



Application Note AN-C-183

USPに則した経口懸濁液のための炭酸水素カリウム発泡錠中のカリウム

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.

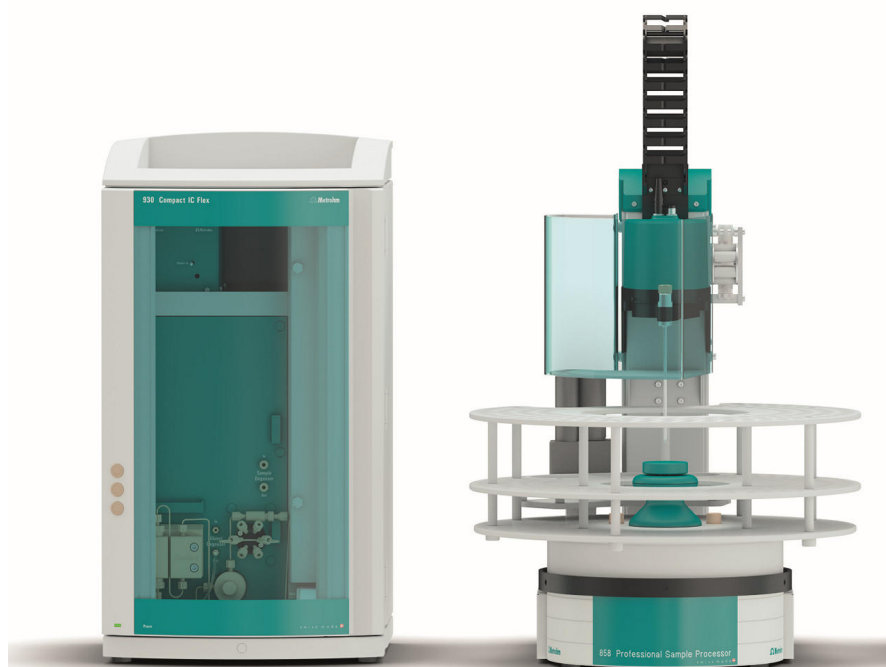


Figure 1. Instrumental setup including a 930 Compact IC Flex Oven/Deg and an 858 Professional Sample Processor.

EXPERIMENTAL

The working standard solution of 15 $\mu\text{g/mL}$ potassium was prepared from a certified 1000 $\mu\text{g/mL}$ 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 $\mu\text{g/mL}$ 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_M6719_4_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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CONFIGURATION



930 Compact IC Flex Oven/Deg

930 コンパクト IC Flex Oven/Deg はカラムオーブンと内蔵式脱気装置を備えたサプレッションの無いインテリジェントコンパクトIC装置です。この装置は任意の分離メソッドおよび検出メソッドによって使用することができます。

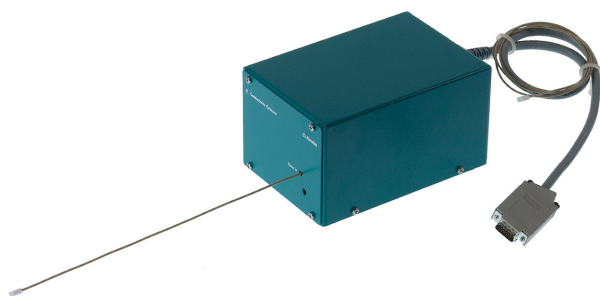
典型的な使用領域:

- 電気伝導度検出器によるサプレッション無しの陰イオンおよび陽イオンの測定
- UV/VIS検出器またはアンペロメトリック検出器によるシンプルな使用



858 Professional Sample Processor – Pump

858 プロフェッショナルサンプルプロセッサ - ポンプは、500 μ Lから500 mLまでのサンプルを処理します。サンプルは内蔵式双方向性の2チャンネルのペリスタリックポンプまたは800 ドジーノ電動ビュレットによって転送されます。



IC Conductivity Detector

インテリジェントIC装置のためのコンパクトかつインテリジェントな高出力電気伝導度検出器。優れた温度安定性、保護された検出器ブロック内の総合的な信号処理、最新版のDSP (Digital Signal Processing) が高精度の測定を保証します。稼動範囲がダイナミックなので測定範囲の変更は(自動のものも含めて)必要ありません。