Application Note AN-CS-021

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## 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**).

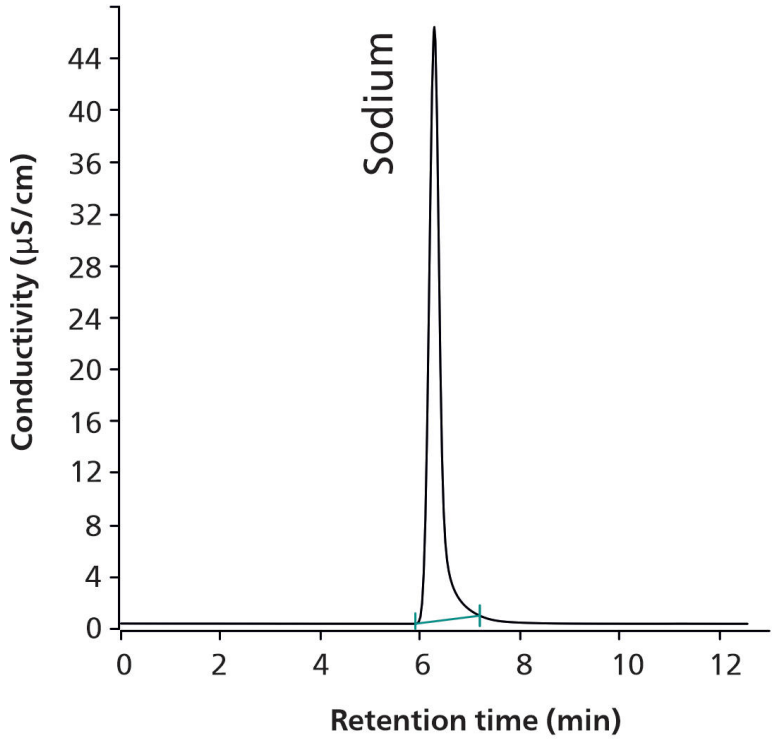


**Figure 2.** Chromatogram for sodium in a sodium bicarbonate compounded injection containing 0.231 mg/mL sodium (100% recovery).

## 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

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## CONFIGURATION

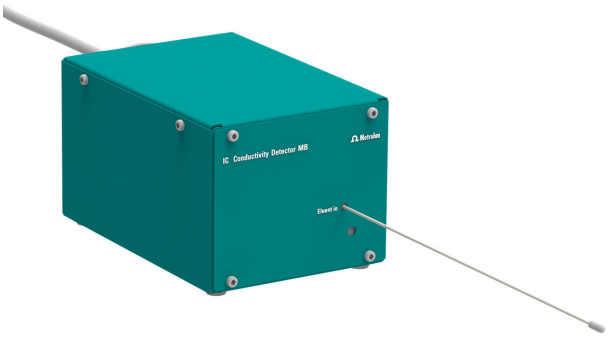
### 930 Compact IC Flex Oven/SeS/PP/Deg

930 Compact IC Flex Oven/SeS/PP/Deg 是智能型 Compact 子色器,有**柱加炉**、**序列抑制**和**蠕**用于抑制器再生,以及内置的**脱气装置**。器可使用各分和方法。典型的用范:

- 子或子定,序列抑制法及

### 919 IC Autosampler plus

919 IC Autosampler plus 足室内理中等品量的要求。使用器,可万通品的各子色分析自化。




## IC Conductivity Detector MB

用于智能型子色的智能型高性能器。微孔柱化。卓越的温度定性,在受保的器端子板内完成整个信号理程以及最新一代的 DSP(数字式信号理)均能保量的最高精性。功于工作范,无需行(也包括非自)范更。

**典型的用范:**

- 子或子定,化学抑制、序列抑制法或无抑制及
- 微孔 (2mm) 用化,尤其合合技(IC-MS 或 IC-ICP/MS)

**格明概:**

- 0 ... 15000 µS/cm 无区段切
- 量池容量:0.3 µL
- 由不 X2CrNiMo17-12-2 (316 L) 制成的形,与 MSA 兼容
- 最大工作力:10.0 MPa (100 bar)
- 池温:20 ... 50 °C,步幅 5 °C
- 温度定性:< 0.001 °C
- 基噪音:<° 0.2° nS/cm,是使用序列抑制法的典型
- 毛管:ID 0.18 mm

支持 MagIC Net 4.1 和以上版本