



Application Note AN-S-398

Phosphate in sodium and potassium phosphates compounded injections

IC assay method validations performed according to USP

INTRODUCTION

Compounded injections of sodium or potassium phosphates are sterile solutions that contain a mixture of monobasic and dibasic phosphates in water for injection [1]. These solutions serve as a phosphate source to either prevent or correct hypophosphatemia (i.e., an abnormally low phosphate level in the blood) in patients with restricted or no oral intake. After dilution, these can be administered intravenously as electrolyte replenishers. They are also useful as additives for preparing specific intravenous fluid formulas.

An ion chromatography (IC) assay with suppressed conductivity detection is the standardized way to accurately quantify phosphate in phosphates compounded injections [2–3]. The Metrosep A Supp 17 column was established as a suitable alternative column within a standardized validation procedure [4] in cooperation with the U.S. Pharmacopoeia (USP). This column guarantees reliable separation, and the Metrohm suppressor module (MSM) ensures low background noise and robust long-term performance.

For the equivalence investigation of the Metrosep A Supp 17 - 150/4.0 column, compounded injections were prepared from the respective mono- and dibasic sodium or potassium salts of phosphate. Anhydrous salts from different manufacturers were used.

Sample stock solutions for the sodium phosphates compounded injection 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. For the potassium phosphates compounded injection, 22.4 g of monobasic

potassium phosphate and 23.6 g of dibasic sodium phosphate were dissolved in 100 mL sterile water for injection.

The sample stock solutions were further manually diluted in ultrapure water (1250-fold) to a nominal concentration of 0.23 mg/mL phosphate. All samples were prepared as individual duplicates.

A single point calibration with 0.230 mg/mL of phosphate, prepared from dibasic potassium phosphate in 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**).

Anionic components were isocratically separated on a Metrosep A Supp 17 - 150/4.0 column, which contains the alternative packing material L91. The conductivity signal was detected after sequential suppression. For the column equivalency, system suitability (e.g., repeatability, tailing factors) and sample recoveries were studied (**Table 2**).



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

RESULTS

Sodium and potassium phosphates compounded injection samples, made from the phosphate salts from different manufacturers, were analyzed for their phosphate content (**Figure 2**). The IC assay for phosphate in sodium and potassium phosphates compounded injections was conducted according to USP General Chapter <621>, Chromatography [4] and fulfilled all suitability and acceptance criteria. Recoveries for phosphate content were determined in the range of 98–99%. Phosphate eluted at approximately 6 minutes as a symmetric peak (tailing factor 1.59 and 1.60) and its peak area was highly reproducible (<0.3% RSD, **Table 2**).

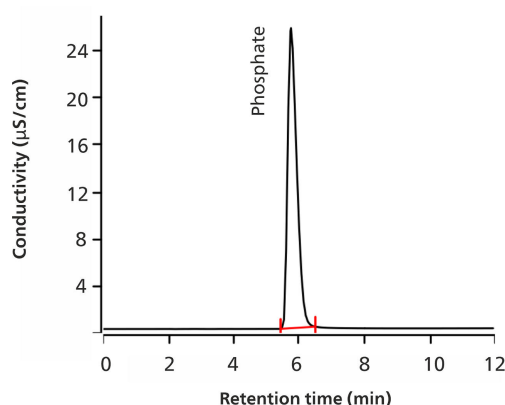


Figure 2 Chromatogram for phosphate in a sodium phosphate compounded injection containing 0.226 mg/mL phosphate (98% recovery).

Table 1. IC method parameters as per the USP monographs «Sodium Phosphates Compounded Injection» [2] and «Potassium Phosphates Compounded Injection» [3].

Column with L91 packing	Metrosep A Supp 17 - 150/4.0
Eluent	40 mmol/L sodium hydroxide
Flow rate	1.0 mL/min
Column temperature	30 °C
Injection volume	10 µL
Detection	Conductivity with sequential suppression

CONCLUSION

The presented IC method with the Metrosep A Supp 17 column that contains the alternative packing material L91 is a robust, reliable, and validated

method suitable to quantify phosphate in both sodium and potassium phosphates compounded injections according to USP requirements.

Table 2. Selected performance characteristics.

Performance characteristics	Acceptance criteria	Results
Tailing factor	Tailing factors (asymmetry) for the phosphate peak is NMT 2.0	1.59–1.60
Repeatability	Relative standard deviation for the phosphate peak area in the standard solution is NMT 2.0% for five replicates	0.2–0.3 %
Accuracy	Average % recovery should be 95.0–105.0% of the manufacturer's CoA value	98–99 %

[1] Sodium Phosphates Injection USP. <https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=e6169d3b-39d2-47f9-8d5b-b53ec069a722&type=display> (accessed 2022-07-15).

[2] Sodium Phosphates Compounded Injection.

https://doi.org/10.31003/USPNF_M10964_06_01.

[3] Potassium Phosphates Compounded Injection. https://doi.org/10.31003/USPNF_M10962_05_01.

[4] 621 Chromatography. https://doi.org/10.31003/USPNF_M99380_01_01.

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CONFIGURATION



930 Compact IC Flex Oven/SeS/PP/Deg

The 930 Compact IC Flex Oven/SeS/PP/Deg is the intelligent Compact IC instrument with **column oven**, **sequential suppression**, **peristaltic pump** for suppressor regeneration and built-in **degasser**. The instrument can be used with any separation and detection methods.

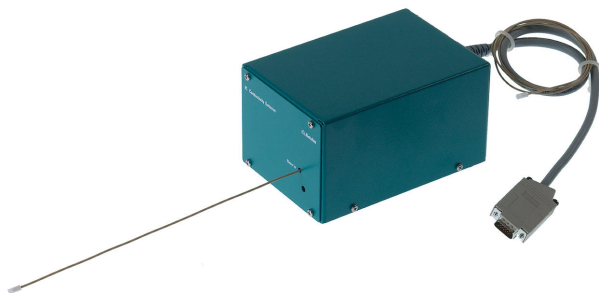
Typical areas of application:

- Anion or cation determinations with sequential suppression and conductivity detection



919 IC Autosampler plus

The 919 IC Autosampler plus fulfills the requirements of laboratories with medium sample numbers. It enables automation of the full range of Metrohm IC instruments.



IC Conductivity Detector

Compact and intelligent high performance conductivity detector for intelligent IC instruments. Outstanding temperature stability, the complete signal processing within the protected detector block and the latest generation of DSP – Digital Signal Processing – guarantee the highest precision of the measurement. No change of measuring ranges (not even automatic ones) is required, due to the dynamic working range.



Metrosep A Supp 17 - 150/4.0

The Metrosep A Supp 17 - 150/4.0 separation column is the column of choice for anion determinations that require good separating efficiency and short separation times at room temperature. The maximum flow rate of 1.4 mL/min then also makes it possible to optimize the determination. The Metrosep A-Supp-17 columns convince with their good price-performance ratio.