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Potassium Assay in OTC Drug Products by Ion Chromatography Hari Narayanan¹, Uvaraj Mani², Michael Chang³, Leonel M Santos³ Metrohm USA Inc¹, Metrohm India Limited², USP³



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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 USP has embarked on a global initiative to modernize monographs with selective and sensitive methodologies to replace outdated wet chemistry methods.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. Omm 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 Table1. 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.

Flow Detection Injection Volume Run time			/-
njection Volume	NA NA	0.9 mL/min Non-Suppressed conductivity	
-	NA NA	20 μL	
	NA NA	20 minutes	1
olumn Temperature	NA	30°C	V.
/orking Standard concentration	NA	15.0 mg/L Potassium standard	
ample concentration pecificity	NA	15.0 mg/L Potassium	
lank	No interference with Potassium peak	No interference with Potassium	1
ailing	Potassium peak Tailing is NMT 2.0 for Standard & Sample Solution	Standard = 1.37 / Sample = 1.38	
sterference/Co-elution	Resolution of the nearest peak from potassium is NLT 2.0 for Resolution Standard	Resolution Standard = 4.17	1
ritical Pair	Resolution between potassium and adjacent impurity should be NLT 1.5 for sample solution	Sample = 11.3	
ystem Suitability			
i.0 mg/L Potassium standard	Six replicate injections RSD is NMT 0.5%	Potassium RSD = 0.15%	
lution Stability			
.0 mg/L Potassium standard & sample solutions	The change in peak area is NMT 2.0% from the initial time point - (μS/cm)×min	Potassium peak area change is 0.8%	1
nearity			
klinearity solutions range from 25 50% (3.75, 7.5, 11.25, 15.0, 18.75	Correlation Coefficient (R) is NLT 0.999 Y-Intercept	0.9999	1
22.5 mg/L)	Y-Intercept bias: ±2.0% of 100% linearity level response	0.51%	
peatability			
peatability solutions analyze against Standard solution	The average Assay result should be NLT 90.0% and NMT 110.0% of the label claim	The average Assay results was 104.8%	
x replicate injections of standard solution)			
	The RSD of the six Assay results should be NMT 1.0%.	The RSD of 6 Assay results was 0.16%	
curacy			
curacy solutions (Sample solutions are spiked with standard solution at 10%, 20%, 30% of nominal	The average recovery result at each spiked level should be within $100\pm3\%$.	Average recovery for potassium Assay was 97.9% 98.7% and 98.1%	,
ncentration (i.e. 110%, 120% and 130%)). Prepare in triplicate at each level and analyze against average response six replicate injections of Standard solution		at 110%, 120% and 130%	
		respectively.	
	Intermediate Precision		
ond Analyst	Column: Metrosep C 6 - 150/4.0; Sl.No: 0033.2363	Date: 17/05/2018 to 18/05/2018	V
ecificity			
ank	No interference with Potassium peak	No interference with Potassium	1
iling	Potassium peak Tailing is NMT 2.0 for Standard & Sample Solution	Standard = 1.44 / Sample = 1.46	V
terference/Co-elution	Resolution of the nearest peak from potassium is NLT 2.0 for Resolution Standard & Sample Solution	Resolution Standard = 4.82 / Sample = 11.01	1
stem Suitability			
.0 mg/L Potassium standard	Six replicate injections RSD is NMT 0.5%	Potassium RSD = 0.28%	1
epeatability			
peatability solutions analyzed against Standard solution (six replicate injections of standard solution) by a different	The average result should be NLT 90.0% and NMT 110.0% of the label claim	The average Assay results was 105.0%	1/
alyst on a different day and using a different batch of column			
	The RSD of the six Assay results should be NMT 1.0%	The RSD of 6 Assay results was 0.22%	
	The two average results for first and second scientists do not differ by more than 2.0%.	The difference was 0.19%	1/
	um in Determine bisochanata and naturaism alla ida (f		
Determination of Potassi	um in Potassium bicarbonate and potassium chloride effervescent tablets for oral suspension		
	HCD Descriptions and	Makesher Decorders	Chatan
arameters	USP Requirement	Metrohm Procedure	Status
llumn (L76)	NA .	Metrosep C 6 - 150/4.0 (L76) & Metrosep C 6 Guard/4.0	🗸
uent	NA .	4.0 mmol/L Nitricacid	1
ow	NA NA	0.9 mL/min	1
etection	NA	Non-Suppressed conductivity	V
jection Volume	NA	20 μL	V
untime	NA	20 minutes	- 1
olumn Temperature orking Standard concentration	NA NA	30°C 15.0 mg/L Potassium standard	
mple concentration	NA .	15.0 mg/L Potassium	- '
ecificity			
	No interference with Potassium peak	No interference with Potassium	
ank	Potassium peak Tailing is NMT 2.0 for Standard & Sample Solution	Standard = 1.37 / Sample = 1.38	
iling	Resolution of the nearest peak from potassium is NLT 2.0 for Resolution Standard	Resolution Standard = 4.17	
ling erference/Co-elution	Resolution of the nearest peak from potassium is NLT 2.0 for Resolution Standard Resolution between potassium and adjacent impurity should be NLT 1.5 for sample solution	Resolution Standard = 4.17 Sample = 11.3	1
ling erference/Co-elution tical Pair			1
iling verference/Co-elution tical Pair stem Suitability			1
ank iiling terference/Co-elution itical Pair //stem Suitability .0 mg/L Potassium standard olution Stability	Resolution between potassium and adjacent impurity should be NLT 1.5 for sample solution	Sample = 11.3	1
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iling rerference/Co-elution tical Pair stem Suitability .0 mg/L Potassium standard lution Stability .0 mg/L Potassium standard & sample solutions	Resolution between potassium and adjacent impurity should be NLT 1.5 for sample solution Six replicate injections RSD is NMT 0.5% The change in peak area is NMT 2.0% from the initial time point - (µS/cm)×min	Potassium RSD = 0.15% Potassium peak area change is 0.8%	
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Table 1: Validation Summary

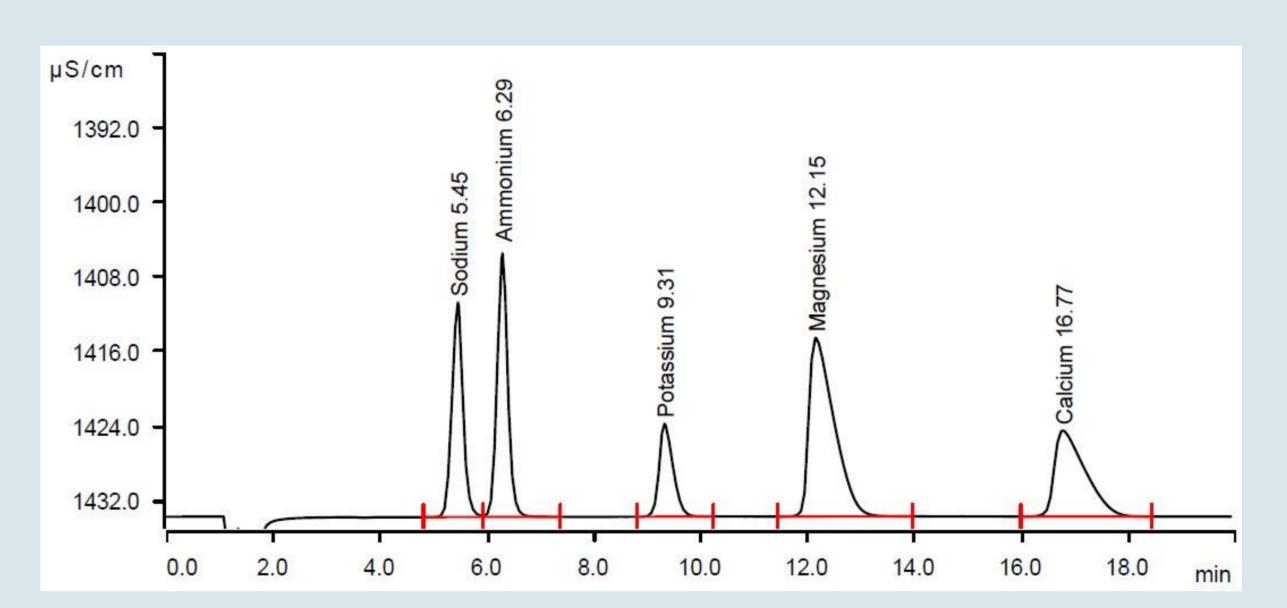


Fig 1: Specificity: Resolution solution

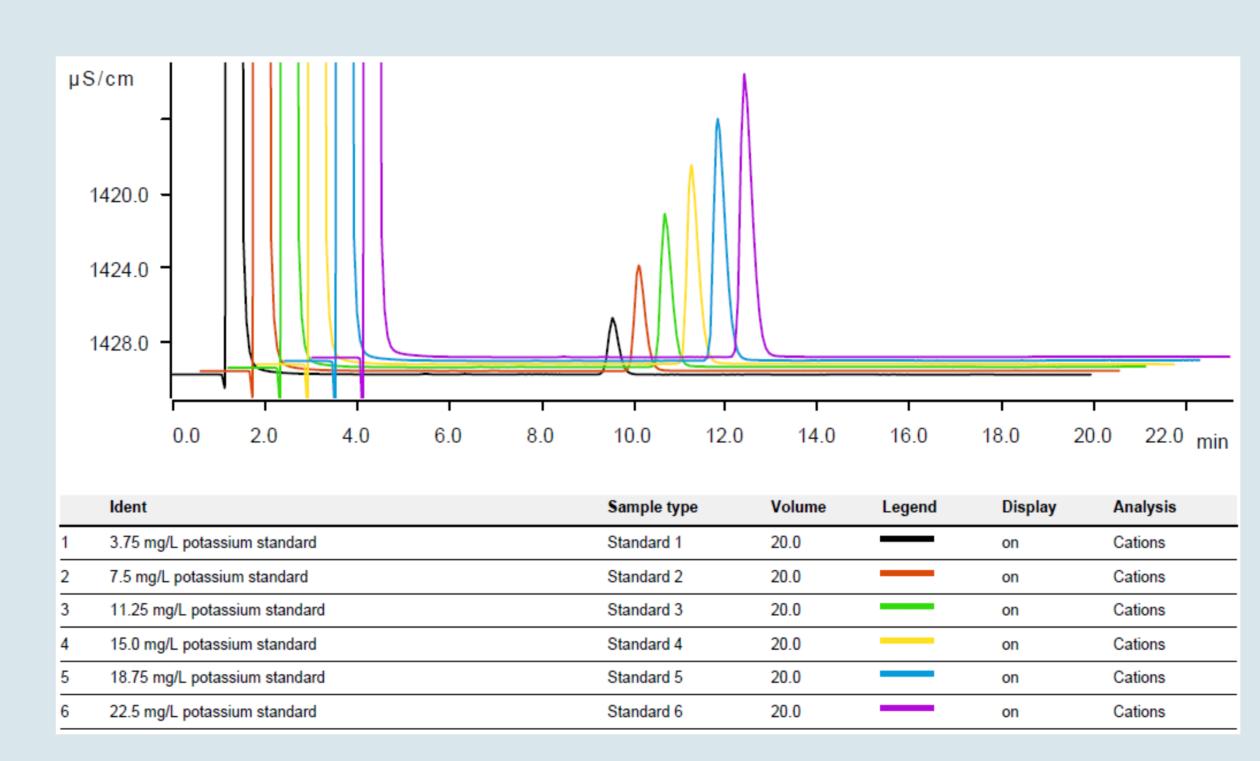


Fig 2: Linearity: Chromatograms overlay

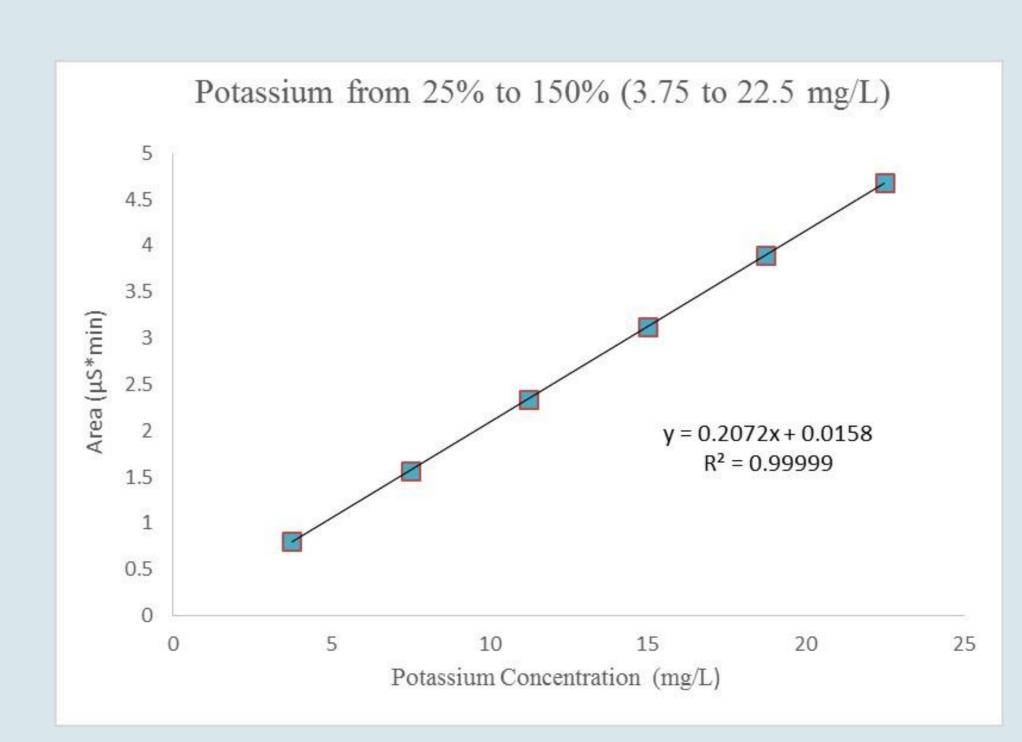


Fig 3: Linearity for Potassium

- 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 × 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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