Application Note AN-C-183

Potassium in potassium bicarbonate effervescent tablets for oral suspension as per USP

Method validation according to the U.S. Pharmacopoeia

Potassium bicarbonate effervescent tablets are used to prevent low levels of potassium in the blood [1]. Pharmaceutical manufacturers and laboratories are obliged to use the monographs from the United States Pharmacopeia (USP) and the National Formulary (NF) to test drugs and formulations.

The USP has embarked on a global initiative to modernize many of their existing monographs. As an alternative to atomic absorption spectroscopy (AAS), ion chromatography (IC) with non-suppressed conductivity detection has been approved by the USP as a validated method to quantify the potassium content in potassium bicarbonate effervescent tablets for oral solution [2].

The Metrosep C 6 - 150/4.0 (L76) column provides the required separation of potassium. All acceptance criteria from the USP monograph «Potassium Bicarbonate Effervescent Tablets for Oral Solution» are fulfilled. The present IC method has been validated according to USP General Chapter <621> Chromatography [3].

SAMPLE AND SAMPLE PREPARATION

Potassium bicarbonate effervescent tablets for oral solution (Effer-K 25 mEq, potassium 978 mg, unflavored) from two different lots were evaluated in this application study.

Sample stock solutions with nominally 4890 mg/L potassium were prepared from at least 20 finely powdered tablets. A small amount (47.2 mg) of the resulting powder was transferred to a 2000 mL volumetric flask. 200 mL of ultrapure water was added, and the flask was swirled until effervescence ceased. Then the solution was diluted to volume with ultrapure water and mixed well.

Sample solutions with nominally 15.0 mg/L potassium were prepared by transferring 1.533 mL of the sample stock solution to a 500 mL volumetric flask, then diluted to volume with ultrapure water and mixed well.

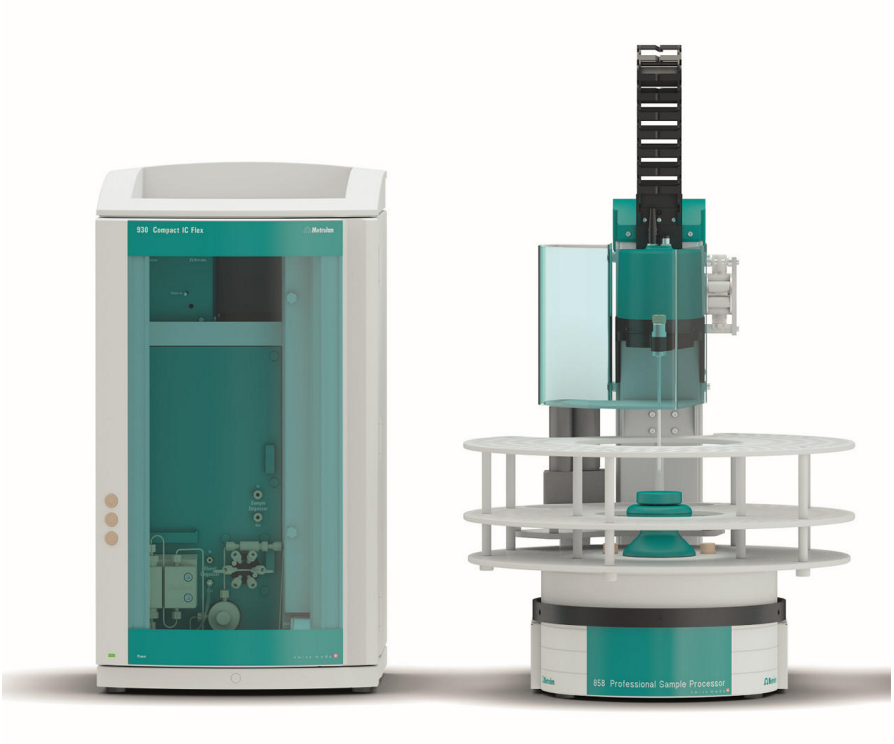

Figure 1. Instrumental setup including a 930 Compact IC Flex Oven/Deg and an 858 Professional Sample Processor.

EXPERIMENTAL

The working standard solution of 15 µg/mL potassium was prepared from a certified 1000 µg/mL potassium USP reference standard.

Samples and standard solutions were injected directly into the IC using an 858 Professional Sample Processor (Figure 1). Potassium was separated from all other cations using a Metrosep C 6 - 150/4.0 column (L76) and the signal was recorded with a conductivity detector.

The calibration was performed using a single standard at 15 µg/mL that was injected six times. The samples were analyzed in duplicate.

Table 1. IC method parameters as per USP monograph «Potassium Bicarbonate Effervescent Tablets for Oral Solution» [2].

Column with L76 packing	Metrosep C 6 - 150/4.0
Eluent	4 mmol/L nitric acid
Flow rate	0.9 mL/min
Temperature	30 °C
Injection volume	20 µL
Detection	Direct conductivity

RESULTS

The IC assay for potassium content was validated according to USP Monograph «Potassium Bicarbonate Effervescent Tablets for Oral Solution» [2]. The accuracy of the potassium determination was calculated as 100% (Figure 2).

All acceptance criteria were fulfilled, e.g., asymmetry (tailing factors) for the potassium peak was <2, or the relative standard deviation (%RSD) of standard solutions was <0.5% (n=6) (Table 2).

Table 2. Required acceptance criteria as per USP monograph «Potassium Bicarbonate Effervescent Tablets for Oral Solution» [2].

Parameter	Actual	USP requirement	Status
% RSD standard solution (n=6)	0.05	NMT 0.5	Pass
Tailing factor	1.5	NMT 2.0	Pass
Resolution	3.89	NLT 3.0	Pass
Solution stability	0.08%	NMT 1.0%	Pass
Assay recovery	100.0%	90–110%	Pass
% RSD assay (n=6)	0.15%	NMT 1.0%	Pass

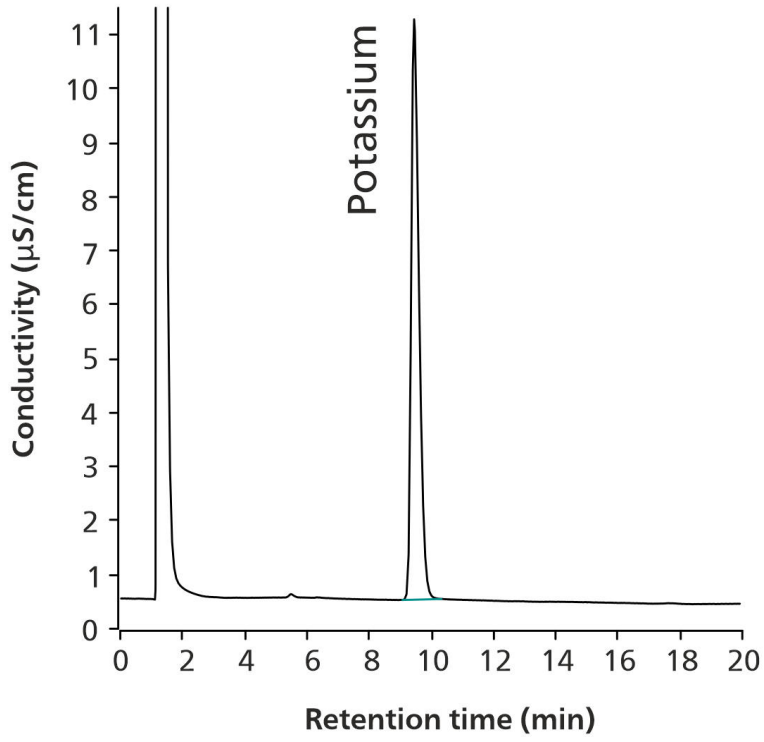

Figure 2. Chromatogram of 15.0 µg/mL potassium in sample solution (100.0% recovery of the nominal concentration).

CONCLUSION

The presented IC method for potassium in potassium bicarbonate effervescent tablets for oral solution with the Metrosep C 6 column (packing material L76) is officially included into the USP. Robustness and reliability of the method was demonstrated following the guidelines of the USP General Chapter <621> [3]. The presented setup is suitable to quantify potassium according to USP requirements.

REFERENCES

1. Kardalas, E.; Paschou, S.S.; Anagnostis, P.; et al. Hypokalemia: a clinical update. *Endocrine Connections* 2018, *7* (4), R135–R146. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5881435/
2. U.S. Pharmacopeia. USP-NF Potassium Bicarbonate Effervescent Tablets for Oral Solution. *Monograph.* https://doi.usp.org/USPNF/USPNF_M67194_02_01.html
3. <621> Chromatography. https://doi.org/10.31003/USPNF_M99380_01_01

Internal references: AW IC IN6-1888-062018

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