# ASSESSING THE STABILITY OF 8.4% SODIUM BICARBONATE INJECTABLE VIALS STORED AT ROOM TEMPERATURE

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## BACKGROUND

Sodium bicarbonate is used to treat a number of conditions including metabolic acidosis, in open heart surgery, and in some cancer chemotherapy regimens. In June 2017, a back-order/shortage of injectable sodium bicarbonate product in Canada was announced. In response to the shortage, the feasibility and stability of an in-house compounded injectable sodium bicarbonate formulation was was evaluated.

## OBJECTIVES

The objective of this study is to evaluate the stability of 8.4% injectable sodium bicarbonate solution compounded in-house, stored at room temperature unprotected from ambient room fluorescent light for 90 days.

## METHODS

### MEASUREMENT OF SODIUM, BICARBONATE, AND BUFFER CAPACITY

On days 0,2,5,7,9,12,14,16,21,23,28,42,56,70 and 91, a 50mL volume (52.8g) of sodium bicarbonate solution was withdrawn from each glass vial and titrated against 2M HCl (three samples per day) to determine buffer capacity. On each study day, three sodium bicarbonate samples were also delivered to the biochemistry lab for determination of initial pH, sodium, and bicarbonate concentrations.

### ASSAY VALIDATION

Both sodium and bicarbonate concentrations were determined using established methods. Sodium was measured by Ion Selective Electrode (ISE) using a sodium-selective PVC Membrane, while bicarbonate was measured using a UV-enzymatic method which quantitated absorbance at 340nm. Quality control of both methods was achieved using commercial materials at two different concentrations, giving long term precision (CVs) of 1.17% for sodium and 1.86% for bicarbonate. During the study, inter and intra-day errors of reproducibility were assessed by the coefficients of variation and the standard deviation of regression.

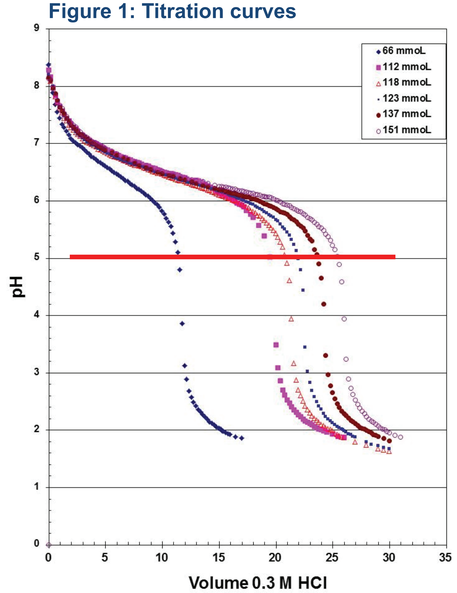
### ACID-BASE TITRATION METHOD

On each study day, a beaker containing 50mL (52.8g) of 8.4% sodium bicarbonate drawn from a vial was titrated with 0.1ml increments of 2M HCl. Titration curves were recorded and analyzed. This titration method serves as a test of the functional capacity of sodium bicarbonate to consume acid. The endpoint measurement of the volume to achieve a pH of 5 was determined to provide greatest resolution between bicarbonate solutions of varying strength and lowest replicate error. (Figure 1 at right shows titration curves for six different bicarbonate concentrations between 66 mmol/L and 151 mmol/L)

### DATA REDUCTION AND STATISTICAL ANALYSIS

Linear regression was used to determine the relationship between sodium, bicarbonate and buffer capacity vs study days. The 95% confidence interval of the percent remaining on the last study day was calculated. Analysis of variance was used to test differences in concentration on different study days. The five-percent level was used as the a priori cut-off for significance.

Figure 1: Titration curves




## RESULTS

Evaluation of titrations of 2M HCL against 50mL volumes of bicarbonate indicated the method was reproducible. Within day reproducibility for buffer capacity as determined by the standard deviation of regression averaged 0.145% for pH 5. Similarly, between days variability for sodium and bicarbonate analysis averaged 1.21% and 1.89%, respectively.

Analysis of sodium and bicarbonate concentrations indicates that less than a 3% change occurred in the study period and that it would take more than 368 and 225 days, respectively, before a 10% change was observed in either concentration, with 95% confidence.

Similarly, analysis of buffer capacity, based on the volume of 2M HCl to achieve a pH of 5, indicates that it would take more than 16,608 days before a 10% change was observed and with 95% confidence and this would not occur sooner than 2,687 days.

The initial pH, before any 2M HCl was added, indicates that solutions stored at room temperature have virtually no change in the initial pH of the 91-day study period, showing a reduction in pH of less than 0.1 pH units over 90 days, with 95% confidence.

Table 1: Results for Sodium, Bicarbonate, Buffer capacity and Initial pH

| | | Sodium | Bicarbonate | Buffer Capacity[1] | Initial pH |
|---|---|---|---|---|---|
| Initial Nominal Value (intercept) | | 1033.29 mmol/L | 1029.11 mmol/L | 25.90 mL | |
| Study Day / | Initial Value | 1030 mmol/L | 1050 mmol/L | 26.0 mL | |
| 0 | | 100.00 | 100.00 | 100.00 | 8.07 |
| 2 | | 99.03 | 97.14 | 99.62 | 8.08 |
| 5 | | 99.03 | 97.14 | 99.49 | 8.03 |
| 7 | | 100.97 | 100.00 | 99.49 | 8.09 |
| 9 | | 99.03 | 97.14 | 99.62 | 8.03 |
| 12 | | 100.00 | 97.14 | 99.49 | 8.05 |
| 14 | | 101.94 | 97.14 | 99.62 | 8.06 |
| 16 | | 100.97 | 97.14 | 99.49 | 8.06 |
| 21 | | 100.97 | 102.86 | 99.49 | 8.05 |
| 23 | | 99.03 | 100.00 | 99.74 | 8.03 |
| 28 | | 98.06 | 97.14 | 99.62 | 8.11 |
| 42 | | 98.06 | 97.14 | 99.74 | 8.06 |
| 56 | | 100.97 | 100.00 | 99.62 | 8.06 |
| 70 | | 100.00 | 100.00 | 99.74 | 8.07 |
| 91 | | 99.03 | 97.14 | 99.62 | 8.01 |
| Degradation rate (%/day) [Slope] | | -0.00127 | 0.00372 | 0.00060 | -0.00025 |
| Intercept (Percent of Initial Concentration) | | 99.96 | 98.38 | 99.61 | 8.06 |
| Correlation coefficient (r) | | -0.1381 | 0.0548 | 0.1149 | -0.2630 |
| Standard Deviation of Regression (Sy.x) | | 1.21 | 1.89 | 0.15 | 0.03 |
| Standard Error in Slope (Sb) | | 0.01196 | 0.01882 | 0.001444 | 0.00026 |
| Confidence Interval for slope | | 0.02585 | 0.04066 | 0.00312 | 0.00056 |
| Fastest Slope 95% Confidence | | -0.02712 | -0.03693 | -0.00252 | -0.00081 |
| Upper Limit 95% Confidence | | 0.02458 | 0.04438 | 0.00372 | 0.00030 |
| T-90 (point Estimate) in days | | 7853.9 | 2687.5 | 16,608.8 | 39,450.7 |
| Shortest T-90 (95% CI) in days | | 368.7 | 225.6 | 2,687.4 | 12,337.2 |

1. Buffer capacity is measured by the volume of 2M HCl required to reduce the pH from 8.06 to 5.0.

## REFERENCES

1. NAPRA. Model Standards for Pharmacy Compounding of Non-Hazardous Sterile Preparations. Available at http://napra.ca/Content_Files/Files/Mdl_Stnds_Pharmacy_Compounding_NonHazardous_Sterile_Preparations_Nov2016_Revised.pdf Accessed August 14, 2017

2. Perks W, Iazzetta J, Chan PC, Brouzas A, Law S, Walker SE. Extended Stability of Sodium Phosphate Solutions in Polyvinyl Chloride Bags. Can J Hosp Pharm. 2017 Jan-Feb;70(1):7-12

## CONCLUSIONS

We observed that injectable sodium bicarbonate solution, compounded in-house, is stable for at least 225 days, with 95% confidence, when stored at room temperature.

The beyond-use date of 225 days should be used only after due consideration of institutional capability, applicable standards, sterility verification and completion of required quality tests

## DISCLOSURE

NONE of the authors of this poster have any personal or financial relationships with any commercial entities that may have a direct or indirect interest in the subject matter of this presentation.
All materials and supplies used in this study were purchased by the Department of Pharmacy, Sunnybrook Health Sciences Centre.

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