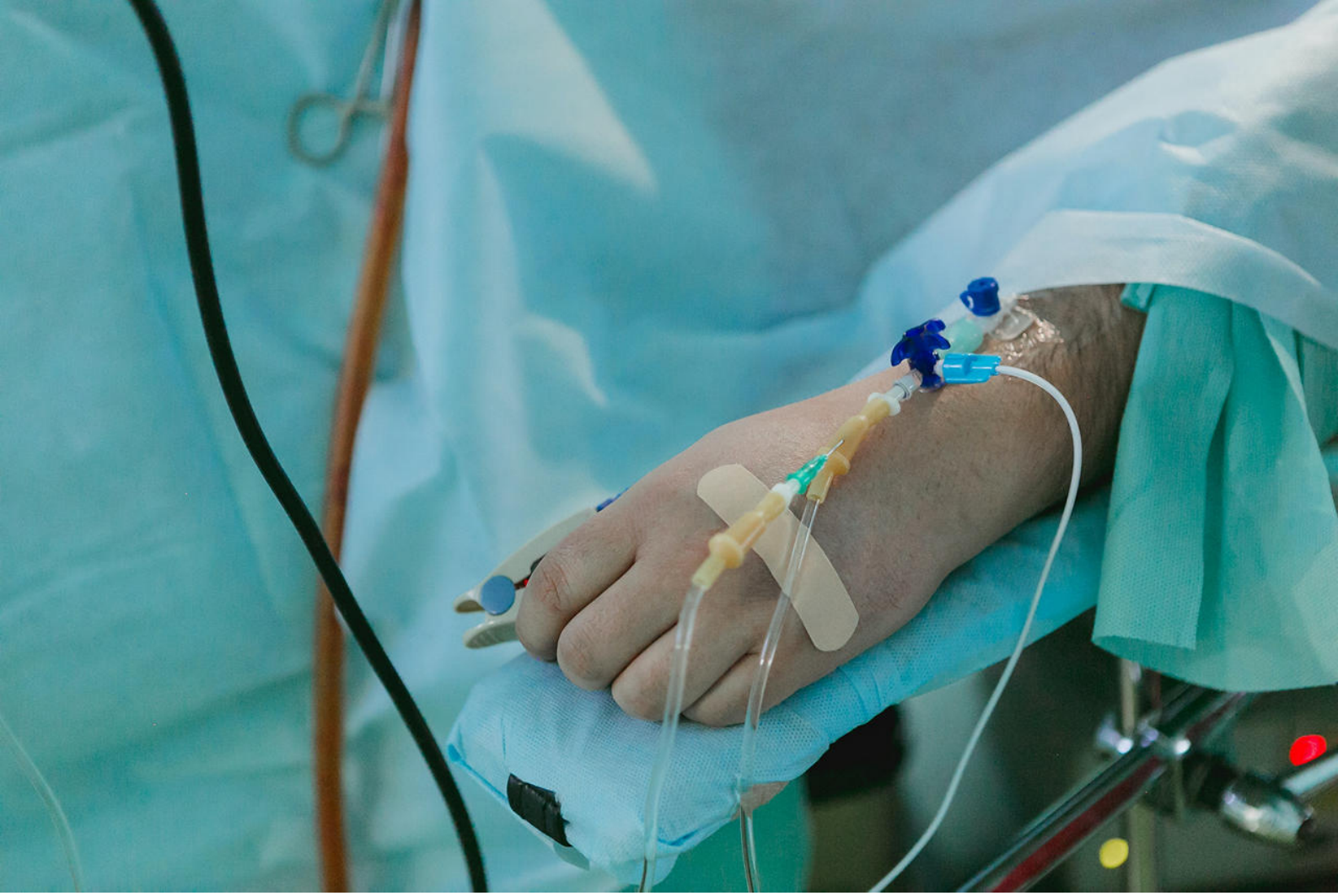

Application Note AN-S-398

Phosphate in sodium and potassium phosphates compounded injections

IC assay method validations performed according to USP

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**).

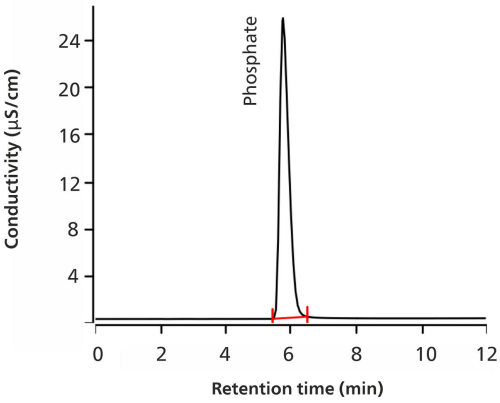

Figure 2 Chromatogram for phosphate in a sodium phosphate compounded injection containing 0.226 mg/mL phosphate (98% recovery).

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 L
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.

REFERENCES

Internal references: AW IC AE6-0121-092021; AW IC AE6-0122-092020

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CONFIGURATION

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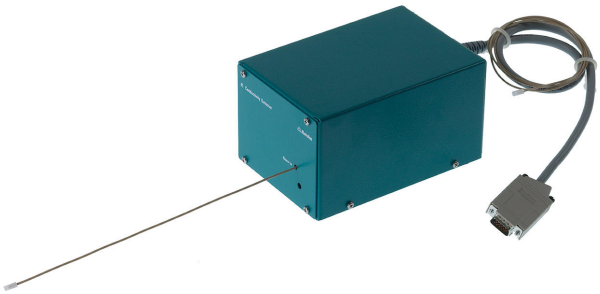

IC Conductivity Detector

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