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ESTIMATION OF INORGANIC (METAL) IONS IN SOME OF THE MARKETED FORMULATIONS BY FLAME EMISSION SPECTROSCOPY

Sumanth Prabhu*, Subhash Kale and Dr. A. Venkatachalam

Pacific University, Pacific Hills, Pratapnagar Extn, Airport Road, Debari, Udaipur, Rajasthan, India.

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***Corresponding Author**
Sumanth Prabhu
Pacific University, Pacific Hills, Pratapnagar Extn, Airport Road, Debari, Udaipur, Rajasthan, India.

ABSTRACT

A metal ion in aqueous solution (aqua ion) is a cation with single or multiple positive charge, dissolved in water, of chemical formula $[M(H2O)n]^{z+}$. Aqua ions are present in most natural waters. Na+, K+, Mg^{2+} and Ca^{2+} are major constituents of sea and ground water. The concentrations of sodium, potassium, magnesium and calcium in blood are similar to those of seawater. Blood also has lower concentrations of essential elements such as iron and zinc. Many are essential in our diets in varying quantities due to their metabolic importance in human body. On the other hand, metals have played an important role in medicine for years in the form of supplement medicines. In addition, a number of drugs and potential pharmaceutical agents also contain metal-binding or metal-recognition sites, which can bind or interact with metal ions and potentially influence (increase or decrease) their bioactivities. Different metal ions which are toxic at higher concentrations are also useful for maintaining life processes at lower concentrations and are even effective in the modification of some well-established drug molecules towards their better action.[1] Controlling and minimizing the side effects of these metal ions[5] (termed metal impurities here) from these drugs is a key issue in assuring the safety of drug therapy. To make drugs serve their purpose various chemical and instrumental methods were developed at regular intervals which are involved in the estimation of drug. The purpose of the present study was to develop estimate the inorganic (metal) ions in some of the oral dosage drug products by Flame emission spectroscopy (FES). An internal standard technique is proposed in order to reduce sample preparation and injection related errors thereby

improving method accuracy. Proposed method is validated as per ICH[4,7] guidelines and was employed to perform the recovery estimation in this study.

KEYWORDS: Inorganic Ions, Metal Ions, Impurities, Method validation, Oral dosage drug products, Flame emission spectroscopy, Internal standard, Cation, Metal impurities.

INTRODUCTION

Atomic spectroscopy is the oldest method for determination of metal elements. The radiation emitted from the flames depends on the characteristic element present in the flame. The developments in the instrumentation area led to the widespread application of atomic spectroscopy. Atomic spectroscopy is an undisputable tool in the field of analytical chemistry. It is divided into three types which are absorption, emission, and luminescence spectroscopy. The different branches of atomic absorption spectroscopy are (1) Flame photometry or flame atomic emission spectrometry in which the species is examined in the form of atoms (2) Atomic absorption spectrophotometry, (AAS), (3) Inductively coupled plasma-atomic emission spectrometry (ICP-AES).

Photoelectric flame photometry, a branch of atomic spectroscopy[8,9,10] is used for inorganic chemical analysis for determining the concentration of certain charged metal ions such as sodium, potassium, lithium, calcium, Cesium, etc. In flame photometry the species (metal ions) used in the spectrum are in the form of atoms. The International Union of Pure and Applied Chemistry (IUPAC) Committee on Spectroscopic Nomenclature has recommended it as flame atomic emission spectrometry (FAES). The basis of flame photometric working is that, the species of alkali metals (Group 1) and alkaline earth metals (Group II) metals are dissociated due to the thermal energy provided by the flame source. Due to this thermal excitation, some of the atoms are excited to a higher energy level where they are not stable. The absorbance of light due to the electrons excitation can be measured by using the direct absorption techniques. The subsequent loss of energy will result in the movement of excited atoms to the low energy ground state with emission of some radiations, which can be visualized in the visible region of the spectrum. The absorbance of light due to the electrons excitation can be measured by using the direct absorption techniques while the emitting radiation intensity is measured using the emission techniques. The wavelength of emitted light is specific for specific elements.

Humans are also exposed to different metal ions either through diet or through different environmental factors[2] (metal contaminated water). Some of which are directly essential for our wellbeing and others are toxic above certain (higher) concentrations. Complexation of drug molecules with metal ions may affect the fate of chemical reaction as their pharmacokinetics may get altered upon metal ion complexation. This may occur in the body in a number of ways (like Changes in drug absorption properties, Changes in drug distribution, Change in allergenicity and potency, Drug interactions, drug metabolism, etc). So controlling and minimizing the side effects of these metal ions (termed impurities here) from drugs is a key issue in assuring the safety of drug therapy. Different sources of metallic impurities in drugs are elaborated through diagrammatic representation in Figure – 1 and Figure – 1a.

To make drugs serve their purpose, various chemical and instrumental methods were developed at regular intervals which are involved in the estimation of drug. In the present study calcium, sodium and potassium metal ions from different tablet/powders commercial formulations sources have been estimated by flame photometric method which was then validated as per ICH guideline[4,6] and compared with the label claim on their packing.

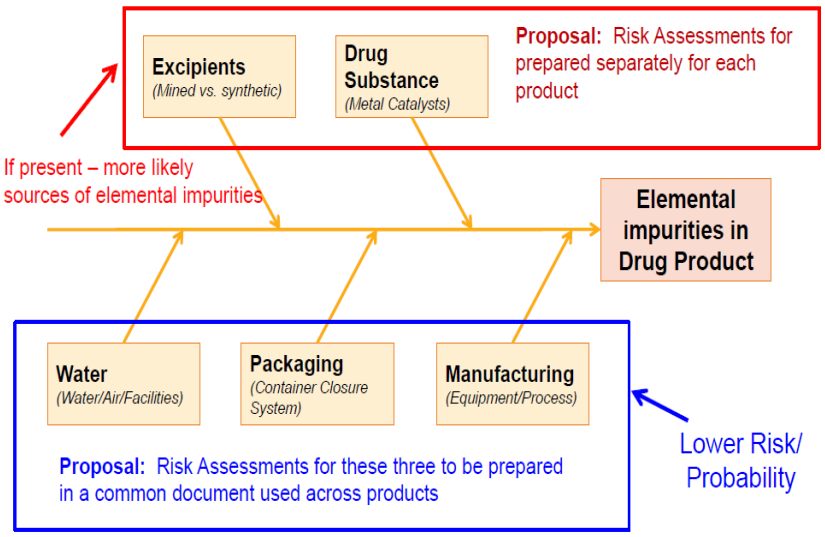
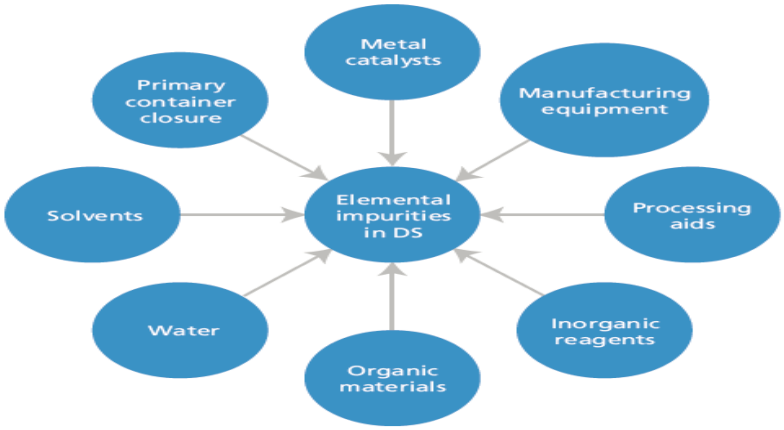


Figure – 1a: Source of elemental impurities in drugs (drug substance).

Figure. 1: Source of elemental impurities in drugs (drug products) [Fishbone diagram].



Chemicals, Instruments and Method

Chemicals: Hydrochloric Acid (AR grade), Calcium carbonate ($CaCO_3$) primary standard, Distilled water, Sodium Chloride (NaCl) primary standard, Potassium chloride (KCl) primary standard.

Formulation Samples: Commercial samples of Drug products containing Calcium, Sodium and Potassium. 10 different formulations were evaluated during the course of this study.

Instruments required: Flame photometer, Analytical precision weighing balance, Sonicator and required precision glassware's.

1.1 Experimental (Estimation of calcium): For the estimation of calcium from tablets, 5 different commercially available Oral dosage forms from different manufacturers were analyzed using the validated analytical method and the results are tabulated in Table-1. Procedure of analysis as follows.

Standard preparation: 0.2528 gm of calcium carbonate (CaCO3) primary standard is weighed and transferred to a 100mL beaker and 6mL of dilute HCL is added, till CaCO3 is dissolved completely. The solution is transferred to a 100mL standard volumetric flask, giving washings to the beaker with distilled water and then making the volume up to the mark. This is 1000ppm calcium standard solution. From this 4,5,6,7,8 and l0mL of solutions are pipetted out separately in100mL standard volumetric flasks and diluted to 100mL, to give 40, 50,60,70,80 and 100ppm solutions respectively. 100ppm solution is taken as maximum standard for aspiration. The solutions are aspirated in to the flame and the readings are noted by using calcium filter. Distilled water is used as a blank and the absorbance is adjusted to zero. The flame photometer readings are given in Table-1.

Sample Preparation: 0.3035gm of "Formulation 1" is weighed and transferred in to a 100mL beaker. It is dissolved in 6mL of dilute HC1 till all the calcium carbonate is dissolved. It is sonicated for 15 minutes for complete dissolution. The solution is transferred to a 100mL standard volumetric flask, giving washings to the beaker with distilled water and then making the volume upto the mark. This is 1000ppm solution. 4,5,6,7 and 8mL of this solution are pipetted out and diluted to 100mL in different 100mL standard volumetric flasks to get 40,50,60,70, and 80ppm solutions respectively. The solutions are aspirated into the flame and the readings are noted, using distilled water as a blank. The readings are given in Table-1.

RESULTS AND DISCUSSION

The linearity in the recovery is maintained. The analysis is precise and accurate (details in **Table-2)** and the method is considered suitable for commercially available samples. The linearity for different concentrations of calcium from calcium standard and "Formulation 1" are given in Fig.2 and Fig. 3 respectively.

Table. 1: Flame Photometer readings for standard as well as sample solutions (Formulation 1) of calcium showing linearity.

Concentration in ppm	Readings (mill equivalence)		Calculated concentration for sample (ppm)	%-Recovery
	Standard	Sample		
40	99	95	38.38	95.95
50	121	120	49.58	99.16
60	147	142	57.95	96.58
70	169	162	67.10	95.85
80	196	188	76.73	95.91
				Avg Recovery = 96.89 % RSD = 1.60

Table. 2: Comparative readings of different Calcium tablets and % recovery.

Source	Concentration of solution (ppm)	Flame photometer reading (Milli equivalence)	Standard Reading	Concentration (ppm)	% Recovery
Formulation 1	50	120	121	49.58	99.16
Formulation 2	50	119		49.17	98.35
Formulation 3	50	122		50.41	100.83
Formulation 4	50	118		48.76	97.52
Formulation 5	50	123		50.83	101.65
					Avg Recovery = 99.50 % RSD = 1.72

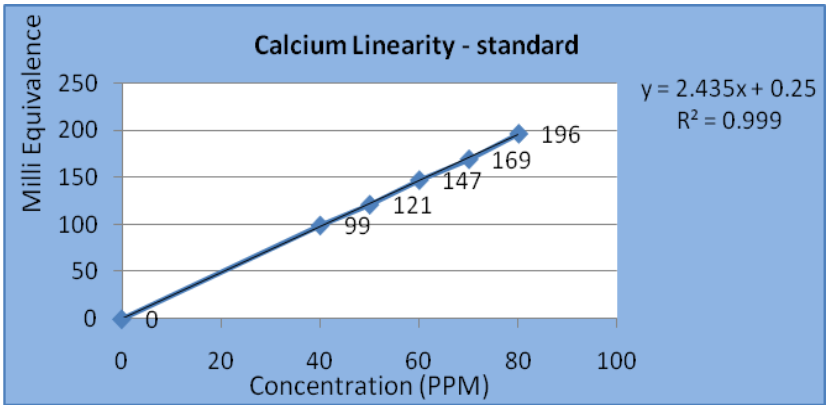


Fig. 2: Linearity of Calcium standard.

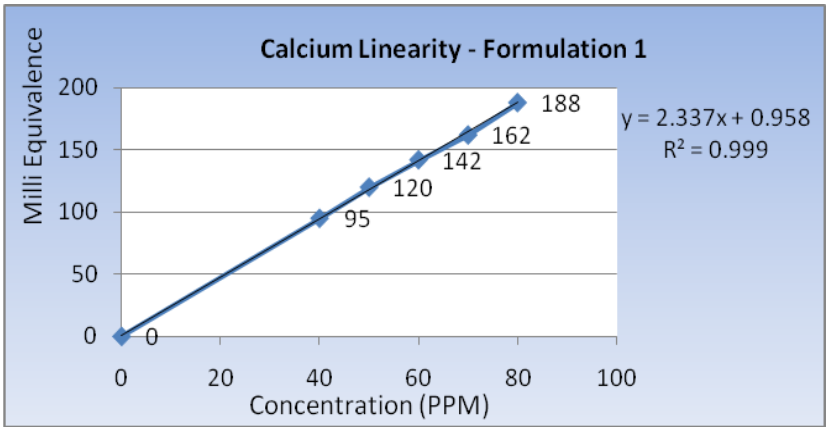


Fig. 3: Linearity of Calcium in Formulation 1.

2.1 Estimation of sodium by Flame photometry

The commercial samples containing Na and K in Formulation 6, Formulation 7, Formulation 8, Formulation 9 and Formulation 10 were analyzed by validated flame photometric method and the accuracy, precision, linearity and recovery studies are done on Formulation 6. The % recovery of the different samples along with their label claim is given in Table 3.

Standard preparation

0.2541 gm of NaCl primary standard is weighed in a 1000mL volumetric flask. It is then dissolved in distilled water making the volume upto the mark. This is 100ppm solution. 2,4,6,8,10 and 14mL of the solution are pipetted out in 100mL standard flasks and diluted with distilled water to get 2,4,6,8,10 and 14ppm solutions respectively. 14ppm is used as the maximum concentration solution for aspiration as maximum standard. The above samples are aspirated into the flame and the readings are noted using distilled water as a blank. The readings are given in Table 4. Sample preparation: 1.3243 gm of Formulation 6 powder is weighed in a 1000mL volumetric flask. It is then dissolved in distilled water making the

volume up to the mark. This is 100ppm solution. From this 2,4,6,8 and 10mL of the solutions are pipetted out in different 100mL standard measuring flasks and diluted with distilled water to get 2, 4, 6, 8 and 10 ppm solutions. They are aspirated into the flame and the flame photometer readings are noted. The readings are given in Table 4.

RESULTS AND DISCUSSION

Table. 3: The data of different sources of sodium.

Source	Label claim (gm)	%Recovery
Formulation 6	0.4304	95.9
Formulation 7	2.1524	96.8
Formulation 8	0.4304	96.9
Formulation 9	0.4304	95.9
Formulation 10	1.2671	98.7
		Avg Recovery = 96.4 % RSD = 0.57

Table. 4: Flame photometric readings for sodium standard and Formulation 6 sample.

Concentration in ppm	Readings (Milli equivalence)		Observed Concentration in ppm
	Standard	Formulation 6 sample	
2	31	27	1.74
4	64	58	3.63
6	93	88	5.68
8	128	116	7.25
10	162	148	9.14
14	240		

The linearity in the recovery is maintained. The analysis is precise and accurate and the method is considered suitable for commercially available samples. The linearity for different concentrations of sodium from sodium standard and "Formulation 6" are given in Fig.4 and Fig. 5 respectively.

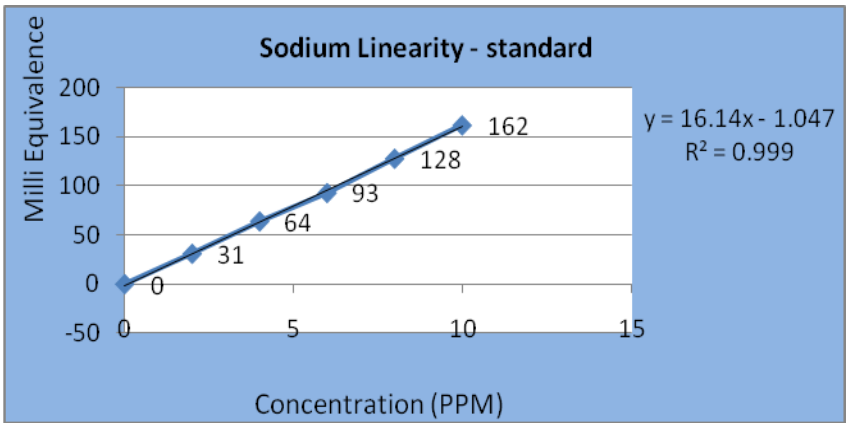


Fig. 4: Linearity of Sodium Standard.

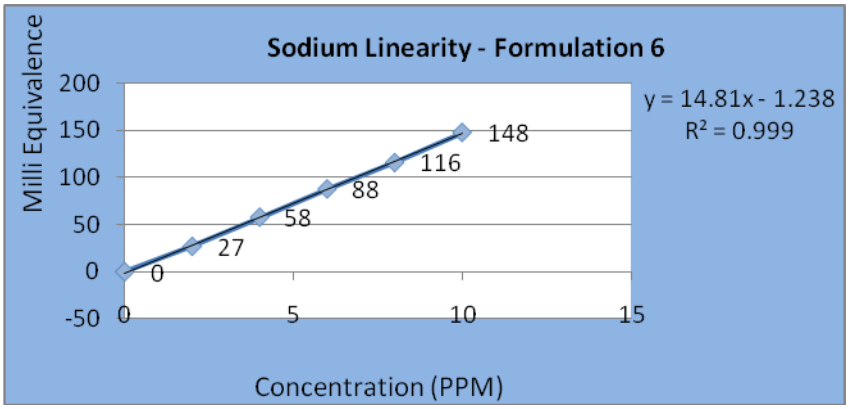


Fig. 5: Linearity of Formulation 6.

3.1 Estimation of potassium by flame photometry

The commercial pharmaceutical powders (in granular form) from Formulation 6, Formulation 7, Formulation 8, Formulation 9 and Formulation 10 also contain K in the form of KCl. Therefore they can be analyzed for the content of K by the validated flame photometric methods using the K filter. The linearity, accuracy precision and recovery of the analysis are discussed. The results are tabulated in Table 5.

Standard Preparation

0.1901 gm of KCl is weighed in a l000mL volumetric flask. It is then dissolved in distilled water making the volume upto the mark. This is l00ppm solution of potassium. From this, 2, 4, 6, 8, 10, and 14mL of solutions are pipetted out in different l00mL standard measuring flasks and diluted up to the mark with distilled water. These give 2, 4, 6, 8, 10, and 14ppm solutions. 14ppm solution is used as maximum standard for aspiration. They are aspirated in to the flame and the readings are noted. The results are given in Tables 5.

Sample preparation

3.6232gm of Formulation 6 powder is weighed in a l000mL volumetric flask. It is then dissolved in distilled water making the volume upto the mark. This gives l00ppm solution. From this 2, 4, 6, 8, and 10 mL of the solutions are pipetted out with distilled water. This gives 2, 4, 6, 8, and 10 ppm solutions. They are aspirated into the flame and the readings are noted. The results are given in Table 5.

Table. 5: Flame photometric readings for potassium standard and sample solution Formulation 6.

Concentration in ppm	Flame photometer Readings (Milli equivalence)		Observed concentration	% Recovery
	Standard	Formulation 6 Sample		
2	36	34	1.88	94.4
4	73	69	3.78	94.5
6	108	104	5.77	96.3
8	143	136	7.61	95.1
10	190	183	9.63	96.3
14	265			Avg Recovery = 95.8 % RSD = 0.92

The linearity in the recovery is maintained. The analysis is precise and accurate and the method is considered suitable for commercially available samples. The linearity for different concentrations of potassium from potassium standard and "Formulation 6" are given in Fig 6 and Fig 7 respectively.

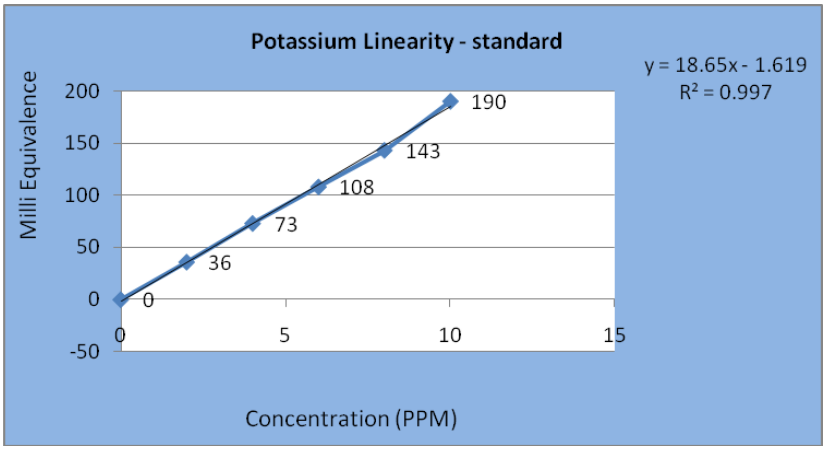


Fig 6: Linearity of Potassium Standard.

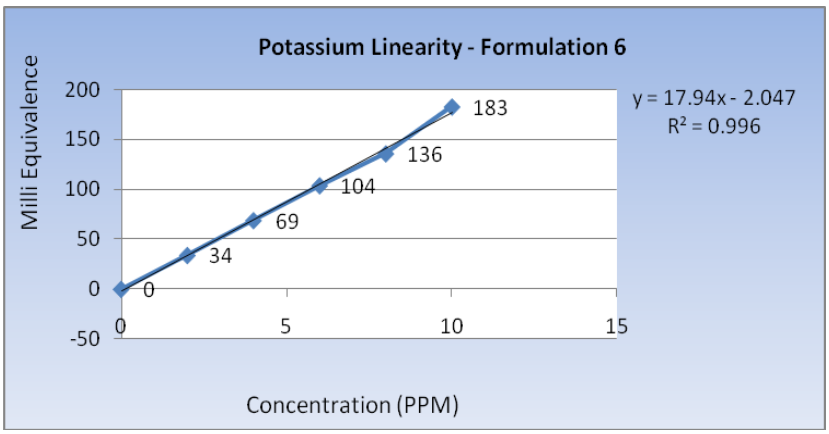


Fig. 7: Linearity of Formulation 6.

Table. 6: Flame photometric readings and the % recovery for Potassium from different samples.

Concentration (ppm)	Source	Readings (Milli equivalence)		Observed Concentration (ppm)	% Recovery
		Standard	Sample		
10	Formulation 6	190	183	9.63	96.3
10	Formulation 7		185	9.73	97.4
10	Formulation 8		182	9.57	95.8
10	Formulation 9		186	9.78	97.9
10	Formulation 10		185	9.73	97.4
					Avg Recovery = 96.9 % RSD = 1.00

Table. 7: Typical recovery targets in general.

Analyte concentration	% Recovery
> 1%	98-102
100-1000 mg/L	95-105
10-100 mg/L	90-107
100 ug/L - 10 mg/L	80-110
10-100 ug/L	60-115
1-10 ug/L	40-120

Based on the results obtained during estimation of calcium, sodium and potassium metal ions in different tablet/powders commercial formulations sources by flame photometric method and the typical recovery targets as in table 7, the employed analytical method is considered to be suitable in the evaluation of different commercial formulations.

CONCLUSION

The expected recovery[3] always depends on the sample matrix, the sample processing procedure, the analytical technique and on the analyte concentration. The table below (Table 7) gives some typical recovery targets in general and not be considered totally binding.

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REFERENCES

1. Kangkana Sarkar and Kamalika Sen., (SOME DRUGS IN ACTION: METAL IONS DO INFLUENCE THE ACTIVITY), International Journal Of Pharmaceutical Sciences And Research, 2017.
2. Guna, R. N., Vyas, J. M., Ramkishan, A., Agrawal, Y. K., Reviews in Anal. Chem., 2012; 31: 193-199.
3. http://simulab.ltt.com.au/6/toolbox/VAL/bookcase/VAL_bc_methodValidation.html
4. ICH, Q2B.Harmonized tripartite guideline, Validation of analytical procedure Methodology. Geneva, Switzerland: International Conference on Harmonization, 1996.
5. Inorganic pharmaceutical chemistry – Block, Roche, Soine, Wilson – Indian edition published by Verghese publishing house, Dadar. Year, 1986.
6. ICH. Guidance on Analytical Method Validation, International Convention on Quality for the Pharmaceutical Industry. Toronto, Canada: International Conference on Harmonization, 2002.
7. ICH. Harmonized Tripartite Guidelines, Validation of Analytical Procedures: Text and Methodology Q2 (R1), 2005.
8. Dean JR, Atomic absorption and plasma spectroscopy, edited by Ando DJ, John Wiley and Sons, 2nd edition, 2008; 42-112.
9. Brown RJC and Milton MJT. Analytical techniques for trace element analysis: an overview. Trends in Analytical Chemistry, 2005; 24(3): 266-274.
10. L'vov BV. Forty years of electrothermal atomic absorption spectrometry. Advances and problems in theory. Spectrochemica Acta, 1997; 52: 1239-1245.