe and Cu. are great importance in life of human beings. The detected accuracy of toxic elemental concentration in selected samples by ICP-MS is given in Table 4. In Cardiol vati Sample A to E, most abundant element was Fe (Iron)) whereas Cd (Cadmium) was found in lowest concentration. The Standard deviation (SD), coefficient variance (CV) and standard error (SE) calculated from the different observations of all
samples are given in table number 6 and table number 7 shows that for most of the target elements, low ppt BEC (background equivalent concentration).

The CV for the Cadmium (Cd) calculated from the different observation was 0.146623698 and the SE was found ± 2.44949E-05.

The CV for the Iron (Fe) calculated from the different observation was 0.010683267 and the SE was found ± 0.012143591.

The CV for the Copper (Cu) calculated from the different observation was 0.101307354 and the SE was found ± 0.002323076.

From the above observation and calculation of CV and SE for the elements cadmium (Cd), iron (Fe) and Copper (Cu) was found in very low concentration and it was found in below toxic limit in all samples.

Figure 3, 4 and 5 shows the standard calibration graph for the elements Cadmium (Cd), Iron (Fe) and Copper (Cu) by ICP-MS.
CONCLUSION

The sufficient quality controlled parameters and condition were followed during the manufacturing process. Results obtained from ICP-MS analysis of tablet samples detected the accurate values of toxic element concentration in ppm. All these values of toxic elements showed less toxicity in herbal medicines, very low CV was found and are detected below LD50. The content of 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. Quantitative estimation of metals is done by atomic absorption spectrophotometer in herbal powder only, not in tablets, therefore, the concentration of the toxic elements are below the hazardous levels to the patient. The standardization and validation of herbal tablets should be mandatory for the preparation of herbal medicines for the more efficiency and accurate results.
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