

PURPOSE

Pharmaceutical laboratories rely heavily on monographs from the United States Pharmacopeia and National Formulary (USP-NF) to build their analytical methods. USP has embarked on a global initiative to modernize monographs with selective and sensitive methodologies to replace outdated wet chemistry methods. In the current monograph for POTASSIUM BICARBONATE AND POTASSIUM CHLORIDE EFFERVESCENT TABLET FOR ORAL SUSPENSION, identification is performed by a wet chemistry method, and assay is determined by Atomic Absorption Spectroscopy (AAS). We propose a selective and sensitive ion chromatography (IC) method for the potassium assay drug product, which can also be used for the identification application.

METHOD

Ion chromatography (IC) is suitable for separation and quantification of mono- and divalent cations and many aliphatic amines in pharmaceutical matrices. Typically, a non-suppressed conductivity detection that resembles a standard HPLC flow path is the preferred method for cation species analysis. Key advantages of non-suppressed conductivity detection are:

- Linear calibration curve over a wide range
- Organic solvents as part of eluent composition
- No metal hydroxide formation
- Economical

In this case, a cation exchange column, Metrosep C6-150/4.0mm with L76 packing and 4 mmol/L nitric acid as the eluent and a flow rate of 0.9 mL/min, was used. We transferred and dissolved approximately 50 g of finely powdered Potassium 25 mEq tablets to a 2000 mL volumetric flask (equivalent to 10 tablets' weight), added 200 mL of DI water, swirled until effervescence ceased, diluted to volume with DI water, and mixed well. The method is validated according to USP General Chapter <1225> VALIDATION OF COMPENDIAL METHODS

RESULT

Optimized chromatographic conditions offered the best selectivity for potassium. Specificity was checked with diluent, resolution solution, standard solution, and sample solution to ensure no interference or co-elution with the potassium peak (Figure. 1). The linearity of potassium was investigated over the concentration range from 3.75 mg/L to 22.5 mg/L of potassium covering 25% to 150% of the expected potassium concentration. An overlay of these chromatograms is shown in Figure 2. The correlation coefficient was found to be 0.9999 and the calculated Y-intercept bias was 0.5% of the 100% linearity level response (figure. 3). Method validation elements of specificity, linearity, system suitability, solution stability, accuracy and precision, and intermediate precision and accuracy were investigated. Validation results met the acceptance criteria and are summarized in Table 1. The data demonstrated that the assay procedure can be used for the ID of potassium in potassium bicarbonate and potassium chloride effervescent tablet for oral suspension.

Determination of Potassium in Potassium bicarbonate and potassium chloride effervescent tablets for oral suspension			
Parameter	USP Requirement	Metrohm Procedure	Status
Column (L76)	NA	Metrosep C6-150/4.0, 4mm x 150mm & Metrosep C6 Guard/4.0	✓
Eluent	NA	4.0 mmol/L Nitric acid	✓
Flow	NA	0.9 mL/min	✓
Detection	NA	Non-suppressed conductivity	✓
Injection Volume	NA	20 µL	✓
Injection Temperature	NA	30 °C	✓
Working Standard Concentration	NA	13.5 mg/L Potassium Standard	✓
Sample Concentration	NA	13.5 mg/L Potassium	✓
Specificity			
Blank	No interference with Potassium peak	No interference with Potassium peak	✓
Resolution	Resolution of the nearest peak from potassium in NLT 2.0 for Resolution Standard	Resolution 1.3/7 Sample 1-3/8	✓
Interference/Co-elution	Resolution of the nearest peak from potassium in NLT 2.0 for Resolution Standard & Sample Solution	Resolution Standard 4.1/7 Sample 1-3/8	✓
System Suitability			
Resolution	Resolution between peaks in NLT 2.0 for Resolution Standard	Resolution Standard 4.1/7 Sample 1-3/8	✓
Retention Time	Retention time of peak in NLT 0.5% of the retention time	Retention Standard 9.3/10 Sample 1-3/8	✓
Linearity			
Linearity	Correlation Coefficient (R) in NLT 0.999	0.9999	✓
Y-intercept	Y-intercept in NLT 0.5% of the 100% response	0.5%	✓
Repeatability			
Repeatability - retention	Retention time of peak in NLT 0.2% of the retention time	The average retention time was 9.3/10 min	✓
Repeatability - response	Response of peak in NLT 0.2% of the response	The average response was 13.5/13.5 µS/cm	✓
Accuracy			
Accuracy	Accuracy of the assay results in NLT 95% of the expected value	The average assay results were 100.0%	✓
Intermediate Precision			
Intermediate Precision	Intermediate precision in NLT 0.5% of the response	Intermediate precision was 0.5%	✓
System Suitability			
Resolution	Resolution between peaks in NLT 2.0 for Resolution Standard	Resolution Standard 4.1/7 Sample 1-3/8	✓
Retention Time	Retention time of peak in NLT 0.5% of the retention time	Retention Standard 9.3/10 Sample 1-3/8	✓
Linearity			
Linearity	Correlation Coefficient (R) in NLT 0.999	0.9999	✓
Y-intercept	Y-intercept in NLT 0.5% of the 100% response	0.5%	✓
Repeatability			
Repeatability - retention	Retention time of peak in NLT 0.2% of the retention time	The average retention time was 9.3/10 min	✓
Repeatability - response	Response of peak in NLT 0.2% of the response	The average response was 13.5/13.5 µS/cm	✓
Accuracy			
Accuracy	Accuracy of the assay results in NLT 95% of the expected value	The average assay results were 100.0%	✓

Table 1: Validation Summary

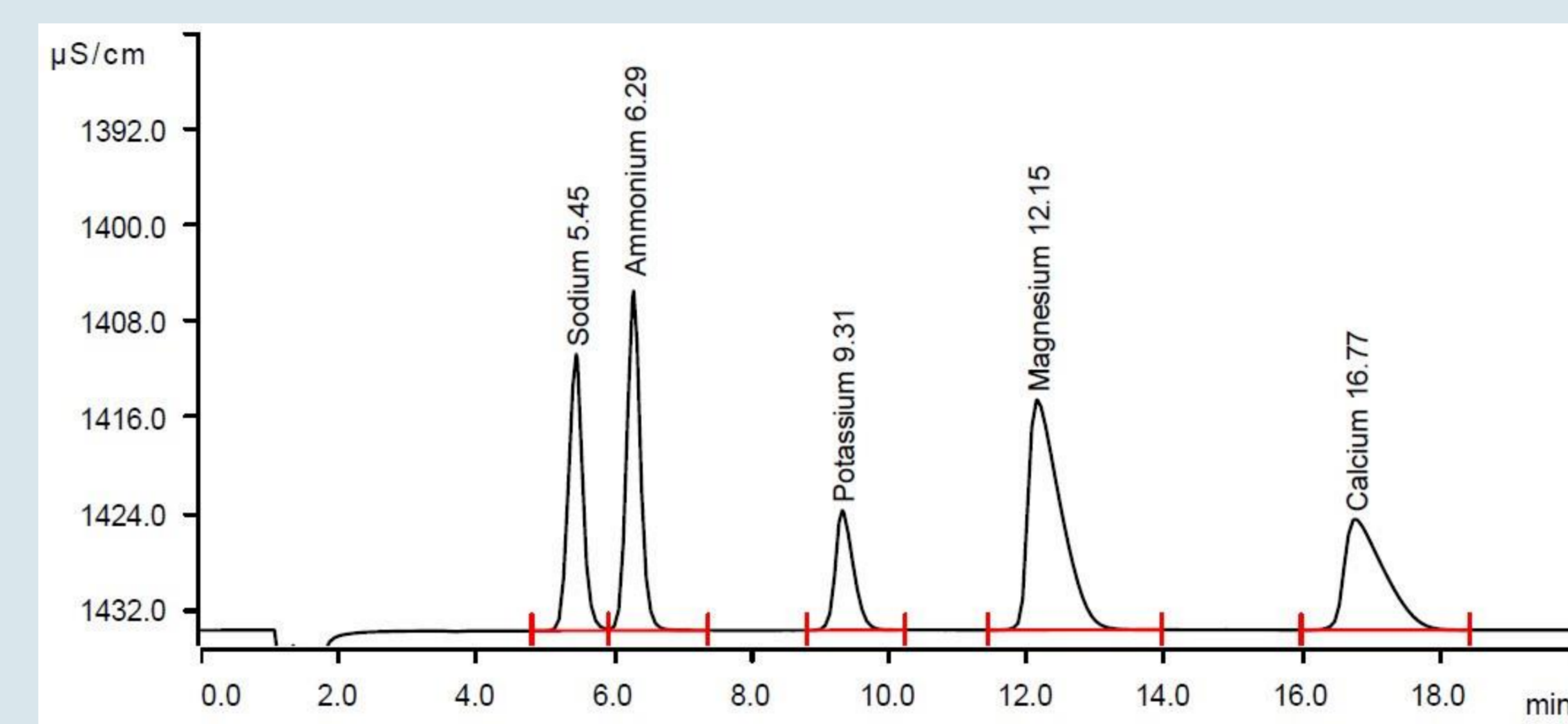
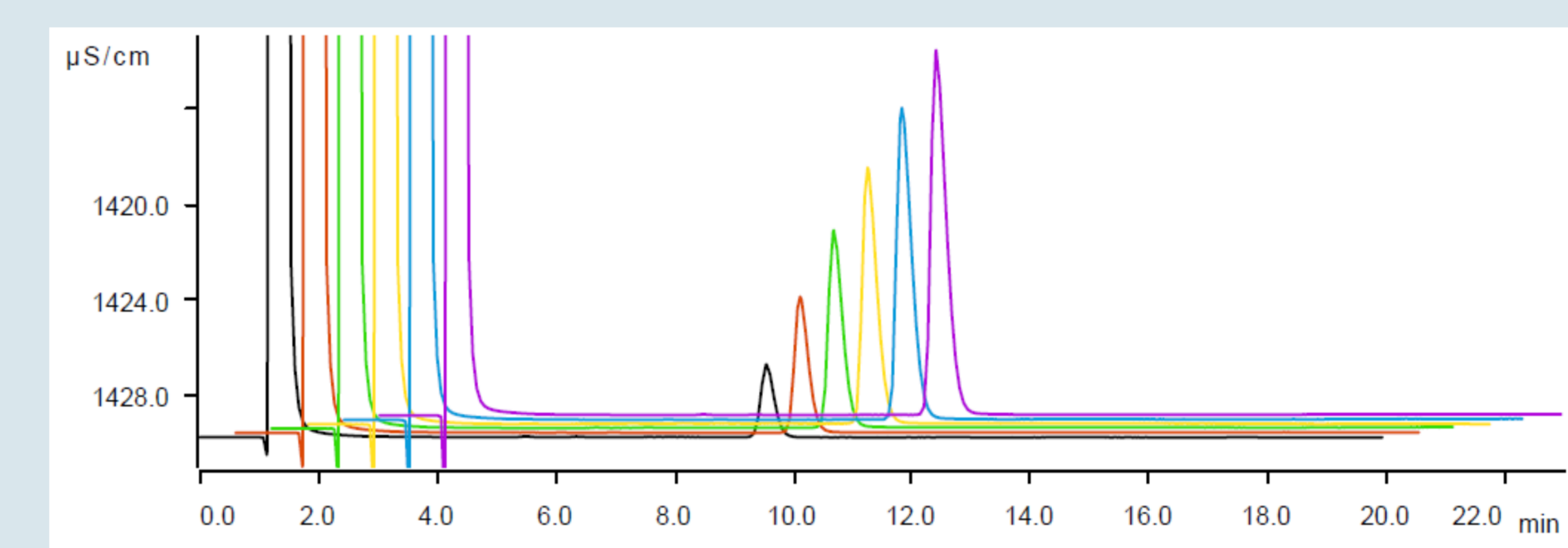


Fig 1: Specificity: Resolution solution



Ident	Sample type	Volume	Legend	Display	Analysis
1	3.75 mg/L potassium standard	20.0	Black	on	Cations
2	7.5 mg/L potassium standard	20.0	Red	on	Cations
3	11.25 mg/L potassium standard	20.0	Green	on	Cations
4	15.0 mg/L potassium standard	20.0	Yellow	on	Cations
5	18.75 mg/L potassium standard	20.0	Blue	on	Cations
6	22.5 mg/L potassium standard	20.0	Purple	on	Cations

Fig 2: Linearity: Chromatograms overlay

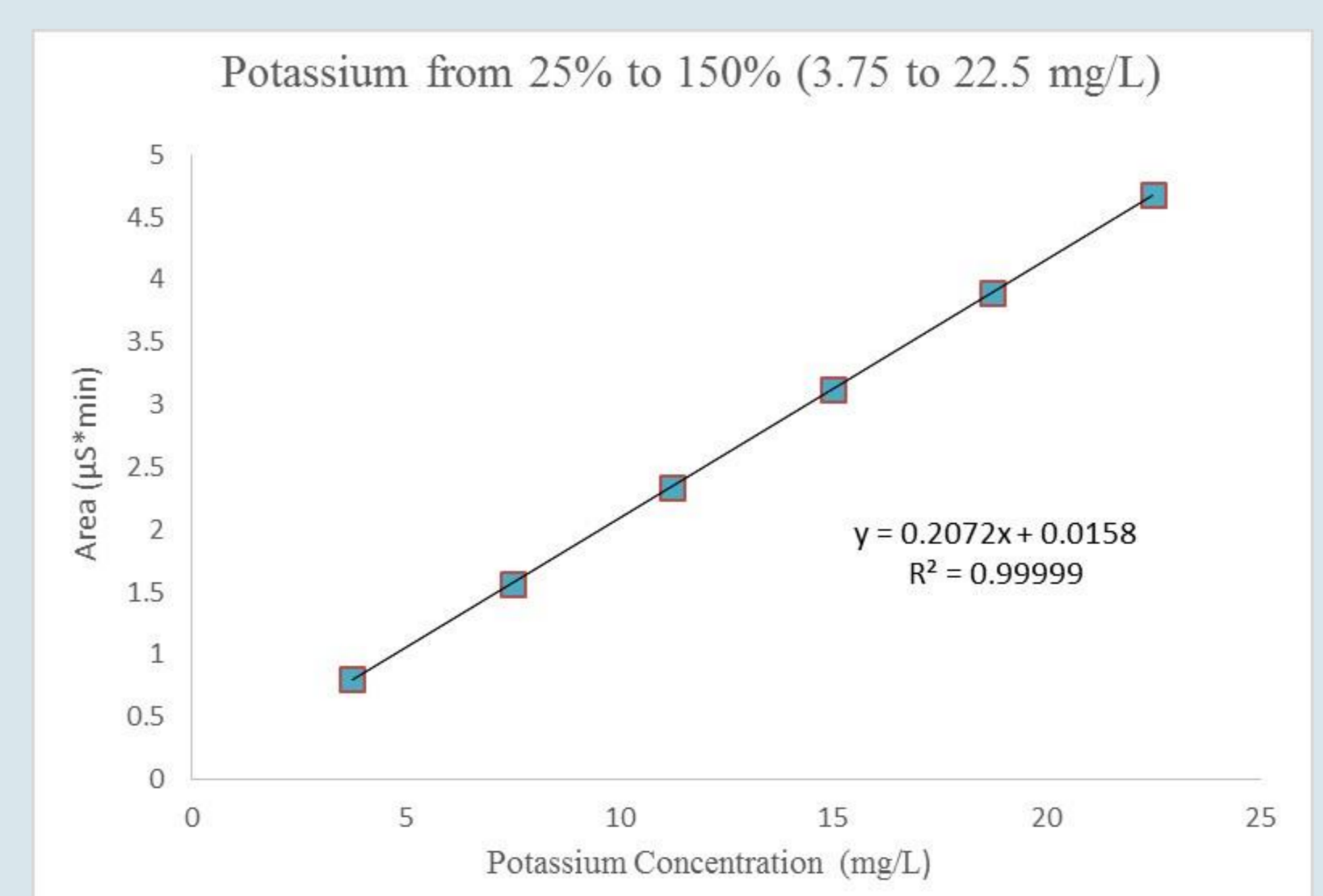


Fig 3: Linearity for Potassium

- Metrohm 940 Professional IC Vario
- Detection: Direct Conductivity Detection
- Column Temperature: 30° C
- Flow Rate: 0.9 mL/min
- Injection Volume: 20 µL
- Run Time: 20.0 min
- Eluent : 4 mmol/L nitric acid - Isocratic separation
- Metrosep C 6 - 150/4.0, 4mm x 150 mm, packing L76
- Metrosep C 6 Guard/4.0



Fig 3: Ion Chromatography instrument used for OTC Assay

CONCLUSION

We successfully developed and validated a single IC procedure for potassium assay and identification in potassium bicarbonate and potassium chloride for effervescent oral suspension. The optimized chromatographic conditions can be used for other cationic impurities, such as magnesium, calcium, sodium, and ammonium in potassium bicarbonate and potassium chloride for effervescent oral suspension. A single chromatographic method for assay and identification simplifies the overall QA/QC workflow.

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