Extended Stability of Sodium Phosphate Solutions in Polyvinylchloride Bags.

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BACKGROUND

Concentrated sodium phosphate injections provide 3 mmol of phosphate per mL, and 4 mmol of sodium per mL. At this concentration the solution is considered a risk to patient safety and must be sufficiently diluted, thoroughly mixed, and infused slowly enough to prevent phlebitis, hysterepamia, hyperphosphatemia and changes in drug concentration and temperature. Pharmacy departments have been preparing dilute solutions of sodium phosphate solutions, frequently in the range of 30 mmol/L to 150 mmol/L of phosphate.

While we are not aware of any literature that aqueous solutions of sodium or phosphate degrade, there is also no supporting published evidence documenting stability in IV solutions to allow the establishment of a beyond use date (BUD).

The objective of this study was to evaluate the stability of both sodium and phosphate in admixtures of 30 mmol/L (phosphate) and 150 mmol/L (phosphate) from sodium phosphate in 5% dextrose in water or 90 mmol/L sodium chloride solutions from sodium phosphate in 5% dextrose in water and 2.5 mg/mL sodium chloride solutions from sodium phosphate NaCl, monitored spectrophotometrically at wavelength of 255 nm. Both methods were routinely quality-controlled by using commercial materials at two different concentrations, giving long term imprecision (CVs) of 0.83-1.67% for sodium and 2.49-3.22% for phosphate.

RESULTS

ASSAY VALIDATION

Phosphate measurements, based on 5 samples with a nominal concentration of 75 mmol/L were accurate (mean bias of -1.17% [range -6.12% to 3.15 percent]; mean absolute bias of 2.86%) and reproducible (mean CV 0.88%). Sodium also measured accurately [mean bias of -1.98% [range -5.66% to 0.08%]; mean absolute bias 1.98%) and reproducible (mean CV 0.70%) based on a nominal concentration of 250.15 mmol/L.

Physical Stability and Bag Weights.

Over the 63-day study period all solutions remained clear and colourless without visible signs of precipitate or particulate matter.

Physical Stability and Bag Weights.

Loss of weight over 63 Days

PVC Bag Volume Surface Area 4°C 23°C

100 mL 176 cm² Loss mg/cm²/day 0.128 0.252

250 mL 346 cm² 0.055 0.117

Stable (≤ change per day) 0.058 0.058

Confidence Interval ±0.037 ±0.030 0.027

Stability Study

On study-day zero, 16 x 100 mL PVC bags containing 150 mmol/L of phosphate (8 solutions in D5W and 8 in NS), and 16 - x 250 mL PVC bags containing 30 mmol/L of phosphate (8 solutions in 5% dextrose, 8 in NaCl) were prepared. Solutions were stored at 4°C and room temperature (23°C), unprotected from fluorescent room light and with the over-wrap removed. On each study day (0, 2, 7, 16, 21, 28, 30, 35, 50 and 63), the sodium and phosphate concentrations were also inspected visually for a precipitate, visual changes, and the weight of the bag determined.

MEASUREMENT OF SODIUM AND PHOSPHATE

Both sodium and phosphate concentrations in the diluted IV solutions were determined using established methods. Sodium was measured by indirect ion Selective Electrode (ISE) based on a sodium-selective PVC Membrane, while inorganic phosphate was measured based on the formation of ammonium phosphomolybdate complex, (NH₄)₂[PO₄MoO₃]₂, monitored spectrophotometrically at wavelength of 340 nm. Both methods were routinely quality-controlled by using commercial materials at two different concentrations, giving long term imprecision (CVs) of 0.83-1.67% for sodium and 2.49-3.22% for phosphate.

METHODS

ASSAY VALIDATION

The initial concentration and the percent remaining observed on each study day during the study period for sodium and phosphate in Tables 1 and 2, respectively.

Sodium and phosphate includes a rate of zero (%/day). The intersection of the lower limit of the 95% CI of the slope and 90%, indicates that concentrations will remain greater than 90% for more than 63 days.

OBJECTIVES

The objective of this study was to evaluate the stability of both sodium and phosphate in admixtures of 30 mmol/L (phosphate) and 150 mmol/L (phosphate) from sodium phosphate in 5% dextrose in water or 90 mmol/L sodium chloride solutions from sodium phosphate NaCl, monitored spectrophotometrically at wavelength of 255 nm. Both methods were routinely quality-controlled by using commercial materials at two different concentrations, giving long term imprecision (CVs) of 0.83-1.67% for sodium and 2.49-3.22% for phosphate.

PHYSICAL STABILITY

The observed percent loss per day, determined by linear regression is listed in Tables 1 and 2.

Sodium and phosphate includes a rate of zero (%/day). The intersection of the lower limit of the 95% CI of the slope and 90%, indicates that concentrations will remain greater than 90% for more than 63 days.

CONCLUSION

We are unaware of any published studies which document the chemical stability of sodium phosphate in standard IV solutions. When considering the stability of sodium phosphate injections, it is recognized that sodium is an element, and while there are known isotypes of sodium, effectively 100% of sodium on earth exists as the stable, non-radioactive form, 23Na. Sodium is generally regarded as stable.

Elemental phosphorus is never found as a free element. Phosphorus has a single naturally occurring isotope, but in biological systems, phosphorus is found as free phosphate ion in solution. Phosphate ion exists in dilute aqueous solutions in four forms. In strongly-acid conditions, aqueous phosphoric acid (H₃PO₄), is the primary form, although some amount of each of the other 3 forms will be present in equilibrium with all other forms. A shift from one form to another is not considered instability. There is no indication that phosphate degrades.

We studied the stability of sodium phosphate solutions in polyvinylchloride bags.

During the 63-day study period PVC bags lost weight proportional to surface area and temperature. With the over-wrap removed, the weight loss was greater for 100 mL bags (1.4% at 4°C; 3.4% at 23°C) compared to (0.9% at 4°C; 1.9% at 23°C) 250 mL bags.

During the 63-day study period, after correction for weight <water> loss, confidence limits were constructed about the rate of change in concentration included a rate of zero for both sodium and phosphate. This indicates that neither sodium nor phosphate was observed to degrade during the 63-day study period.

When establishing a BUD for intravenous admixtures of sodium phosphate injection, USP 797 guidelines for compounded sterile products (CSP) based on risk level, institutional compliance and storage conditions should be considered.