



Application Note AN-CS-021

碳酸氢钠和磷酸钠复方注射剂中的钠

IC assay method validation performed according to USP

Patients may be unable to use commercially available medical formulations for many reasons and therefore require specific compounded formulations [1]. Compounded injections of sodium bicarbonate are sterile solutions for correcting metabolic acidosis and other conditions requiring systemic alkalinization [2]. Compounded injections of sodium phosphates (a mixture of monobasic and dibasic phosphates [3]) serve as a phosphate source to either

prevent or correct hypophosphatemia in patients with restricted oral intake. After dilution, these injections can be administered intravenously as electrolyte replenishers. Ion chromatography (IC) with suppressed conductivity detection is the standardized way to accurately quantify sodium in these solutions [4,5]. The Metrosep C Supp 2 column was evaluated as an alternative column [6,7] in cooperation with the U.S. Pharmacopoeia (USP).

SAMPLES AND STANDARDS

For the equivalence investigation of the Metrosep C Supp 2 - 250/4.0 column, compounded injections were prepared from the

respective sodium salts. Anhydrous salts from different manufacturers were used.



Figure 1. Instrumental setup including a 930 Compact IC Flex with the IC Conductivity Detector MB (L) and the 919 IC Autosampler plus (R).

For **sodium bicarbonate compounded injections**, 8.4 g of sodium bicarbonate was dissolved in 100 mL sterile Water for Injection [4]. Further manual dilution was performed using ultrapure water (100-fold dilution) to achieve a nominal concentration of 0.23 mg/mL. Sample stock solutions for the **sodium phosphates compounded injections** were prepared from 24 g of monobasic sodium phosphate and 14.2 g of

dibasic sodium phosphate – both dissolved in 100 mL sterile Water for Injection. Both solutions were further diluted in ultrapure water (100-fold) to a nominal concentration of 0.92 mg/mL sodium. All samples were prepared as individual duplicates.

A single-point calibration with 0.250 mg/mL of sodium, prepared from sodium chloride in ultrapure water, was used.

EXPERIMENTAL

The samples were injected directly into the ion chromatograph (**Figure 1**) and analyzed using the method parameters given in the respective USP monograph (**Table 1**). Cationic components

were isocratically separated on a Metrosep C Supp 2 - 250/4.0 column which contains the alternative packing material L97 (**Figure 2**).

Table 1. IC method parameters as per the USP monographs «Sodium Bicarbonate Compounded Injection» [4] and «Sodium Phosphates Compounded Injection» [5].

Column with L97 packing	Metrosep C Supp 2 – 250/4.0
Eluent	8 mmol/L methanesulfonic acid (MSA)
Flow rate	1.0 mL/min
Column temp.	30 ° C
Injection volume	10 µL
Detection	Conductivity with sequential suppression

A Metrohm Suppressor Module for cation suppression, regenerated with a solution of sodium carbonate and sodium bicarbonate (70 mmol/L each), was used to reduce the background noise in the chromatograms. The

conductivity signal was detected after sequential suppression. For the column equivalency study, system suitability (e.g., repeatability, tailing factors) and sample recoveries were evaluated (**Table 2**).

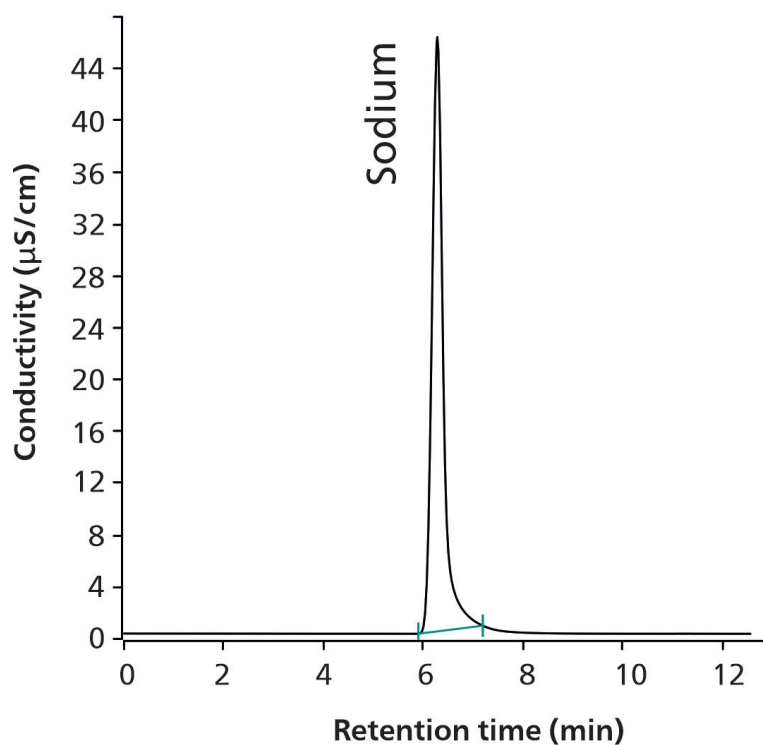


Figure 2. Chromatogram for sodium in a sodium bicarbonate compounded injection containing 0.231 mg/mL sodium (100% recovery).

RESULTS

Sodium bicarbonate and sodium phosphates compounded injection samples, made from the sodium salts from different manufacturers, were analyzed for their sodium content (**Figure 2**) within less than 12 minutes. The IC assay for sodium was conducted according to USP General Chapter <621>, Chromatography [6] and fulfilled all suitability and acceptance

criteria. Sodium eluted after approximately six minutes as a symmetric peak (tailing factor <1.8). The peak area was highly reproducible (<1.4 % RSD for five replicates, **Table 2**).

Recoveries for the sodium content were determined in the range of 98–102%, within the acceptance criteria of USP.

Table 2. Selected performance characteristics.

Performance characteristics	Acceptance criteria	Results
Tailing factor	Tailing factors (asymmetry) for the sodium peak is NMT 2.0	1.39–1.79
Repeatability	Relative standard deviation for the sodium peak area in the standard solution is NMT 2.0% for five replicates	0.3–1.3%
Accuracy	Average % recovery should be 95.0–105.0% of the manufacturer's CoA value	98–100% sodium in sodium bicarbonate 98–102% sodium in sodium phosphates

CONCLUSION

The presented IC method with the **Metrosep C Supp 2** column that contains the **alternative packing material L97** is a robust, reliable, and validated method suitable to quantify sodium in

both **sodium bicarbonate and sodium phosphates compounded injections** according to USP requirements.

REFERENCES

1. USP General Chapter <797>. <https://www.usp.org/compounding/general-chapter-797> (accessed 2023-03-27).
2. Exela Pharma Sciences, LLC. *Sodium Bicarbonate Injection, USP*. [dailymed](#). (accessed 2023-01-16).
3. Fresenius Kabi USA, LLC. *Sodium Phosphates Injection USP*. [dailymed](#). (accessed 2022-07-15).
4. U.S. Pharmacopeia. USP-NF Sodium Bicarbonate Compounded Injection. *Monograph*. https://doi.org/10.31003/USPNF_M10963_04_01.
5. *Sodium Phosphates Compounded Injection*. https://doi.org/10.31003/USPNF_M10964_06_01.
6. <621> Chromatography. https://doi.org/10.31003/USPNF_M99380_01_01.
7. <1225> Validation of Compendial Procedures; General Chapter; U.S. Pharmacopeia/National Formulary: Rockville, MD. https://doi.org/10.31003/USPNF_M99945_04_01.

CONTACT

瑞士万通中国
北京市海淀区上地东路1号
院1号楼7层702
100085 北京

marketing@metrohm.com.cn

CONFIGURATION



930 Compact IC Flex Oven/SeS/PP/Deg

930 Compact IC Flex Oven/SeS/PP/Deg 是智能型 Compact 离子色谱仪器,带有柱加热炉、序列抑制和蠕动泵用于抑制器再生,以及内置的脱气装置。该仪器可使用各种分离和检测方法。

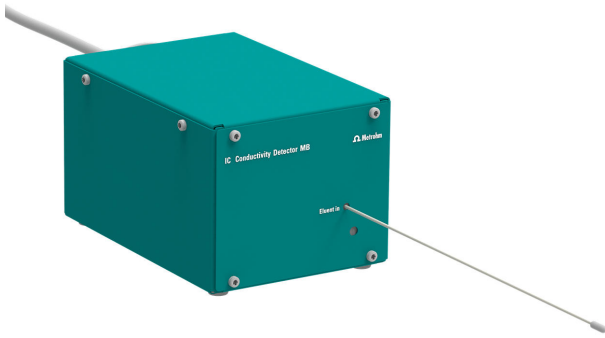
典型的应用范围:

- 阴离子或阳离子测定,序列抑制法及电导检测



919 IC Autosampler plus

919 IC Autosampler plus 满足实验室内处理中等样品量的要求。使用该仪器,可实现万通产品的各种离子色谱分析自动化。



IC Conductivity Detector MB

用于智能型离子色谱仪的紧凑智能型高性能电导检测器。针对微孔柱经过优化。卓越的温度稳定性,在受保护的检测器端子板内完成整个信号处理过程以及最新一代的 DSP(数字式信号处理)均能确保测量的最高精确性。归功于动态工作范围,无需进行(也包括非自动)范围变更。

典型的应用范围:

- 阴离子或阳离子测定,化学抑制、序列抑制法或无抑制及电导检测
- 针对微孔 (2mm) 应用经过优化,尤其适合耦合技术(IC-MS 或 IC-ICP/MS)

规格说明书概览:

- 0 ... 15000 $\mu\text{S}/\text{cm}$ 无区段切换
- 测量池容量:0.3 μL
- 由不锈钢 X2CrNiMo17-12-2 (316 L) 制成的环形电极,与 MSA 兼容
- 最大工作压力:10.0 MPa (100 bar)
- 池温:20 ... 50 ° C,步幅为 5 ° C
- 温度稳定性: 0.001 ° C
- 基线噪音:° 0.2° nS/cm,是使用序列抑制法的典型值
- 毛细管:ID 0.18 mm

支持 MagIC Net 4.1 和以上版本