DETERMINATION OF FOURTEEN PREFERRED ELEMENTAL IMPURITIES EMPLOYING ICP-MS AND MICROWAVE ACID DIGESTION APPROACH IN PARENTERAL OFLOXACIN SAMPLES

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ABSTRACT

The method of "Inductively Coupled Plasma Mass Spectrometry" (ICP-MS) may be interpreted as a trend in pharmaceutical determination of elemental impurities. The development of a specific process that is precise for all elemental impurities, however, is still a task. The ICP-MS technique using microwave acid digestion as a sample processing method was used to determine 14 elemental impurities (lithium, vanadium, chromium, manganese, iron, cobalt, nickel, copper, arsenic, molybdenum, cadmium, antimony, mercury and lead) existing in parenteral ofloxacin in this study. The strategy proposed was verified as per "United States Pharmacopeia Convention". The detection limits achieved by the proposed approach suggest that the ICP-MS technique is quite well fit for the measurement of the 14 chosen elemental impurities. Good linearity was achieved with correlation coefficient values higher than 0.99 over the range of quantification limit level concentration to 200 % level of the individual elemental impurity specification values. The values obtained for accuracy, precision, robustness, selectivity and ruggedness are also satisfactory. Six distinct batches of parenteral ofloxacin samples were subjected to analysis by the ICP-MS technique proposed. In all the batch samples, the fourteen chosen elemental impurities were noticed to be less than detection levels.

INTRODUCTION

Elemental impurities are remnants of metals that could be observable in the penultimate drug product. The evaluation of elemental impurities is important to explain the concentrations of heavy metals in the ultimate drug product. They can meddle with the effectiveness of the medication or have a direct harmful impact on the patient[1]. Elemental impurities in drug products can emerge from formulation ingredients, catalysts, packaging systems and processing vessels[2,3]. The ICH Q3D directives framed allowed regular exposures ($\mu g \, day^{-1}$) for 24 metal elements categorised into five groups[4,5]. In this categorization, the metal elements were also differentiated by path of administration and hazard classification on the criteria of toxicity and probability of occurrence.

One of the concerns of contemporary pharmaceutical quality management and research & development centers is the development of innovative approaches and protocols for the quick, precise and accurate evaluation of elemental impurities in different drug finished forms. For more than 100 years, compendial analytical techniques, including the colorimetric analysis procedure and the sulphide precipitation procedure, are often exploited to evaluate heavy metals[6,7]. The conventional colorimetric approach, besides the compendial processes used in Pharmacopoeias, have significant limitations: these approaches do not differentiate among different metal elements, their reproducibility, accuracy and precision are poor, and necessitate a weighty sample size. These approaches have recently been increasingly replaced by new analytical strategies, like plasma dependent spectrochemical instrumentational methods[8]. The "Inductively Coupled Plasma Mass Spectrometry" (ICP-MS) technique is generally accepted as an exceptionally stable and fast multi-element analysis technique in different sample matrices. Since this methodology has larger sensitivity, it is extended to ultra-trace investigations[9-11].

Ofloxacin, a broad-spectrum antibiotic of fluoroquinolone category, is used in therapy of bacterial

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infectivity which sets off pneumonia, bronchitis, chalmydia, skin infections, gonorrhea, urinary tract infections, and prostrate infections[12,13]. Latest literature reviews do not disclose published studies on the concurrent assessment of 14 metal elements (lithium, vanadium, chromium, manganese, iron, cobalt, nickel, copper, arsenic, molybdenum, cadmium, antimony, mercury and lead) in parenteral ofloxacin. The specification limitations for the chosen 14 metal elements were set on the rationale of the maximum standard dose of parenteral ofloxacin (3 g day^{-1}). The specification limits set were 75 ppm (lithium), 3 ppm (vanadium), 330 ppm (chromium), 25 ppm (manganese), 1000 ppm (iron), 1.5 ppm (cobalt), 6 ppm (nickel), 90 ppm (copper), 4.5 ppm (arsenic), 450 ppm (molybdenum), 0.6 ppm (cadmium), 27 ppm (antimony), 0.9 ppm (mercury) and 1.5 ppm (lead). Hence, the concurrent evaluation of 14 metal elements in parenteral ofloxacin with ICP-MS applying a microwave digestion methodology for sample processing was reported. The ICP-MS procedure was checked in fulfilment with USP Pharmacopoeia[14-16].

MATERIALS AND METHODS

Apparatus

Agilent Technologies ICP-MS model 7700 X, Sartorius Secura balance model 225D-10 IN, Merck Milli pore water processing system and CEM corporation microwave digester was employed in concurrent evaluation of 14 metal elements in parenteral ofloxacin.

Chemicals

Trace metal quality nitric acid, suprapure quality hydrochloric acid and ACS reagent quality peroxide were provided from Merck, India. Milli Q water was provided inhouse from Merck Milli pore water processing system. Traceable quality metal elements of the "National Institute of Standards and Technology" grade were used in the whole study. Lithium, vanadium, manganese, cobalt, copper, arsenic, cadmium, antimony, lead, yttrium, bismuth, indium, scandium standards of 1000 ppm concentrations were provided by Merck, India. Nickel, mercury and rhodium standards of 1000 ppm concentrations were provided by Sigma, India. Chromium, iron and molybdenum standards of 10000 ppm concentrations were provided by Inorganic Ventures, India.

ICP-MS and microwave digester conditions to evaluate the selected 14 metal elements

ICP-MS was run in Multi tune acquisition mode with forward and reflected power of 1550 W and 1-20 W, respectively. The plasma gas flow was 15 L min^{-1} and number of repetitions were 6. Collision gas and nebulizer gas employed were helium and argon, respectively. The flow auxiliary, collision gas and nebulizer gas were 1.2 L min^{-1}, 3.5 mL min^{-1} and 0.9 L min^{-1}, respectively. Scandium, rhodium and indium were internal standards for lithium, cadmium and antimony, respectively. Bismuth was internal standard for Mercury and Lead. Yttrium was internal standard for vanadium, chromium, manganese, iron, cobalt, nickel, copper, arsenic and molybdenum. The mass, mode of collision and integration time are provided in Table I. The peristaltic pump programming is provided in Table II. The solution of 5.0 % V/V nitric acid and 1.5 % V/V hydrochloric acid was utilized as diluent. The microwave digester conditions were 1600 W power, 215 ^{0}C temperature, 25 min of holding time and 20 min of ramp time.

Table I: ICP-MS conditions for metal elements

Metal element		Collision mode	Integration Time/Mass [sec]
Name	Mass		
Lithium	7	Helium	0.3
Vanadium	51	Helium	0.3
Chromium	53	Helium	0.3
Manganese	55	Helium	0.3
Iron	56	Helium	0.3
Cobalt	59	Helium	0.3
Nickel	60	Helium	0.3
Copper	63	Helium	0.3
Arsenic	75	Helium	1.0
Molybdenum	98	Helium	1.0
Cadmium	111	Helium	1.0
Antimony	121	Helium	0.3
Mercury	202	Helium	1.0
Lead	208	Helium	1.0
Yttrium	89	Helium	0.3
Rhodium	103	Helium	0.3
Indium	115	Helium	0.3
Bismuth	209	Helium	0.3
Scandium	45	Helium	0.3

Table II: Peristaltic pump program

Peristaltic pump program	Time (Sec)	Speed (rps) Nebulizer pump	Vial
Pre-Run			
Sample uptake	60	0.50	-
Stabilize	60		-
Post-Run			
Probe Rinse (sample)	15	0.35	-
Probe Rinse (standard)	15		-
Rinse 1 (2% V/V nitric acid)	45	0.35	1
Rinse 2 (Water)	45		2
Rinse 3 (Water)	45		3

Standard metal elements solution

Standard metal elements solution (lithium – 3750 ppb, vanadium – 150 ppb, chromium – 16500 ppb, manganese – 1250 ppb, iron – 50000 ppb, cobalt – 75 ppb, nickel – 300 ppb, copper – 4500 ppb, arsenic – 225 ppb, molybdenum – 22500 ppb, cadmium – 30 ppb, antimony – 1350 ppb, mercury – 45 ppb and lead – 75 ppb) for ICP-MS analysis were prepared earlier to use by successive dilutions of stock solutions containing 1000 ppm (lithium, vanadium, manganese, cobalt, copper, arsenic, cadmium, antimony, lead, yttrium, bismuth, indium, scandium, nickel, mercury and rhodium) and 10000 ppm (chromium, iron and molybdenum) concentrations of metal elements in solution containing 5.0 % V/V nitric acid and 1.5 % V/V hydrochloric acid. 1000 ppm concentration of stock scandium, rhodium, indium, bismuth and yttrium internal standards were also successively diluted with solution containing 5.0 % V/V nitric acid and 1.5 % V/V hydrochloric acid to acquire solution with concentration 0.5 ppm of each internal standard. The diluted internal standard was added to standard metal elements solution.

The preparation of a range of six standard linearity solutions was carried out in 10 mL volumetric bottles using the above-stated solution (14 metal elements + 5 internal standards) freshly processed in a solution containing 5.0 % V/V nitric acid and 1.5 % V/V hydrochloric acid. The concentration ranges prepared were 0.9 – 6 ppb (for cadmium), 6.75 – 45 ppb (for arsenic), 1.35 – 9 ppb (for mercury), 2.25 – 15 ppb (for lead), 2.25 – 15 ppb (for cobalt), 4.5 – 30 ppb (for vanadium), 9 – 60 ppb (for nickel), 112.5 – 750 ppb (for lithium), 40.5 – 270 ppb (for antimony), 675 – 4500 ppb (molybdenum), 37.5 - 250 ppb (manganese), 495 – 3300 ppb (for chromium), 135 – 900 ppb (for copper) and 1500 – 10000 ppb (for iron).

Blank solution preparation

To the microwave digestion container, 1.5 mL of peroxide, 1.5 mL of nitric acid and 0.1 mL of hydrochloric acid were added. After waiting for at least 10 min and including 0.2 mL of standard internal solution and 4 mL of water, digestion was resumed according to the schedule, i.e. 25 min to touch 215 ^{0}C and 25 min hold at 215 ^{0}C. The contents were moved to a 20 mL volumetric container after completion of digestion and processed to volume with water and blended properly.

Test ofloxacin solution preparation

Approximately 100 mg ofloxacin was accurately measured into a microwave digestion jar and 1.5 mL of peroxide, 1.5 mL of nitric acid and 0.1 mL of hydrochloric acid were added. After waiting for at least 10 min and then including 0.2 mL of standard internal solution followed by 4 mL of water, digestion process was continued according to the schedule, i.e. 25 min to touch 215 ^{0}C and 30 min hold at 215 ^{0}C. The contents were moved to a 20 mL volumetric container after completion of digestion and processed to volume with water and blended properly. The test ofloxacin solution concentration was 0.005 g mL^{-1}.

Procedure

The blank solution was aspirated followed by six linearity standard solutions. The six linearity standard solutions were analysed using the conditions proposed in section "ICP-MS and microwave digester conditions to evaluate the selected 14 metal elements". The linearity curve of the 14 metal elements selected were plotted by concentration (ppb) versus response (counts per sec) ratio of the standard to internal standard.

The blank solution was aspirated and then the test ofloxacin solution. These two samples were analysed by using the ICP-MS settings proposed in section "ICP-MS and microwave digester conditions to evaluate the selected 14 metal elements". The content of selected 14 metal elements in test ofloxacin solution was assessed utilizing corresponding metal element calibration curve.

RESULTS AND DISCUSSION

In the current study, ofloxacin parenteral digestion using the microwave digester method was assessed for further determination of 14 metal elements by ICP-MS. As ofloxacin is having acid groups, nitric acid and peroxide cannot form any salts with the analyte. Therefore, nitric

acid and peroxide were used for decomposing the ofloxacin sample matrix. Regarding the digestion effectiveness, use of 1.5 mL of peroxide, 1.5 mL of nitric acid and 0.1 mL of hydrochloric acid, and temperature of 215 °C for 25 min resulted in suitable digests permitting further evaluation of all chosen 14 metal elements. The internal standards for chosen 14 metal elements were founded on observations like: near as close as possible to analyte mass number, internal standard ionisation was identical to the metal element, chemical properties are similar to the metal element, absence of the internal standard in the sample, stable in matrix, having mass to charge ratio similar to the metal element and internal standards are not used at any stage of compound preparation. Based on above, scandium, rhodium and indium were chosen as internal standards for lithium, cadmium and antimony, respectively. Bismuth was opted as internal standard for mercury and lead. Yttrium was employed as internal standard for vanadium, chromium, manganese, iron, cobalt, nickel, copper, arsenic and molybdenum.

Validation

The developed digestion system and ICP-MS procedure was checked in fulfilment with USP Pharmacopoeia[14-16].

System suitability

Performed system suitability with the six standard linearity solutions using settings described in segment "ICP-MS and microwave digester conditions to evaluate the selected 14 metal elements". System suitability reports were viewed as the value of the correlation coefficient (Table III). The values for each metal element were greater than 0.99, suggesting the suitability of the ICP-MS system for the study of the chosen 14 metal elements.

Quantification limit (QFL) and detection limit (DTL)

The strategy applied to the evaluation of QFL and DTL was dependent on linearity and a blank solution. After evaluating the system suitability, 10 blank injections were pumped into the ICP-MS system. Recorded the standard deviation for ten blank ratios and measured the QFL and DTL for each metal using the slope of metal element's linearity curve characterised in the system suitability (Table III). The QFL and DTL values acquired were checked by means of precision experiments with a solution of metal elements at the concentrations of QFL and DTL levels. The precision experiment reports were viewed as the value of relative standard variation (RSV) percent (Table

Table III: System suitability, QFL and DTL reports

Metal element	Correlation coefficient (R^2)	Slope (m)	QFL		DTL	
			Value (ppb)	RSV* (%)	Value (ppb)	RSV* (%)
Lithium	0.9995	0.0055	112.5	1.21	22.5	0.68
Vanadium	0.9997	0.0994	4.5	0.48	0.9	0.46
Chromium	0.9997	0.0152	495	0.58	99	0.37
Manganese	0.9995	0.0721	37.5	0.43	7.5	0.41
Iron	0.9997	0.1026	1500	0.51	300	0.32
Cobalt	0.9997	0.2021	2.25	0.31	0.45	0.73
Nickel	0.9998	0.0525	9	0.63	1.8	0.69
Copper	0.9998	0.1428	135	0.54	27	0.27
Arsenic	0.9998	0.0164	6.75	0.45	1.35	0.54
Molybdenum	0.9998	0.1234	675	0.40	135	0.17
Cadmium	0.9998	0.0149	0.9	0.75	0.18	1.14
Antimony	0.9994	0.0816	40.5	0.41	8.1	0.42
Mercury	0.9998	0.0288	1.35	0.79	0.27	0.75
Lead	0.9999	0.1406	2.25	0.49	0.45	0.11

Relative standard variation for values

III). The values suggest enough sensitivity of the ICP-MS approach for the study of the chosen 14 metal elements.

Selectivity

The blank solution and solution of metal elements at the concentrations of DTL level were prepared and evaluated using settings given in segment "ICP-MS and microwave digester conditions to evaluate the selected 14 metal elements". The response ratio of each metal element in DTL level solution and blank solution were determined (Table IV). The response ratio of all metal elements in DTL level solution was more than the response ratio of all metal elements in blank solution. The values prove the appropriate selectivity of the ICP-MS procedure for the assessment of the selected 14 metal elements.

Linearity

The linearity of the ICP-MS procedure was validated in the range of QFL level to 200 % level (QFL level, 50 %, 75 %, 100 %, 150 % and 200 %) concentrations with regard to the individual specification value of each metal element. The six-linearity standard metal element solutions were injected into ICP-MS system and analysed via the suggested conditions described in "ICP-MS and microwave digester conditions to evaluate the selected 14 metal elements" section. The regression equation, correlation coefficient and percent Y intercept for each

Table IV: ICP-MS approach selectivity report

Metal element	Response ratio of metal elements in	
	Blank solution	Standard solution
Lithium	0.0057	0.1915
Vanadium	0.0283	0.1756
Chromium	0.0185	2.5541
Manganese	0.1265	0.9804
Iron	2.285	50.9748
Cobalt	0.0050	0.1511
Nickel	0.0283	0.1751
Copper	1.2991	7.4669
Arsenic	0.0008	0.0378
Molybdenum	0.0516	26.0068
Cadmium	0.0001	0.0042
Antimony	0.0347	1.1105
Mercury	0.0006	0.0130
Lead	0.0611	0.0859

Table V: Linearity reports for chosen 14 metal elements

Metal element	Linearity range (ppb)	Correlation coefficient (R^2)	Y intercept (%)	Regression equation
Lithium	112.5-750	0.9999	0.02	y = 0.005617 c + 0.026509
Vanadium	4.5-30.0	0.9999	0.01	y = 0.099935 c + 0.009494
Chromium	495-3300	0.9999	0.01	y = 0.014491 c + 0.134819
Manganese	37.5-250	0.9999	0.01	y = 0.067597 c + 0.071270
Iron	1500-10000	0.9999	0.01	y = 0.098087 c - 0.600461
Cobalt	2.25-15.0	0.9999	0.01	y = 0.197766 c + 0.002122
Nickel	9.0-60.0	0.9999	0.01	y = 0.052831 c + 0.013282
Copper	135-900	0.9999	0.01	y = 0.135422 c + 0.618607
Arsenic	6.75-45.0	0.9999	-0.01	y = 0.016785 c - 0.001084
Molybdenum	675-4500	1.00	-0.01	y = 0.114980 c − 1.405898
Cadmium	0.9-6.0	0.9999	0.00	y = 0.015081 c − 0.000030
Antimony	40.5-270.0	1.00	0.01	y = 0.080006 c + 0.128449
Mercury	1.35-9.0	0.9999	0.01	y = 0.029162 c + 0.000750
Lead	2.25-15.0	0.9999	0.02	y = 0.133262 c + 0.021151

Y = response ratio; c = concentration of metal element (ppb)

Table VI: Precision reports for ICP-MS approach

Metal element	Spiked (ppm)	Quantified (ppm)*	Recovered (%)*	RSV (%)**
Lithium	75.00	78.292	103.98	0.949
Vanadium	3.00	3.100	102.91	0.480
Chromium	330.00	344.687	104.50	0.395
Manganese	25.00	26.113	104.04	0.450
Iron	1000.00	1033.984	103.00	0.401
Cobalt	1.50	1.548	102.80	0.347
Nickel	6.00	6.175	102.52	0.325
Copper	90.00	93.928	103.96	0.485
Arsenic	4.50	4.643	102.77	0.522
Molybdenum	450.00	469.560	103.94	0.437
Cadmium	0.60	0.612	101.50	0.694
Antimony	27.00	26.668	98.39	0.515
Mercury	0.90	0.892	98.70	0.632
Lead	1.50	1.511	100.29	0.351

*Average of six quantified/recovered values

**Relative standard variation for six quantified/recovered values

metal element were calculated (Table V). The values of percent Y intercept and correlation coefficient for each metal element were in between – 1.405898 to + 0.618607 and greater than 0.99, respectively, suggesting the better linearity of the ICP-MS system for the study of the chosen 14 metal elements.

Precision

Precision was executed with test ofloxacin solution (0.005 g mL^{-1}) spiked with 14 metal elements at their individual specification value level. Precision was accomplished by injecting the spiked test ofloxacin solution 6 times and analysed via the suggested conditions described in "ICP-MS and microwave digester conditions to evaluate the selected 14 metal elements" section. The percentiles of recovery and relative standard variation of recovery values for the 14 metal elements spiked were measured (Table VI). The percent relative standard variation of recovery values for 14 chosen metal elements were between 0.15 % to 2.12 %, suggesting the better preciseness of the ICP-MS approach for the study of the chosen 14 metal elements.

Accuracy

Accuracy was checked by a recovery experiment using a standard add-on methodology. Accuracy was executed with a test ofloxacin solution (0.005 g mL^{-1}) spiked with 14 metal elements at the QTL level, 50 %, 100 % and 200 % levels of their individual specification values. Each specification level solution was infused 3 times and analysed via the recommended conditions designated in "ICP-MS and microwave digester conditions to evaluate the selected 14 metal elements" section. The percentiles of recoveries of 14 metal elements spiked at all specification levels were measured (Table VII). The percent recovery values for 14 chosen metal elements were between 96.40 % to 107.09 %, suggesting the better accurateness of the ICP-MS approach for the investigation of the chosen 14 metal elements.

Robustness

Robustness of the ICP-MS approach was accomplished by small variations in digestion conditions at specification

Table VII: Accuracy reports for ICP-MS approach

Metal element	QTL level		50% level	
	Spiked (ppm)	Recovered (%)*	Spiked (ppm)	Recovered (%)*
Lithium	22.50	103.97	37.50	103.08
Vanadium	0.90	103.24	1.50	102.47
Chromium	99.00	107.09	165.00	106.05
Manganese	7.50	102.82	12.50	102.69
Iron	300.00	103.73	500.00	103.69
Cobalt	0.45	104.01	0.75	103.48
Nickel	1.80	103.14	3.00	102.04
Copper	27.00	106.49	45.00	105.02
Arsenic	1.35	102.76	2.25	101.17
Molybdenum	135.00	104.59	225.00	104.20
Cadmium	0.18	102.63	0.30	100.44
Antimony	8.10	96.72	13.50	96.40
Mercury	0.27	98.69	0.45	99.18
Lead	0.45	99.82	0.75	100.63
Metal element	100% level		200% level	
	Spiked (ppm)	Recovered (%)*	Spiked (ppm)	Recovered (%)*
Lithium	75.00	102.63	150.00	105.05
Vanadium	3.00	101.42	6.00	102.45
Chromium	330.00	102.96	660.00	103.45
Manganese	25.00	102.24	50.00	102.34
Iron	1000.00	101.61	2000.00	103.15
Cobalt	1.50	101.06	3.00	102.75
Nickel	6.00	100.84	12.00	102.18
Copper	90.00	102.55	180.00	103.53
Arsenic	4.50	101.90	9.00	101.40
Molybdenum	450.00	102.87	900.00	104.16
Cadmium	0.60	99.00	1.20	100.13
Antimony	27.00	96.90	54.00	96.61
Mercury	0.90	96.87	1.80	100.01
Lead	1.50	98.16	3.00	100.76

*Average of six recovered values

Table VIII: Robustness reports for ICP-MS approach

Metal element	Spiked (ppm)	Conditions applied			RSV (%)**
		16.5 % V/V HNO$_3$ + 1.1 % V/V HCl	15 % V/V HNO$_3$ + 1.0 % V/V HCl	13.5 % V/V HNO$_3$ + 0.9 % V/V HCl	
		Recovered (%)*	Recovered (%)*	Recovered (%)*	
Lithium	75.00	104.27	102.63	104.43	1.67
Vanadium	3.00	101.89	101.42	101.72	1.09
Chromium	330.00	103.52	102.96	103.17	1.12
Manganese	25.00	103.82	102.24	102.68	1.31
Iron	1000.00	102.33	101.61	101.97	1.09
Cobalt	1.50	101.71	101.06	101.31	1.07
Nickel	6.00	101.90	100.84	100.94	1.35
Copper	90.00	103.22	102.55	102.50	1.30
Arsenic	4.50	103.41	101.90	102.53	1.35
Molybdenum	450.00	103.63	102.87	103.73	1.19
Cadmium	0.60	99.45	99.00	99.57	1.19
Antimony	27.00	101.30	96.90	99.22	2.10
Mercury	0.90	97.28	96.87	97.09	1.30
Lead	1.50	101.15	98.16	100.69	1.76

Average of six recovered values

**Relative standard variation for eighteen recovered values

value concentration level by purposely changing the percentage of nitric acid (±1.5 %) and hydrochloric acid (±0.1 %). Robustness was executed with a test ofloxacin solution (0.005 g mL^{-1}) spiked with 14 metal elements at their individual specification values. The spiked test ofloxacin solution was analysed with altered conditions and also with optimized ICP-MS conditions. The percentiles of recoveries of 14 metal elements spiked and relative standard variation of percentile recoveries were measured (Table VIII). The percent relative standard variation values were between 1.07 % to 2.10 %, suggesting the better robustness of the ICP-MS approach for the investigation of 14 metal elements selected.

Ruggedness

Robustness was executed with a test ofloxacin solution (0.005 g mL^{-1}) spiked with 14 metal elements at their individual specification values. The spiked test ofloxacin solution was analysed with two analysts on two days with optimized ICP-MS conditions (see section - ICP-MS and microwave digester conditions to evaluate the selected 14 metal elements). Recovery percentiles of 14 spiked metal elements and relative standard variance of percentile recoveries have been gauged (Table IX). For the 14 metal elements chosen, the percent relative standard variance values varied from 0.54 % to 2.38 %, showing the sounder robustness of the ICP-MS strategy.

Table IX: Ruggedness reports for ICP-MS approach

Metal element	Spiked (ppm)	Day 1 and analyst 1 Recovered (%)*	Day 2 and analyst 2 Recovered (%)*	RSV (%)**
Lithium	75.00	98.99	102.63	2.13
Vanadium	3.00	101.37	101.42	1.13
Chromium	330.00	102.74	102.96	1.19
Manganese	25.00	103.10	102.24	1.40
Iron	1000.00	101.85	101.61	1.13
Cobalt	1.50	101.09	101.06	1.59
Nickel	6.00	101.23	100.84	1.33
Copper	90.00	101.90	102.55	1.43
Arsenic	4.50	101.15	101.90	0.54
Molybdenum	450.00	101.31	102.87	1.36
Cadmium	0.60	102.31	99.00	2.23
Antimony	27.00	99.29	96.90	1.78
Mercury	0.90	100.64	96.87	2.38
Lead	1.50	101.40	98.16	2.05

*Average of six recovered value
**Relative standard variation for twelve recovered values

Application of ICP-MS strategy for parenteral ofloxacin batch analysis

Six batch samples (OFCI304002, OFCI405012, OFCI405015, OFCI506008, OFCI607009, OFCI607010) of parenteral ofloxacin were analysed for 14 chosen metal elements by the proposed ICP-MS strategy. In all parenteral ofloxacin batch samples, the contents of lithium, vanadium, chromium, manganese, iron, cobalt, nickel, copper, arsenic, molybdenum, cadmium, antimony, mercury and lead were noticed to lower the detection limits.

CONCLUSION

Based on the reports of the current study, it was concluded that lithium, vanadium, chromium, manganese, iron, cobalt, nickel, copper, arsenic, molybdenum, cadmium, antimony, mercury and lead content determination by ICP-MS methodology in parenteral ofloxacin can be used for the release testing of ofloxacin.

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