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Pharma

Determination of ammonia in sodium bicarbonate using a compact RFIC ion chromatography system

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Introduction

Sodium bicarbonate, or sodium hydrogen carbonate, is used in a wide variety of pharmaceutical and food products, and ammonia is one of the impurities that is assayed. Previously published Thermo Scientific Application Note 1073[1] demonstrated the capability of an ion chromatography (IC) based method to determine a trace amount of ammonia (as ammonium). The method described in this note was later updated in the United States Pharmacopeia-National Formulary (USP-NF) Sodium Bicarbonate monograph[2].

In this application proof note, the performance of the easy-to-use, compact Thermo Scientific™ Dionex™ Inuvion™ ion chromatography system equipped with a Thermo Scientific™ Dionex™ IonPac™ CS16 (3 × 250 mm) cation-exchange column was evaluated to show that the new instrument is suitable for this application.

Method

Reagents and standards

- Deionized (DI) water, Type I reagent grade, 18 MΩ·cm resistance or better
- Ammonium Standard, 1,000 µg/mL, Agilent Technologies (P/N ICC-101)
- Sodium bicarbonate, EM Science (SX0320-1)

Instrument method parameters

Instrument	Dionex Inuvion IC system (P/N 22185-60108), including column heater, pump degas module, and eluent generation
Autosampler	Thermo Scientific™ Dionex™ AS-DV autosampler (P/N 068907) with 5 mL Thermo Scientific™ Dionex™ PolyVials™ and filter caps, (P/N 038141)
Columns	Dionex IonPac CS16, Analytical, 3 × 250 mm (P/N 059596) Dionex IonPac CG16, Guard, 3 × 50 mm (P/N 079931)
Eluent	7 mM methanesulfonic acid (MSA) for 28 min, 70 mM MSA from 28.1 to 36 min, re-equilibrate to 7 mM MSA from 36.1 to 42 min*
Eluent source	Thermo Scientific™ Dionex™ EGC 500 MSA cartridge (P/N 075779), Thermo Scientific™ Dionex™ CR-CTC 600 (P/N 088663), Thermo Scientific™ Dionex™ RFIC™ eluent degasser module (P/N 106-60001)
Flow rate	0.43 mL/min
Column temp.	40 °C
Injection volume	25 µL
Detection	Suppressed conductivity, Thermo Scientific™ Dionex™ CDRS 600 (2 mm) suppressor (P/N 088670CMD or 088670), 89 mA, recycle mode
System backpressure	~2,400 psi (100 psi = 689.5 kPa)
Background conductance	<0.3 µS/cm
Noise	<1.0 nS/cm
Run time	42 min
Software	Thermo Scientific™ Chromeleon™ Chromatography Data System (CDS) software version 7.3.2

*Analysis time was adjusted from the original method due to the retention time shift of the ammonium peak caused by within specification column variation.

Results

The separation of trace ammonia in a high concentration of sodium was achieved. Figure 1 shows chromatograms comparing a 1.0 mg/mL sodium bicarbonate sample solution, the same sample solution spiked with 0.02 µg/mL ammonium ion, and a DI water blank. The USP ammonia limit test compares the sample to the sodium bicarbonate solution spiked with 0.02 µg/mL ammonium ion to determine if the sodium bicarbonate is acceptable.

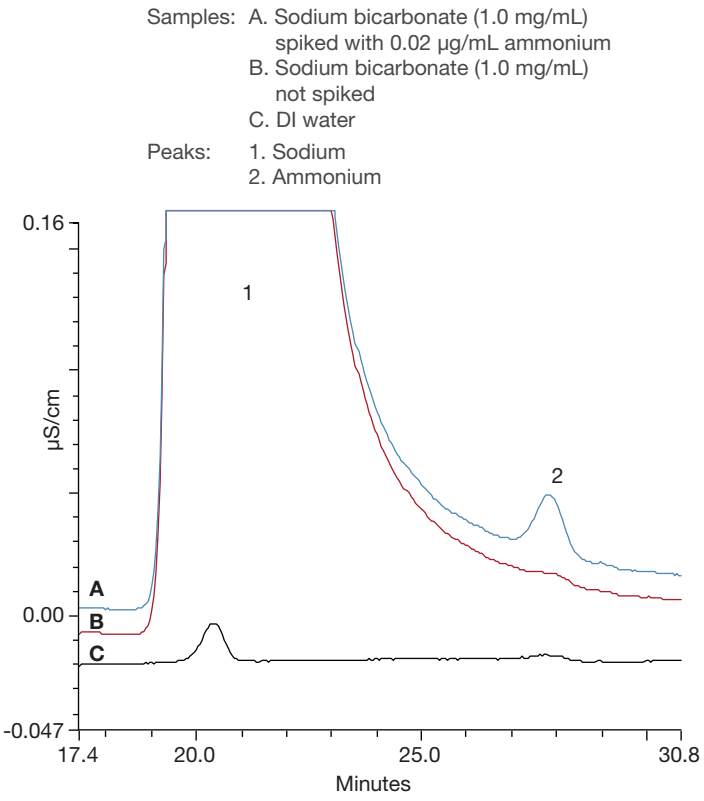

Figure 1. Determination of ammonia in sodium bicarbonate

Precision

Table 1 shows the precisions of the retention time and the peak area for ammonia in 1.0 mg/mL sodium bicarbonate. They were determined by assaying ammonia at three different concentrations in triplicate and calculating the relative standard deviations. The retention time and peak area RSDs were <0.1% and <0.6%, respectively.

Table 1. Precision for ammonia in 1.0 mg/mL sodium bicarbonate

Ammonia (µg/mL)	Retention time (min)	Retention time RSD	Peak area (µS*min)	Peak area RSD
0.02	27.838	0.05	0.0159	0.59
0.1	27.791	0.03	0.0768	0.18
0.5	27.727	0.03	0.3939	0.44

Linearity, LOD, and LOQ

Nine concentration levels of ammonium standards were prepared in the range of 0.02–2 mg/L to create the calibration curve. A quadratic fit was used. The coefficient of determination was 0.9997.

To determine LOD and LOQ, a low concentration of ammonium standard was injected, and the signal-to-noise ratio was determined using the formula 2H/h. H is the peak height from the middle of the noise band to the top of the peak, and h is the noise measured in a time range as wide as five times peak width at 50% of the peak height. LOD was calculated to be 0.0004 µg/mL at S/N = 3, and LOQ was calculated to be 0.0013 µg/mL at S/N = 10.

Accuracy

The accuracy of the method was verified by determining recoveries of spiked ammonia in the sample solution in three replicates, repeated over three consecutive days. Three concentrations of ammonia in 1.0 mg/mL sodium bicarbonate were tested. The average recoveries ranged from 74% to 94% as shown in Table 2.

Table 2. Recovery for ammonia in sodium bicarbonate

Spike level (µg/mL)	Recovery (%)
0.02	74
0.1	84
0.5	94

Conclusions

The study successfully demonstrates the performance of a Dionex Inuvion IC system using a Dionex IonPac CS16 column for determining ammonia in sodium bicarbonate.

References

1. Thermo Scientific Application Note 1073: Determination of Ammonia in Sodium Bicarbonate.
2. Sodium Bicarbonate. U.S. Pharmacopeia National Formulary USP43 NF38 (2023) 4056.

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