Application Note AN-C-197

柠檬酸钾和柠檬酸口服液中的钾测定

Method validation according to the U.S. Pharmacopeia (USP)

Potassium citrate and citric acid oral solutions are systemic alkalizers beneficial for health conditions where long-term maintenance of alkaline urine is desirable, and administration of sodium salts is contraindicated [1,2]. To comply with the strict quality standards for pharmaceutical products, validated methods such as those from the United States Pharmacopeia – National Formulary (USP-NF) are mandatory for manufacturers and laboratories. As part of the USP modernization initiative, the potassium monograph was updated, replacing the previous identification procedure of titration with ion chromatographic (IC) analysis [3]. For quality control, the USP specifies ion chromatography using a cation-exchange column with L76 column material and non-suppressed conductivity detection to quantify the potassium content [3].

The present IC method uses the Metrosep C 6 - 150/4.0 column (L76) to separate potassium from other potentially present ions. This method has been validated according to USP General Chapters <621> Chromatography [4] and <1225> Validation of Compendial Procedures [5]. All acceptance criteria for the potassium assay of the USP monograph «Potassium Citrate and Citric Acid Oral Solution» are fulfilled [3].

SAMPLE AND SAMPLE PREPARATION

The sample solutions are made using two distinct commercially available oral solutions of potassium citrate and citric acid. The labeled content was 1100 mg/334 mg potassium citrate monohydrate/citric acid monohydrate per 5 mL solution. For a sample stock solution (1000 mg/mL of potassium from potassium citrate and citric acid oral solutions), 1.26 mL of sample are transferred quantitatively to a 100 mL volumetric flask, then diluted to volume with ultrapure water and mixed well. For a sample solution (nominally 15.0 µg/mL of potassium), 1.5 mL of sample stock solution are added to a 100 mL volumetric flask, diluted to volume with ultrapure water, and mixed well.

The USP Reference Standard Potassium Citrate monohydrate (Cat#1548225 RS) is used as a standard solution.

EXPERIMENTAL

An 858 Professional Sample Processor with a peristaltic pump is used to aspirate samples or standard solutions into a 20 µL loop for direct injection (**Figure 1**). Cations are separated using the Metrosep C 6 - 150/4.0 column (L76) with a nitric acid eluent and detected with non-suppressed conductivity (**Table 1**).

The IC system is calibrated with a 6-point linear calibration fit in the concentration range of 3.0 to 22.5 µg/mL potassium. System suitability tests and solution stability tests are done with a working standard of 15.0 µg/mL potassium. Spiking recoveries are evaluated as triplicates. Repeatability studies are done with a 6-fold injection.

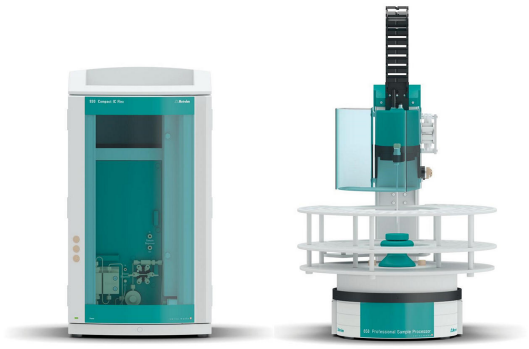

Figure 1. Instrumental setup including a 930 Compact IC Flex Oven/Deg and an 858 Professional Sample Processor.

Table 1. Parameters for the IC method as per USP Monograph «Potassium Citrate and Citric Acid Oral Solution» [3].

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 method validation for the potassium assay in potassium citrate and citric acid oral solution was carried out according to the USP Monograph «Potassium Citrate and Citric Acid Oral Solution» [3]. The potassium peak was well resolved from other typical cations. The tailing factor was 1.3. Recovery results for samples spiked at three different levels were 99.2% (Table 2 and Figure 2).

Replicate tests for standards and samples always reached relative standard deviations (RSD) of less than 0.4%. Six standard solutions ranging from 322.5 mg/L potassium showed correlation coefficients of 0.99999 with a linear curve fit (only 0.999 was required). Intermediate precision was tested with two independent systems and analysts. The average results for the first and the second analyst did not differ by more than 0.5% (2% deviation was allowed) (Table 2).

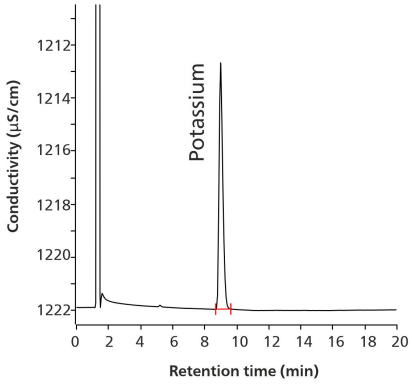

Figure 2. Chromatogram of a potassium citrate and citric acid oral solution containing 19 µg/mL potassium.

Table 2. Exemplary results and USP requirements from the IC method validation for potassium in potassium citrate and citric acid oral solution as per USP [3].

Parameter	Result	USP requirement
Tailing factor	1.3	NMT 2.0
Resolution K^+/Mg^{2+}	4.6	NLT 2.0
RSD % (n = 6)	<0.4%	NMT 0.5%
Linear correlation coefficient R	0.99999	NLT 0.999
Spiking recovery	99.2%	100 ± 3%
Intermediate precision	0.5%	NMT 2%

CONCLUSION

As per USP «Potassium Citrate and Citric Acid Oral Solution» [3], the assay for potassium is carried out with an IC using a Metrosep C 6 separation column (packing material L76). All validation results fulfilled the requirements of the monograph and followed the guidelines of the USP General Chapters <621> [4] and <1225> [5]. The presented IC method is suitable to quantify potassium in potassium citrate and citric acid oral solutions.

REFERENCES

1. National Institutes of Health (NIH) (.gov). *Potassium Citrate and Citric Acid Oral Solution USP*. https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=ce42122f-8087-471f-b0a3-5524bdbd4526&type=display (accessed 2024-08-26).
2. Doizi, S.; Poindexter, J. R.; Pearle, M. S.; et al. Impact of Potassium Citrate vs Citric Acid on Urinary Stone Risk in Calcium Phosphate Stone *Formers. Journal of Urology* 2018. DOI:10.1016/j.juro.2018.07.039
3. U.S. Pharmacopeia. USP-NF Potassium Citrate and Citric Acid Oral Solution. *Monograph*. DOI:10.31003/USPNF_M67530_04_01
4. *<621> Chromatography, General Chapter*; U.S. Pharmacopeia/National Formulary: Rockville, MD.
5. *〈1225〉 Validation of Compendial Procedures*; General Chapter; U.S. Pharmacopeia/National Formulary: Rockville, MD. DOI:10.31003/USPNF_M99945_04_01

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CONFIGURATION

Metrosep C 6 - 150/4.0

高容量的 C 6 材料使分离柱 Metrosep C 6 - 150/4.0 成为在浓度差异很高时的正常保留时间内分离标准阳离子的解决方法。可用此柱测定铵含量很高的饮用水。

930 Compact IC Flex Oven/Deg

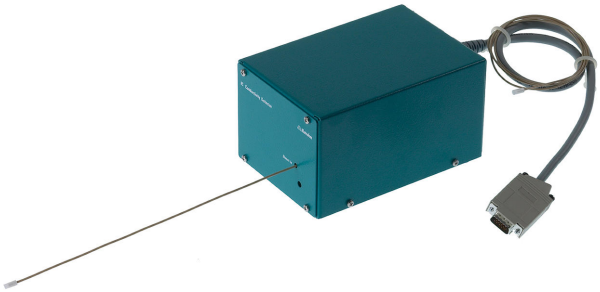
930 Compact IC Flex Oven/Deg 是智能型带**柱加热炉**、**无抑制**的 Compact IC 仪器,并且内置**脱气装置**。 该仪器可使用各种分离和检测方法。

典型的应用范围:

- 阴离子和阳离子测定,无抑制的电导检测
- 使用 UV-VIS 或安培检测的简单应用

858 Professional Sample Processor – Pump

858 Professional Sample Processor – Pump 可处理体积在 500 µL 至 500 mL 之间的样品。进行样品转移时,既可以使用内置的双向双通道蠕动泵、也可通过 800 Dosino 来进行。



IC Conductivity Detector

用于智能型离子色谱仪的紧凑智能型高性能电导检测器。不凡的温度稳定性,受保护的检测器端子板内的整个信号处理过程以及新一代的 DSP(数字式信号处理)均能确保测量的准确性。归功于动态工作范围,无需进行范围变更(也不是自动进行)。