Application Note AN-C-184

Potassium and sodium in bicarbonates and citric acid effervescent tablets for oral solution as per USP

Method validation according to the U.S. Pharmacopoeia

Potassium and sodium bicarbonates and citric acid effervescent tablets for oral solution are used to prevent hypokalemia (low levels of potassium in blood) [1]. Pharmaceutical manufacturers and laboratories are obliged to use USP monographs to test drugs and formulations.

As an alternative to flame photometry, ion chromatography with non-suppressed conductivity detection has been approved by the USP as a validated method to quantify potassium and sodium content in potassium and sodium bicarbonates and citric acid effervescent tablets for oral solution [2].

The Metrosep C 6 - 150/4.0 column (L76) provides the required separation of sodium, ammonium, and potassium. All acceptance criteria from the USP monograph «Potassium and Sodium Bicarbonates and Citric Acid Effervescent Tablets for Oral Solution» are fulfilled [2]. The present IC method has been validated according to USP General Chapter <621> Chromatography, system suitability [3].

SAMPLE AND SAMPLE PREPARATION

Sample solutions are prepared from commercially available citric acid effervescent tablets for oral solution. Standard analyses are performed with a solution of ultrapure potassium bicarbonate. No additional sample preparation is required.

EXPERIMENTAL

A sample stock solution is prepared by adding powdered citric acid effervescent tablets for oral solution into ultrapure water. Approximately 20 citric acid effervescent tablets for oral solution are finely ground, then 27.6 g of the resulting fine powder is added to 200 mL ultrapure water in a 1000 mL volumetric flask. After effervescence ceases, the volumetric flask is filled up to the mark. This stock solution contains nominally 1343.44 mg/L potassium and 2873.38 mg/L sodium. A 1.740 mL aliquot of the sample stock solution is transferred to a 500 mL volumetric flask and diluted with ultrapure water up to the mark. This final sample solution nominally contains 4.68 µg/mL potassium and 10.0 µg/mL sodium.

The working standard solution of 4.5 µg/mL potassium chloride and 10.0 µg/mL sodium chloride is prepared from USP RS reference standards.

Samples and standard solutions are injected directly into the ion chromatograph (Figure 1) using an 858 Professional Sample Processor. Potassium is separated from all other cations using a Metrosep C 6 -150/4.0 column (L76).

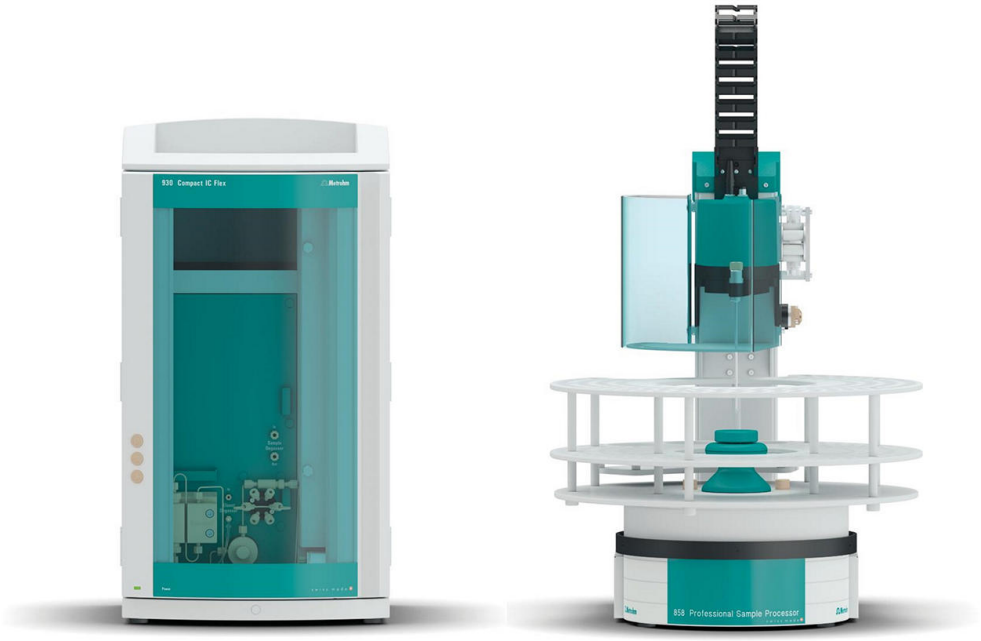

Figure 1. Instrumental setup including a 930 Compact IC Flex Oven and an 858 Professional Sample Processor.

The calibration is performed by using a 6-point linear calibration curve in the concentration ranges of 1.1–6.75 µg/mL for potassium and 2.5–15 µg/mL for sodium. The sample is then analyzed in duplicate.

Table 1. Requirements for the IC method as per USP Monograph «Potassium and Sodium Bicarbonates and Citric Acid 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 assays for potassium and sodium content were validated according to USP Monograph «Potassium and Sodium Bicarbonates and Citric Acid Effervescent Tablets for Oral Solution» [2]. The accuracy of the determinations were calculated as 101% for potassium and 106% for sodium (Table 2 and Figure 2).

Table 2. Required acceptance criteria according to USP Monograph «Potassium and Sodium Bicarbonates and Citric Acid Effervescent Tablets for Oral Solution» [2] (abbreviations: Na+, sodium; K+, potassium; NH4+, ammonium).

Parameter	Actual K^+/Na^+	USP requirement	Status
% RSD	0.27/0.08	NMT 2.0	Pass
Tailing factor	1.24/1.0	NMT 2.0	Pass
Recovery	101/106%	90–110%	Pass
Resolution Na^+ /NH_4^+	2.59	NLT 2.0	Pass

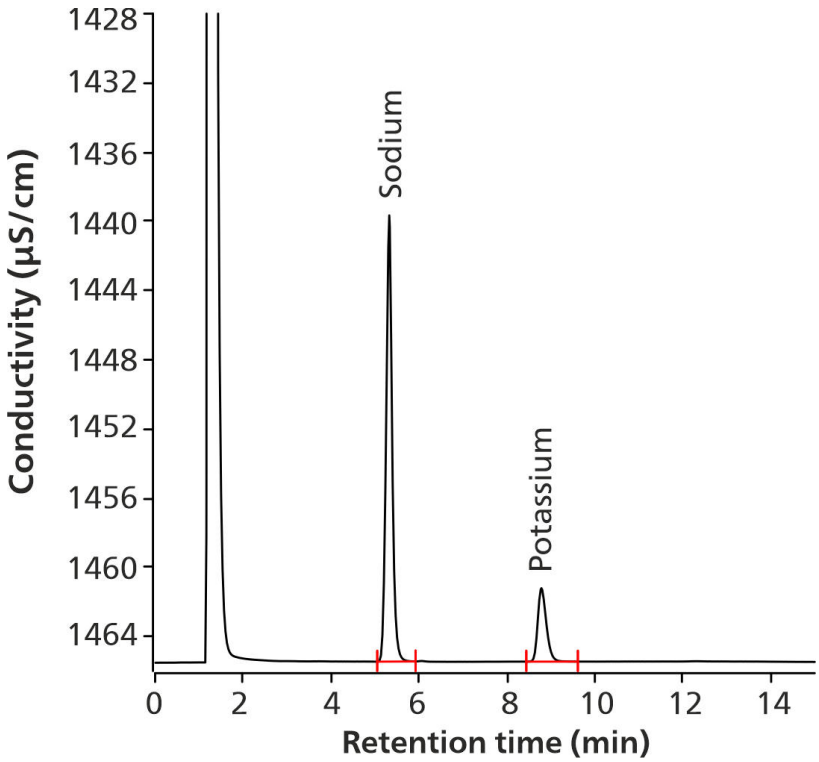

Figure 2. Chromatogram of the sample solution (101% and 106% recovery of the nominal concentration for potassium and sodium, respectively). Resolution between sodium and potassium was 11.7.

All acceptance criteria were fulfilled, e.g., correlation coefficients for potassium and sodium were 0.99996 and 0.99999, respectively, and the relative standard deviation of standard solutions was <0.3% (n = 6) (Table 2).

CONCLUSION

The presented IC method to determine potassium and sodium content in potassium and sodium bicarbonates and citric acid effervescent tablets for oral solution with the Metrosep C 6 column (packing material L76) is officially included into the USP [2]. 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 and sodium according to the USP requirements. Additional USP methods are summarized in the flyer «Bring your USP methods up to date!» [4].

REFERENCES

1. Kardalas, E.; Paschou, S. A.; Anagnostis, P.; et al. Hypokalemia: A Clinical Update. *Endocr Connect* **2018**, *7* (4), R135–R146. https://doi.org/10.1530/EC-18-0109.
2. *Potassium and Sodium Bicarbonates and Citric Acid Effervescent Tablets for Oral Solution*; Monograph; U.S. Pharmacopeia/National Formulary: Rockville, MD. https://doi.org/10.31003/USPNF_M67260_04_01.
3. *<621> Chromatography, General Chapter*; U.S. Pharmacopeia/National Formulary: Rockville, MD. https://www.uspnf.com/notices-gc-621-nitr-20220826.
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Internal reference: AW IC IN6-1889-052018

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