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ICP-MS, ICP-AES AND FLAMEPHOTOMETRIC QUANTITATIVE DETERMINATION AND VALIDATION OF ELECTROLYTES FROM HERBAL CARDIOL VATI

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ABSTRACT

Cardiol vati is one of the most popular herbal medicines in Indian market for Cardiac patients. Minerals and Electrolytes are naturally occurring elements present in herbal medicines. The vati content Manganese(Mn), Calcium(Ca), Magnesium(Mg), Sodium(Na) and Potassium(K). Though they are essential elements it is utmost necessary to determine the quantitatively because it most effects on heart and kidney. The daily requirement of minerals, Electrolytes is in micrograms, but there is no proper method to detect the accurate concentration of minerals, electrolytes present in herbal medicines. Herbal medicines require implementation and good manufacturing practices and effective quality control methods. In addition, various parameters such as dosage, stability, toxicity, chemical factors such as pesticides residue, aflatoxin content and heavy metals contamination and age should be taken in to consideration. Diseases occur due to their deficiency and toxicity due to overdose. These minerals can bind to vital cellular components and interfere with their normal functions. In human being, these minerals can cause severe physiological and health effects. The rapid development of metro cities in developing as well as in developed countries it causes adverse life style effects like unhealthy food, pollutions and a sedentary job and transportation mode are likely to be risk factors for cardiac diseases. Electrolytes are needed for metabolism, normal cellular activities and help to maintain the acid-base balance. Herbal medicines required standardization with implementation and constant review of technical standards of herbal product and effective quality control methods. Therefore, it is thought necessary about the efficacy and standardization of Cardiol

vati. Hence in present study Herbal Cardiol vati was scanned for the analysis of Electrolytes like Manganese(Mn), Calcium(Ca), Magnesium(Mg), Sodium(Na) and Potassium(K). These Electrolytes can cause several physiological and health effects. These Electrolytes can determine by quantitatively and validated by using modern technique such as ICP-MS, ICP-AES and Flame photometer.

KEYWORDS: Cardiol vati, Standardization, Herbal medicine, Electrolytes, ICP-MS, ICP-AES and Flame photometer.

INTRODUCTION

Electrolyte are salts found in body fluids, tissue and blood. Proper balance is essential for muscle coordination, heart function, fluid absorption and excretion, nerve function and concentration. The kidneys regulate fluid absorption and excretion and maintain the electrolyte fluctuation. Normally, sodium and potassium are filtered and excreted in the urine and feces according to the body's needs. Small or large quantity of sodium or potassium, caused by poor diet, dehydration, medication and disease, results in an imbalance. Electrolytes are needed for metabolism, for movement of fluids and for normal cellular activities, for proper fluid movement between cell to cell, from tissue to tissue, from organ to organ, for normal metabolism and help to maintain the acid-base level for normal cellular activities. World health organization states that around 85-95% of the world population uses traditional medicines.[1] In the preparation of herbal medicines various parts of the plants are used as a raw material. After passing through many process they are converted in to finished herbal products. Herbs include crude plant materials such as leaves, flowers, fruit, seeds, stems, wood, bark, roots, rhizomes or other plant parts, which may be whole, fragmented or powdered. Herbal materials include, in addition to herbs, fresh juices, gums, fixed oils, essential oils, resins and dry powders of herbs.[2] But patients are not aware about their content, standards and validation. World health Organization gives some guidelines[3] for the preparation of herbal medicines and listed some methods for the standardization of herbal medicines[4] and also give maximum permissible limit of heavy metal[5] 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[6], GC-gas chromatography[7], electrophoresis and TLC -thin layer chromatography.[8] However, those methods cater to mostly organic active ingredients. Therefore XRPD-Ray diffraction[9] and ICP methods are developed for the

quality control from inorganic prospective such as Manganese(Mn), Calcium(Ca), Magnesium(Mg), Sodium(Na) and Potassium(K) elements. Standardized herbal medicines maintained the quality and containing well defined constituents are required for reliable, beneficial therapeutic effects without any toxic effects.

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.

Sr. No	Brand and Company Name	Medicines Name	Plants as per label *
1	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,

***Data as per container labelled.**

Experimental design

Methods for the ICP-MS

Samples

Cardiol vati, taking five tablets code number was given B1, B2, B3, B4 and B5. 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-ionzed 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 as collision gas. The general analytical condition set for the ICP-MS are given in table number 2.

Table – 2. General analytical condition.

Sr. No	Parameter	Value
1	Spray Chamber Temperature	2.7
2	Cool Flow	14
3	Sampling Depth	5
4	Plasma Power	1550
5	Auxiliary Flow	0.8
6	Nebulizer Flow	1.0079
7	Spray Chamber Temperature	2.7
8	Peristaltic Pump Speed	25

Table -3. Standard Preparation Stock Standards Available of 10 ppm 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

MATERIALS AND METHOD FOR ICP-AES AND FLAME PHOTOMETER

Chemicals

1) Double Deionized water used for all dilution**.**

2) Hydrogen peroxide **(**H_2O_2**)** AR **(**100 Volume, SDFSL**.**M**.**W**.** 34**.**04**).**

3) Concentrated Sulphuric Acid **(**H_2SO_4**) (**98**%).**

4) Acetone**.**

5) Paraffin**.**

Sampling

In the present study, the marketed herbal tablets of Cardiol Vati was selected for the analysis. The brand names of products, license number and content as per company's label are included in table 1.

Experimental design

Code numbers namely B1, B2, B3, B4 and B5 was assigned for Cardiol Vati. By taking the weight of each tablet of Cardiol Vati on digital balance, each tablet sample was gently ground to fine powder using mortar and pestle and packed in butter paper until the analysis. To determine the concentration and validation of heavy metals, a wet digestion of the powder sample was done according to the new method developed. Table number 4 shows the weight of Cardiol Vati samples and dilution. Each sample was placed separately in 100 mL round bottom flask and 3 mL concentrated sulphuric acid was added. The mixture was allowed to stand for 30 minutes at room temperature. After 30 minutes about 4 mL of 30% hydrogen peroxide was added to the round bottom flask and allowed to cool at room temperature. The sample was then refluxed at 190^{o}C for 40 minutes. The sample was cooled down to room temperature. 2 mL of 30% hydrogen peroxide was added and the solution heated once again until the digest was clear upon cooling. it was filtered through Whatman 42 filter paper and transferred quantitatively to a 25 mL volumetric flask by adding distilled water. The concentration of Electrolytes Magnesium (Mg) in the final solution were determined by using ICP-AES similarly Sodium (Na) and Potassium (K) in the final solution were determined by using Elico Flame Photometer CL 378 for the analysis of samples. Analysis made much simpler because of the multiple calibration curves saving facility. The instrument carries advanced features like automatic ignition, automatic gas shut off in case of a power failure.

Table 4- Sample weight and dilution

Sr. No	Sample	Weight (g)	Dilution	Final volume
1	Cardiol Vati [B1]	0.443	25 mL in conc H_2SO_4	1 mL in 25 mL de-ionized H_2O
2	Cardiol Vati [B2]	0.447	25 mL in conc H_2SO_4	1 mL in 25 mL de-ionized H_2O
3	Cardiol Vati [B3]	0.446	25 mL in conc H_2SO_4	1 mL in 25 mL de-ionized H_2O
4	Cardiol Vati [B4]	0.442	25 mL in conc H_2SO_4	1 mL in 25 mL de-ionized H_2O
5	Cardiol Vati [B5]	0.444	25 mL in conc H_2SO_4	1 mL in 25 mL de-ionized H_2O

RESULTS AND DISCUSSION

Biological Role of Electrolytes[19]

Manganese

Manganese is an important electrolyte for human health, essential for development of metabolism and the antioxidant system. It is also important in photosynthetic.

Calcium

calcium is not only necessary for the formation of bones and teeth, but also critical for transmission of nerve impulses, blood clotting and muscle contraction. The excess calcium in the body, is pretty uncommon, but can come from excessive consumption of calcium-rich foods, certain bone diseases or extreme inactivity e.g., quadriplegic/paraplegic conditions where the bones bear no weight. Symptoms may include digestive problems and nausea in minor cases, but can cause brain dysfunction, coma or even death in extreme instances. Deficiency of calcium may not cause immediate symptoms, but over time can also affect the brain, leading to delirium, memory loss and depression; severe cases may lead to muscle spasms, seizures and abnormal heart rhythms.

Magnesium

Magnesium is necessary for over 300 biochemical reactions in the body, it also plays an important role in the synthesis of both DNA and RNA, essential to every cell of every known living organism. The fourth most prevalent mineral in the human body, magnesium helps maintain normal nerve and muscle function, boosts the immune system, maintains stable heart rate, stabilizes blood sugar and promotes the formation of bones and teeth. Magnesium toxicity can occur in cases of kidney failure or excessive supplementation, however and may lead to nausea, vomiting, impaired breathing or irregular heartbeat.[19]

Sodium

Increasing incidence of hypertension and heart disease all over the world can be attributed to the rising occurrences of sodium imbalances.

Sodium is the major positive ion in fluid outside of cells. Excess sodium is excreted in the urine. the transmission of sodium into and out of individual cells also plays a role in critical body functions. Many processes in the body, especially in the brain, nervous system and muscles, require electrical signals for communication. The movement of sodium is critical in the generation of these electrical signals. Therefore, too much or too little sodium can cause

cells to malfunction, and extremes in the blood sodium levels can be fatal. Increased sodium in the blood occurs whenever there is excess sodium in relation to water it may cause kidney disease, loss of water and vomiting. A decreased concentration of sodium occurs whenever there is a relative increase in the amount of body water relative to sodium it causes liver, kidney and heart disease. Sodium is responsible for controlling the total amount of water in the body. It is also important for regulating blood volume and maintaining muscle and nerve function. Sodium mostly found in blood, plasma and lymph fluid. It may cause hypertension and increased risk of heart disease.

Potassium

Potassium is the major positive ion found inside of cells. Among the many functions of potassium in the body are regulation of the heartbeat and the function of the muscles. A seriously abnormal increase in potassium or decrease in potassium can profoundly affect the nervous system and increases the chance of irregular heartbeats, which, when extreme, can be fatal. Potassium is normally excreted by the kidneys, so disorders that decrease the function of the kidneys can result in hyperkalemia. potassium, can arise due to kidney diseases; excessive losses due to heavy sweating, vomiting, diarrhea, eating disorders or other causes. The proper balance between potassium and sodium is very important to maintaining our health, imbalance of potassium and sodium can further increase risk of hypertension, heart disease and even stroke. Loss of electrolytes can result vomiting, diarrhea and dehydration**.** In healthy person PH is between 6**.**4 and 7**.**00**.** Change in PH may cause several problems in body like damaging tissue, kidney disease. Deficiency of electrolytes may cause muscle weakness or sever cramping in excess it causes high blood pressure and increase your risk of heart disease. Diluted samples of Cardiol vati were used for the further analysis on ICP-MS Icap Q model, ICP-AES and Flame photometer. As an electrolytes Manganese (Mn), Calcium (Ca), Magnesium(Mg), Sodium(Na) and Potassium(K) are great importance for life and the fluids which are present in body. Detected accurate concentration of Electrolytes in selected samples by ICP-MS, ICP-AES and Flame Photometer are given in table number 5 and the SD, SE and CV are given in Table 7.

Table – 5. Accuracy of elemental concentration per Tablet.

Sr. No	Tablet Code	Concentration of Elements in ppm				
		Mn	Ca	Mg	Na	K
1	B1	0.20572	0.0019	6.498	2.9	5.6
2	B2	0.28564	0.00199	6.557	2.926	5.65

3	B3	0.21035	0.00145	6.542	2.919	5.637
4	B4	0.215	0.00178	6.483	2.893	5.587
5	B5	0.29965	0.00187	6.512	2.906	5.612

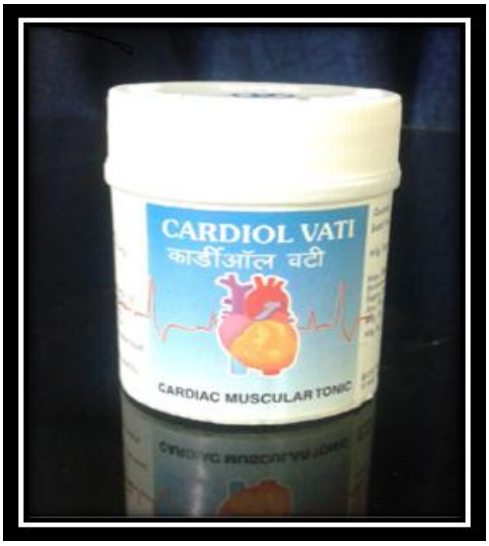

Figure-1A. Cardiol vati Sample.

Figure-1B. 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).

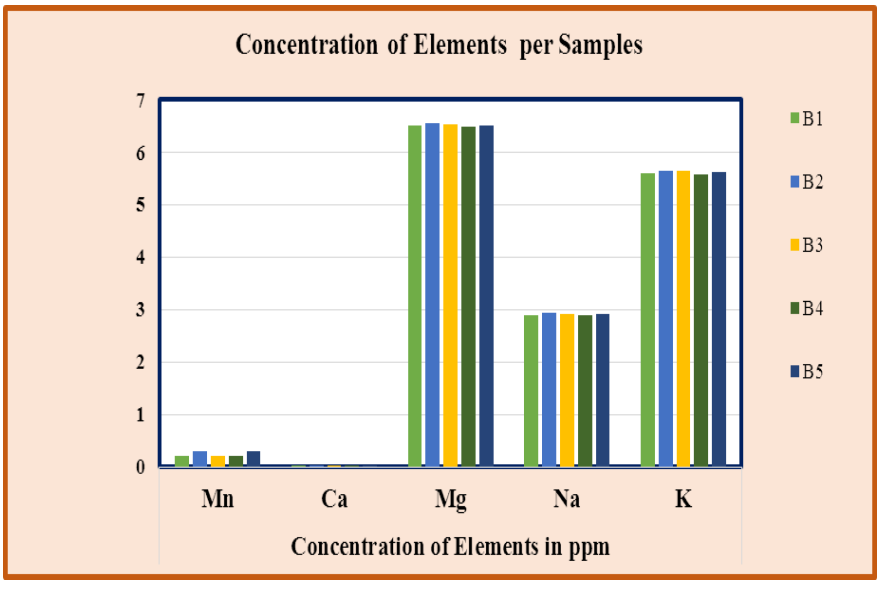

Fig -2. Graphical representation of Elements presents in different samples

Table- 6. LD 50 FROM MERCK INDEX - 11TH EDITION AND ACGIH Threshold Limit Value[7,12,13]

Sr. No	Elements	Compounds	LD50	ATS (Airborne Threshold Limit)
1	Mn	Manganese dioxide	45 mg/kg in rabbit	0.02 mg/m^3
2	Ca	Calcium acetate	04.28 g/kg orally on rat	2.0 mg/m^3
3	Mg	Magnesium Acetate	18 mg / kg iv in mice	10.0 mg/m^3
4	Na	Sodium chloride	3.75 g / kg orally in rat	2.0 mg/m^3
5	K	Potassium carbonate	1.87 g / kg orally in rat	2.0 mg/m^3

Table- 7. Standard deviation, standard errors and Coefficient variance of Electrolytes Calculated in Cardiol Vati

Sr. No	Observations	Concentration of Elements in ppm				
		Mn	**Ca**	**Mg**	**Na**	**K**
1	1	0.20572	0.0019	6.498	2.9	5.6
2	2	0.28564	0.00199	6.557	2.926	5.65
3	3	0.21035	0.00145	6.542	2.919	5.637
4	4	0.215	0.00178	6.483	2.893	5.587
5	5	0.29965	0.00187	6.512	2.906	5.612
6	**Mean**	**0.243272**	**0.001798**	**6.5184**	**2.9088**	**5.6172**
7	**SD**	**± 0.045461**	**± 0.000208**	**± 0.030648**	**± 0.013553**	**± 0.025994**
8	**SE**	**± 0.020330**	**± 9.324162E-05**	**± 0.013706**	**± 0.006061**	**± 0.011624**
9	**CV**	**0.186873**	**0.115959**	**0.004701**	**0.004659**	**0.004627**

Table- 8. Calibration correlation coefficient R and BEC (ppb) data.

Sr. No	Isotope	R	BEC (ppb)
1	55Mn	0.993	0.612
2	40Ca	0.995	-1.230

Table-9. Approximate Elementary Composition of the Human Body (Dry Weight Basis).[18]

Sr. No	Elements	Percent
1	Manganese(Mn)	0.001
2	Calcium(Ca)	4.0
3	Magnesium(Mg)	0.1
4	Sodium(Na)	0.4
5	Potassium(K)	1.0

Electrolytes Manganese(Mn), Calcium (Ca), Magnesium (Mg), Sodium (Na) and Potassium (K) are great importance in life. The detected accurate concentration of electrolytes in selected samples by ICP-MS, ICP-AES and by Flame Photometer are given in table number 5. In Herbal Cardiol vati sample B1 to B5, most abundant element was Magnesium (Mg) whereas Calcium (Ca) was found in lowest concentration. The Standard deviation (SD),

standard error (SE) and coefficient variance (CV) calculated from the different observations of all samples are given in table number 7 and table number 8 shows that for most of the target elements, low ppt BEC (background equivalent concentration). Table number 6 shows the LD50 and Airborne Threshold Limit of electrolytes**.**

The CV for the Manganese (Mn)calculated from the different observation was **0.18687350** and the SE was found **± 0.020330817.**

The CV for the Calcium(Ca)calculated from the different observation was **0.11595917** and the SE was found **± 9.32416216E-05.**

The CV for the Magnesium(Mg)calculated from the different observation was **0.00470176** and the SE was found **± 0.01370620**.

The CV for the Sodium(Na)calculated from the different observation was **0.00465951** and the SE was found **± 0.00606135**.

The CV for the Potassium(K) calculated from the different observation was **0.00462761** and the SE was found **± 0.01162497**.

From the above observation and calculation of Coefficient Variance(CV) and Standard Error (SE) for the Electrolytes Manganese(Mn), Calcium (Ca), Magnesium (Mg), Sodium (Na) and Potassium(K) was found in very low concentration and it was found in below toxic and Airborne threshold limit in all Tablets of Herbal Cardiol Vati.

Figure 3 and 4 shows the standard calibration graph for the electrolyte Manganese (Mn) and Calcium (Ca) by ICP-MS.

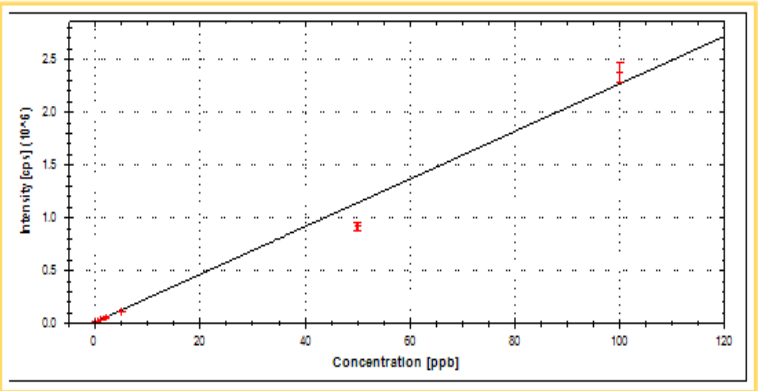

Fig-3. Calibration graph of Manganese (Mn)

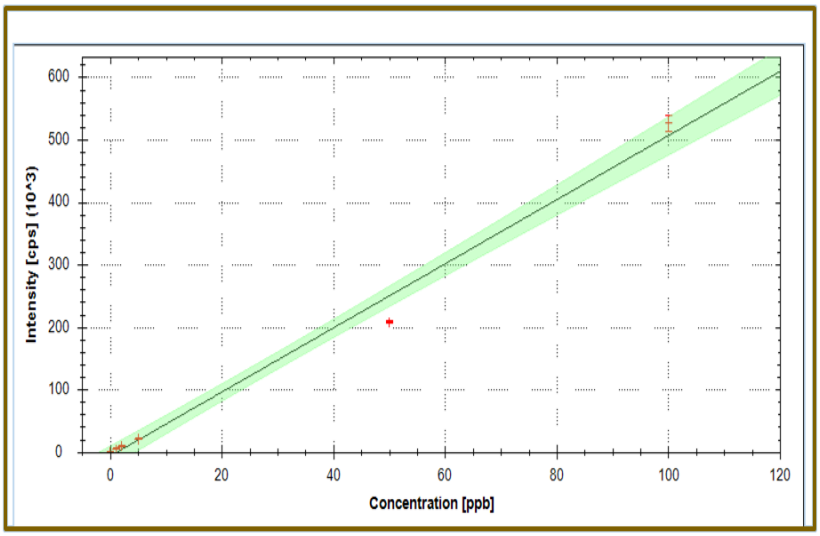

Fig-4. Calibration graph of Calcium (Ca)

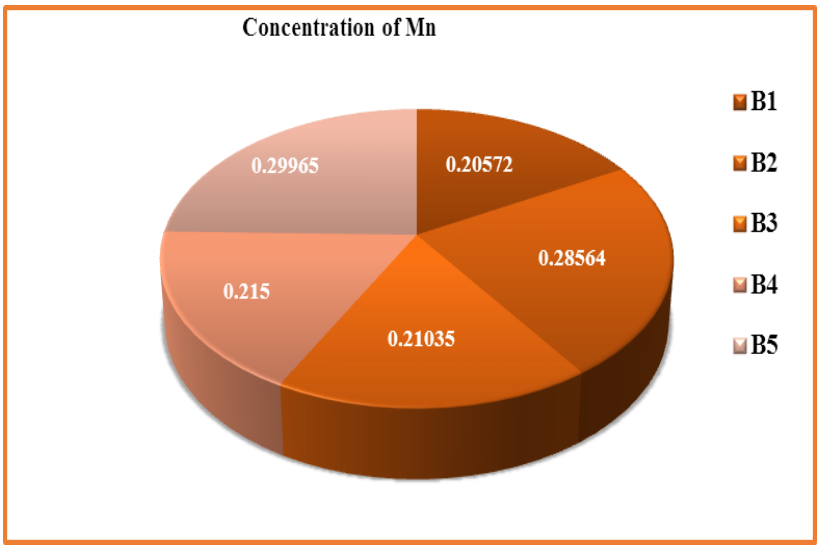

Fig-5. Concentration of Manganese

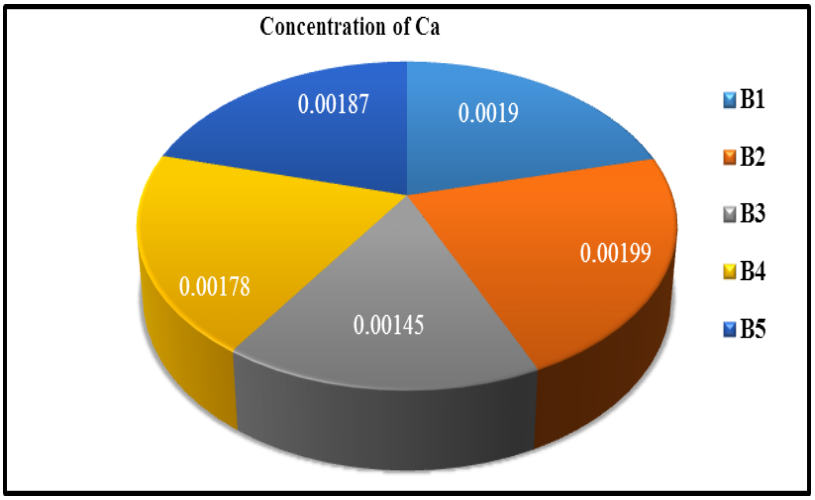

Figure -6 Concentration of Calcium

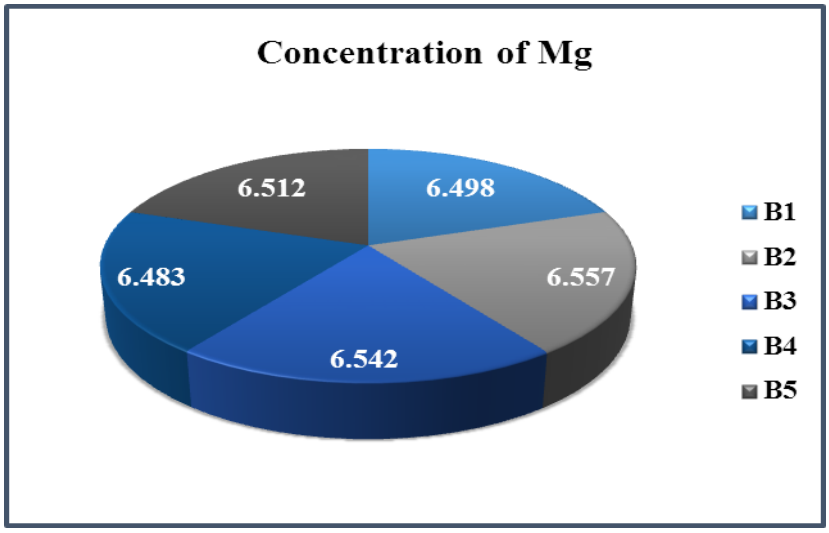

Figure -7 Concentration of Magnesium

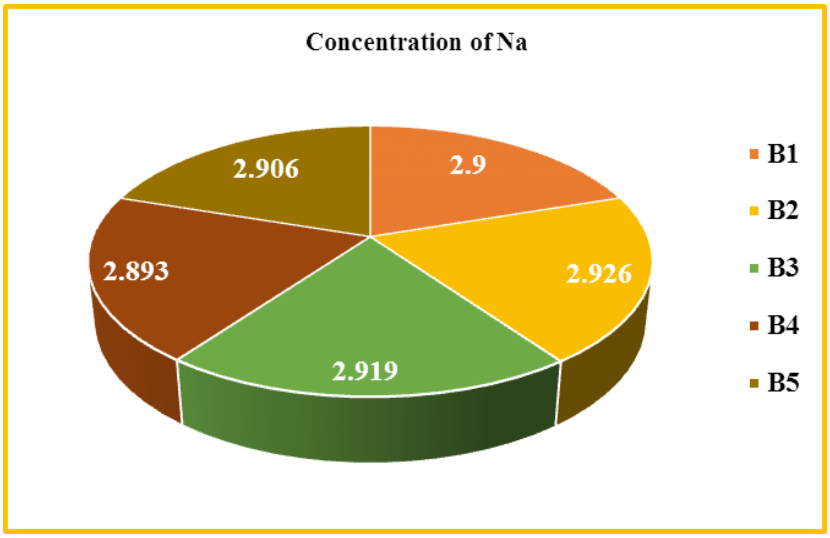

Figure -8 Concentration of Sodium

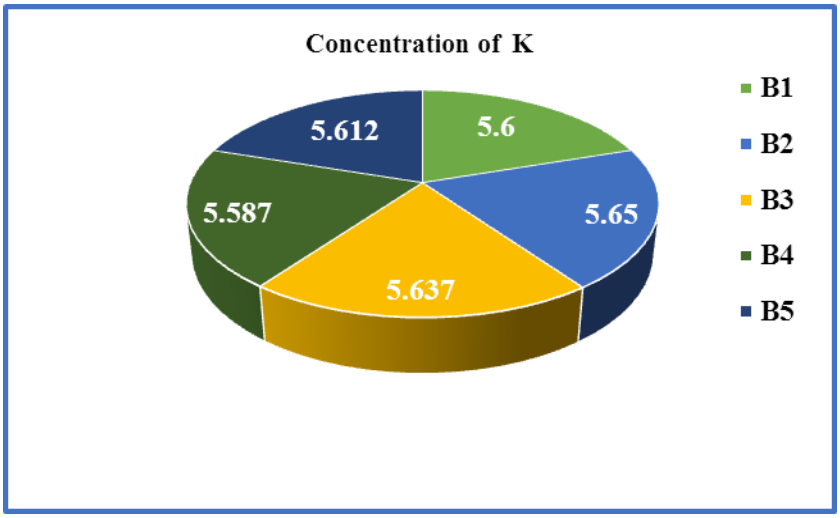

Figure -9 Concentration of Potassium

The above figure number 5, 6, 7, 8, 9 shows the concentration of Electrolytes Manganese(Mn), Calcium (Ca), Magnesium (Mg), Sodium (Na) and Potassium (K) respectively. It observed that the difference between each electrolyte in all samples was very low concentration.

CONCLUSION

The coefficient variance (CV) of the samples are less than one are consider as low variance and coefficient variance (CV) is greater than one are consider as high variance in all samples very low coefficient variance (CV) was found. All these values of electrolytes showed less toxicity in herbal medicines and are detected below LD50 and Airborne threshold limit and within permissible limit by World Health Organization (WHO). A low Standard deviation(SD) means that the data is very closely related to the average thus very reliable. The sufficient quality controlled parameters and condition were followed during the manufacturing process. Results obtained from ICP-MS, ICP-AES and Flame photometer of Herbal Cardiol vati samples detected the accurate values of electrolytes concentration in ppm. The content of Electrolytes and Minerals are not indicated on the tablet label. Elemental analysis by ICP-MS and ICP-AES are recent techniques which gives more accurate concentration of electrolytes contain in the Herbal Cardiol vati samples (Tablets) which is not previously reported by researchers. Quantitative estimation of metals, minerals, trace elements is done by atomic absorption spectrophotometer in herbal powder only, not in tablets, therefore, the concentration of the electrolytes is below the hazardous levels to the patient. In Ayurvedic medicines, the minerals, electrolytes are not reported with the daily intake of tablet, it is essential to know the amount of individual minerals consumed by 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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