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N-nitrosodimethylamine (NDMA) Analysis in Water Using GC Triple Quadrupole Mass Spectrometry in Positive Chemical Ionization Mode

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Background

N-nitrosodimethylamine (NDMA) is highly active carcinogen produced during chlorination or chloramination of nitrogen containing wastewater (Njam et al., 2001). The compound is regulated, having an admissible concentration of 7ng/L in drinking water as determined by the EPA, although current permitting levels can reach as low as an order of magnitude below this value (Andrzejewski et al., 2005). Analysis of NDMA is most commonly performed by liquid-liquid extraction and gas chromatography mass spectrometry. Recent interest in low level NDMA occurrence in water sources has pushed method development forward using higher precision analytical instruments to reach new detection limits. EPA 521, the current drinking water method for detection and quantification of NDMA recommends the use of gas chromatography ion trap MS/MS mass spectrometry with positive chemical ionization and a liquid reagent such as methanol or acetonitrile.

Focus

The focus of this work was to develop a method for analysis of NDMA and related compounds using positive chemical ionization (PCI) GC/MS/MS analysis. Low level detection was a particular focus of this method. Chemical ionization, is a "soft" ionization process, resulting in less molecular fragmentation and greater sensitivity for amino compounds (Charrois et al., 2004). Ammonia reagent gas also produces selective [M+18] and [M+H] adducts for quantification, compared to the common low mass ions produced during EI fragmentation (Charrois et al., 2004).

Figure 1: 7890A/7000B GC/MS/MS in the Snyder Research Group Lab.
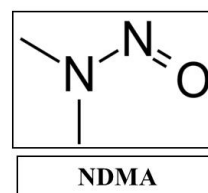
Experimental

Standards and Reagents

NDMA standard was obtained from Supelco, and d6-NDMA surrogate and N-Nitrosodi-n-propylamine-d14 (NDPA-d14) internal standard were obtained from Cambridge Isotope Laboratories Inc. Standards were made up by weight in dichloromethane. Coconut charcoal SPE cartridges, 80/120 mesh, were obtained from Restek. Dichloromethane and methanol were obtained from Fisher Scientific. HPLC grade water was used to prepare the calibration standards.

Sample Preparation

One-half liter of each water sample spiked with NDMA standard at a given concentration was extracted using solid phase extraction (SPE) procedures similar to those described elsewhere (Munch and Basset, 2004). NDMA-d6- was added to samples as a surrogate prior to sample preparation to monitor extraction efficiency. The eluent from the SPE column was reduced to 0.5 mL using a gentle stream of nitrogen at room temperature. The sample was then brought to 1.0 mL with dichloromethane. The final concentration factor was 500 fold. NDPA-d14 was then added as an internal standard.

Instruments

This method was developed on an Agilent 7890A gas chromatograph equipped with an S/S inlet and coupled to an Agilent 7000B Triple Quadrupole GC/MS in positive chemical ionization (PCI) mode. The instrument conditions are listed in Table 1

NDMA

N-nitrosodimethylamine (NDMA) Analysis in Water Using GC-TQ MS in Positive Chemical Ionization Mode

Experimental

GC run conditions

Analytical columns	DB-WAXETR 30 m × 0.25 mm, 0.25 µm (p/n 122-7332)
Inlet temperature	200 °C
Injection mode	Splitless 5-µL injection.
Flow	Constant flow at 1.7 mL/min
Oven program	40 °C for 3 minutes then 10 °C/min to 110 °C for 0 minutes then 15 °C/min to 200 °C for 0 minutes then 40 °C/min to 240 °C for 0 minutes
Carrier gas	Helium Ultra High Purity.
Transfer line temperature	240 °C

PCI MS conditions

Tune	PCI Autotune
EMV gain	15
Acquisition parameters	PCI positive mode with single reaction monitoring (SRM)
Reagent gas	Ammonia, 20 % flow
Collision gas	Nitrogen, constant flow, 1.5 mL/min
Quench gas	Helium, constant flow, 2.25 mL/min
Solvent delay	6.0 minutes
MS temperatures	Source 200 °C; Quadrupole 150 °C

Nitrosamine	RT (min)	SRM	PCI with ammonia mode		
			Dwell time (ms)	Collision energy (EV)	Gain
N-Nitrosodimethylamine (NDMA)	9.141	92 → 75	30	12	15
Deuterated N-Nitrosodimethylamine (NDMA-d6)	9.133	98 → 81	30	12	15
Deuterated N-Nitrosodi-n-propylamine (NDPA-d14)	11.862	162 → 50	30	12	15
		162 → 145	30	12	15

Table 1: GC/MS conditions.

Results and Discussion

PCI with Ammonia

Using the Agilent 7000 Triple Quadrupole GC/MS in positive chemical ionization (PCI) mode with ammonia as the reagent gas and single reaction monitoring (SRM) enables the low detection limits that may be required to monitor NDMA in environmental water samples. Figure 1 illustrates a limit of quantification with a signal-to-noise (S/N) ratio of 12:1 for NDMA at 0.56 ppt (height, Peak-to-Peak, 30 second noise region over 8.4 minutes – 8.9 minutes).

Results and Discussion

S/N = 12.7 (height, peak-to-peak, 0.5 min noise)
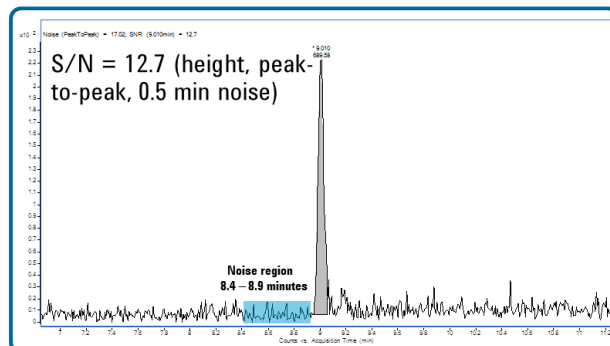
Noise region 8.4 – 8.9 minutes

Figure 1: NDMA signal to noise (S/N) at 0.56 ppt.

Figure 2 shows an overlay of the SRM chromatograms of the 7 calibration levels and Figure 3 illustrates the corresponding calibration curve with a linear correlation coefficient of > 0.999.

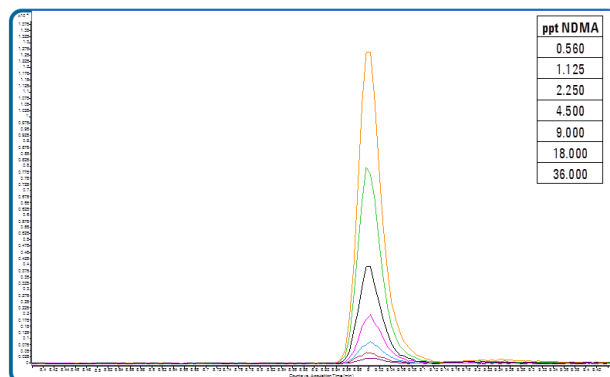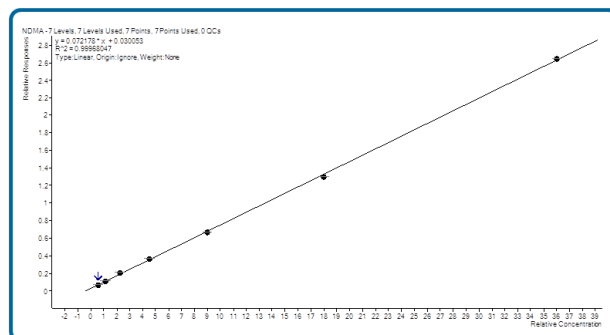| ppt NDMA |
|---|
| 0.560 |
| 1.125 |
| 2.250 |
| 4.500 |
| 9.000 |
| 18.000 |
| 36.000 |

Figure 2. Overlay of NDMA at 7 levels

Figure 3:. Linear calibration curve from 0.56 ppt to 360 ppt.

Results and Discussion

With this data, minimum reportable limits such as the limit of detection and the limit of quantification were determined as 0.20 ppt and 0.56 ppt, respectively at the 99% confidence level for ten replicate injections by using a one-tail Student's-T test with n-1 degrees of freedom. Figure 4 shows typical lab and field blank samples containing approximately 0.6 ppt NDMA and Figure 5 illustrates the NDMA and NDMA-d6 SRM channels of dichloromethane solvent blank and actual drinking water sample from a western city determined to contain 3.4 ppt NDMA.
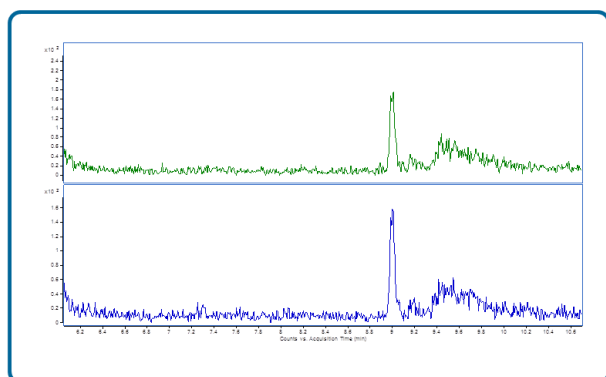

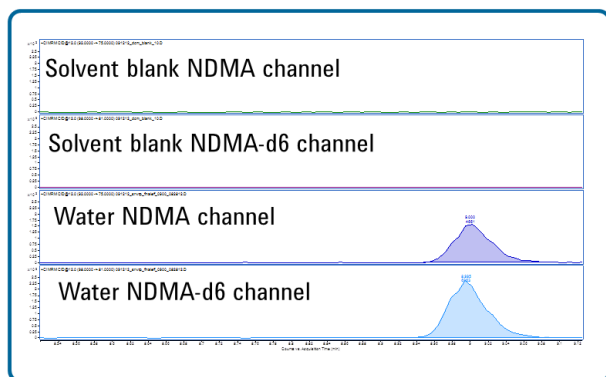Figure 4: Lab (top) and field (bottom) blanks containing approximately 0.6 ppt NDMA

Figure 5. NDMA and NDMA-d6 SRM channels of dichloromethane solvent blank and water sample

Conclusions

The method described herein using the Agilent 7890A GC and 7000B Triple Quadrupole GC/MS system yields limits of detection and quantification of less than part per trillion NDMA in water matrices.

The method was validated by a calibration curve of at least 7 points, with an R2 value of 0.99 or greater for both external and internal standards. Deuterated surrogate was added to samples prior to extraction to correct for recovery during preparation.

References

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Acknowledgements