Application Note AN-C-185

USPに則した経口懸濁液のための炭酸水素カリウムおよび塩化カリウム発泡錠中のカリウム

Method validation according to the U.S. Pharmacopoeia

Potassium bicarbonate and potassium chloride effervescent tablets for oral solution are used to prevent hypokalemia (low levels of potassium in blood) [1]. Pharmaceutical manufacturers and laboratories must use approved quality monitoring techniques for drugs and formulations as stipulated by U.S. Pharmacopoeia (USP) monographs.

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 content in potassium bicarbonate and potassium chloride effervescent tablets for oral solution [2].

The Metrosep C 6 - 150/4.0 column provides the required separation of potassium and magnesium. All acceptance criteria from the USP monograph «Potassium Bicarbonate and Potassium Chloride 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 potassium bicarbonate and potassium chloride effervescent tablets for oral solution. Standard analyses are performed with a solution of USP Potassium Chloride RS. No additional sample preparation is required.

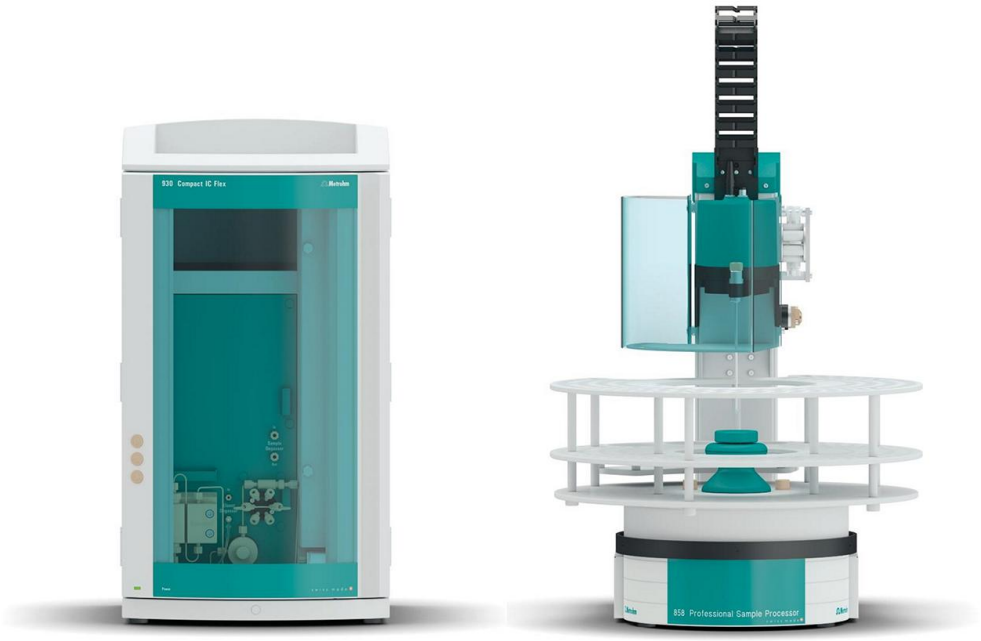

Figure 1. Instrumental setup including a 930 Compact IC Flex Oven and an 858 Professional Sample Processor.

EXPERIMENTAL

The sample stock solution is prepared through the addition of 25 g finely powdered potassium bicarbonate and potassium chloride effervescent tablets for oral solution to a 1000 mL volumetric flask. The powder is dissolved in 200 mL ultrapure water. After effervescence ceases, the volumetric flask is filled up to the mark. This stock solution contains nominally 4809.48 mg/L potassium. A 1.533 mL aliquot of this stock solution is transferred to a 500 mL volumetric flask and is filled up to the mark with ultrapure water. This final sample solution nominally contains 15.0 µg/mL potassium.

A working standard solution of 15 µg/mL potassium chloride is prepared from the respective USP reference standards.

All solutions (i.e., samples and standards) are injected directly into the ion chromatograph (Figure 1) using an 858 Professional Sample Processor. Potassium is separated from all other cations using the Metrosep C 6 - 150/4.0 column.

The calibration is performed by using a 6-point linear calibration curve in the concentration range of 3.75–22.5 µg/mL potassium. The sample is then analyzed in duplicate.

Table 1. Requirements for the IC method as per USP Monograph «Potassium Bicarbonate and Potassium Chloride 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 and Potassium Chloride Effervescent Tablets for Oral Solution» [2]. The accuracy of the potassium determination was calculated as 105% (Table 2 and Figure 2).

All acceptance criteria were fulfilled, e.g., the correlation coefficient for potassium was 0.9999, the resolution of adjacent peaks, and the relative standard deviation of the standard solutions was <0.15% (n = 6) (Table 2).

Table 2. Required acceptance criteria according to USP Monograph Potassium Bicarbonate and Potassium Chloride Effervescent Tablets for Oral Solution [2] (Abbreviations: K+, potassium; Mg2+, magnesium).

Parameter	Actual	USP requirement	Status
% RSD	0.15	NMT 1.0	Pass
Tailing factor	1.37	NMT 2.0	Pass
Recovery	104.8%	90–110%	Pass
Resolution K^+/Mg^{2+}	4.17	NLT 2.0	Pass

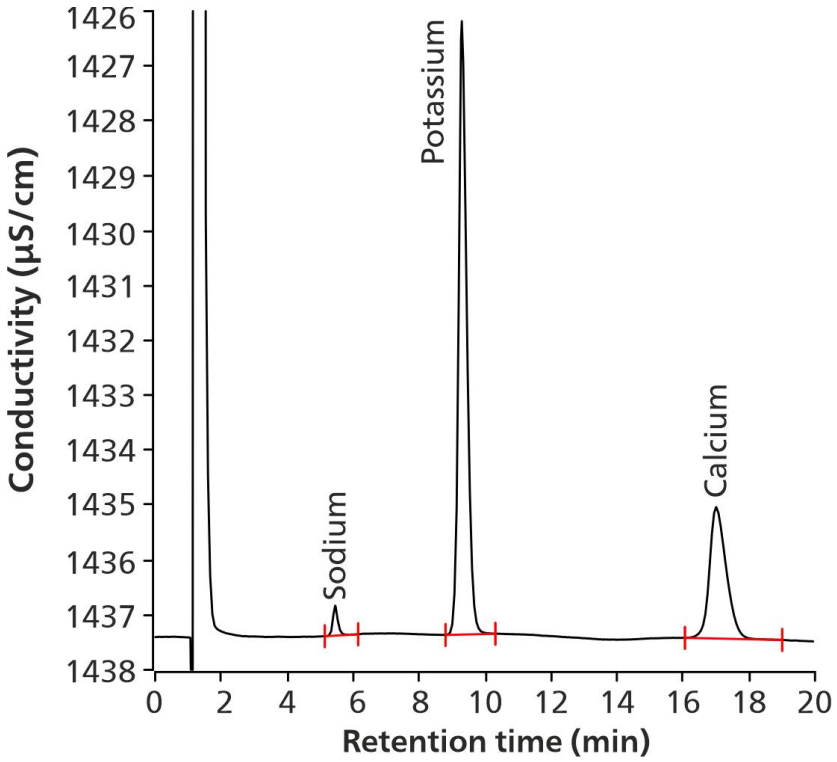

Figure 2. Chromatogram of the sample solution (105% recovery of the nominal concentration for potassium). Sodium and calcium were not quantified. The resolution was 11, for both pairs sodium/potassium and potassium/calcium.

CONCLUSION

The presented IC method for the determination of potassium content in potassium bicarbonate and potassium chloride effervescent tablets for oral solution using the Metrosep C 6 column (packing material L76) for separation 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 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 Bicarbonate and Potassium Chloride Effervescent Tablets for Oral Solution*; Monograph; U.S. Pharmacopeia/National Formulary: Rockville, MD. https://doi.org/10.31003/USPNF_M67253_02_01.
3. *<621> Chromatography, General Chapter*; U.S. Pharmacopeia/National Formulary: Rockville, MD. https://www.uspnf.com/notices-gc-621-nitr-20220826.
4. Metrohm AG. Bring Your USP Methods up to Date!, 2023. 8.000.5436EN

Internal reference: AW IC IN6-1887-052018

CONTACT

メトロームジャパン株式会社
143-0006 東京都大田区平和島6-1-1
null 東京流通センター アネックス9階
metrohm.jp@metrohm.jp

CONFIGURATION

Metrosep C 6 - 150/4.0

C 6 の材料の容量か大きいため、分離カラム Metrosep C 6 - 150/4.0 は、妥当な保持時間の場合、濃度差の大きな標準陽イオンを分離するのに最も適したソリューションてす。アンモニウム含有量の少ない飲料水は、このカラムて測定することかてきます。

Metrosep C 6 Guard/4.0

Metrosep C 6 Guard/4.0にはC 6カラムの材料か含まれており、粒子や汚れから保護します。これにより、分析の分離カラムの耐用期間か格段に長くなります。Metrosep C 6 Guard/4.0は «On Column Guard System» に則して機能し、それぞれの分離カラムにほほテットホリュームなして直接取り付けることかてきます。

930 Compact IC Flex Deg

930 コンハクト IC Flex Degは内蔵式**脱気装置**付きの**サフレッションの無い**インテリシェントコンハクトIC装置てす。この装置は任意の分離メソットおよひ検出メソットによって使用することかてきます。
典型的な使用領域:
- 電気伝導度検出器によるサフレッション無しの陰イオンもしくは陽イオンの測定
- UV/VIS検出器またはアンヘロメトリック検出器によるシンフルな使用

858 Professional Sample Processor

858 フロフェッショナルサンフルフロセッサは、500 µLから500 mLまてのサンフルを処理します。サンフルは850 フロフェッショナル IC システム のヘリスタリックホンフまたは800 トシーノ電動ヒュレットを使用することによって転送されます。