

LC-MS/MS Solution for Determination of Nitrosamine Disinfection Byproducts in Drinking Water

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Following the 2016 publication of the article, “Nitrosamine Carcinogen, ‘Silent Killer’ - Urgent Water Quality Standards,” nitrosamine compounds have rapidly drawn the widespread attention of the public and of those in the field of analytical monitoring. N-Nitrosodimethylamine (NDMA) is one of the known byproducts of nitrosamine disinfection and has been classified as a Group 2A carcinogen by the International Agency for Research on Cancer. The World Health Organization (WHO) has established a limit of 100 ng/L NDMA in drinking water, although no such quality standards for limiting nitrosamines in drinking water exist in China. In response to public concern, this document presents the use of the QTRAP® 4500 liquid chromatography mass spectrometry system to actively respond to national and societal appeals, partnering with the state to build multi-layered safety protections and full-process monitoring systems spanning from water sources to faucets. The method described for quantifying 8 nitrosamines offers a simple and rapid solution for the accurate determination of nitrosamine disinfection byproducts in drinking water.

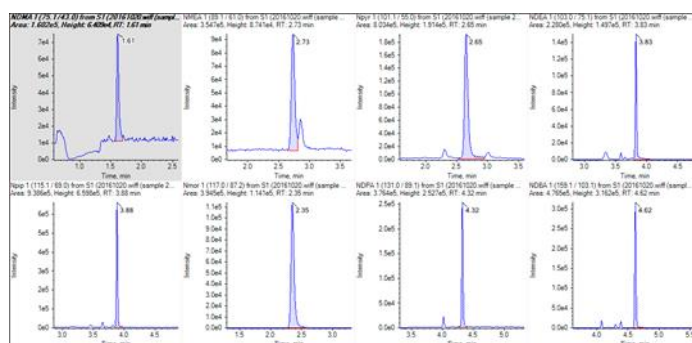
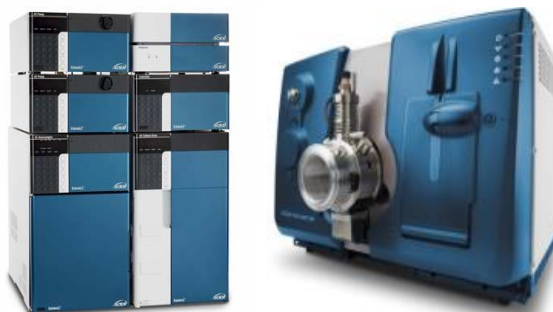


Figure 1: Standard LC-MS/MS Chromatograms of 8 Nitrosamine Compounds. Detection limit below 10 ng/L, far below the standard WHO limit of 100 ng/L.

Nitrosamines Analysis Features

- Simple sample pretreatment with Agela Cleanert SPE
- Total sample runtime is less than 10 min, while still achieving separation of nitrosamine analytes on the Phenomenex Kinetex F5 stationary phase
- Sensitive detection limits below 10 ng/L, far below the standard WHO limit of 100 ng/L
- Method can be easily deployed to any SCIEX QTRAP® or triple quadrupole systems.

Experimental

The SCIEX ExionLC™ system and the QTRAP® 4500 mass spectrometry system were employed during method development and data collection.

Sample Pretreatment: SPE

Cleanert PEP-2 SPE 200mg/6mL (Agela Technologies) + activated carbon column.

Procedure for SPE as follows:

1. Weigh a defined quantity of ammonium bicarbonate to adjust the water pH to around 8
2. Use dichloromethane and methanol in succession to activate, and use water to equilibrate the SPE column
3. Load the sample at 3-5 mL/min, and rinse with ultrapure water after loading
4. Elute with dichloromethane, evaporate to a defined quantity using nitrogen, and add water to make up to a defined volume for LC-MS/MS analysis to be undertaken
5. Transfer a 0.25 mL aliquot to a polypropylene vial and archive the remaining volume

Liquid Chromatography Method:

Chromatographic column: Phenomenex 2.6 μ m F5 100Å. Mobile phase A: water; Mobile phase B: acetonitrile. Gradient elution. Flow rate: 0.5 mL/min. Quantity injected: 20 μ L. Time Program details can be found in Table 1.

Table 1: LC Gradient Program. Flow Rate of 0.5 mL/min.

Time (min)	A% (water)	B% (acetonitrile)
0	95	5
1.5	95	5
3.5	10	90
5.1	95	5
7	95	5

Mass Spectrometry Method:

Ion source: APCI source, positive ion mode. Ion source parameters: CUR: 30psi GS1: 50psi, NC: 5, TEM: 400°C, CAD: medium. Figure 2 shows the structure of nitrosamines, while Figure 3 shows the parameters of the MRM transitions for each.

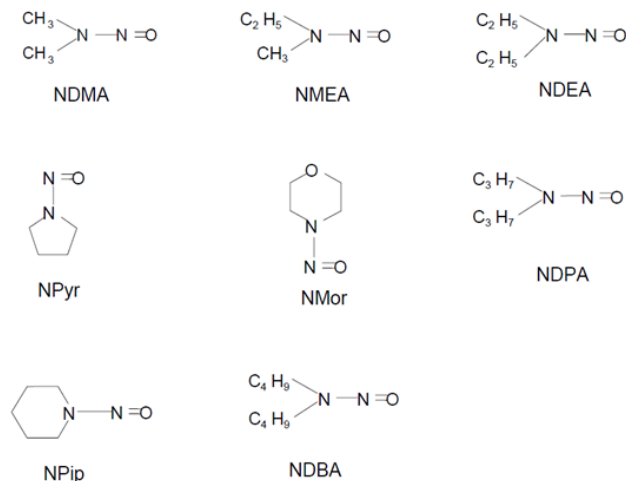


Figure 2: Structures of 8 Nitrosamine Compounds Selected for Quantitative Analysis.

Results

The analyzed standards showed sensitivity down to 10ng/L (Figure 1) and the linear response of all eight nitrosamines was demonstrated with calibration curve r – values > 0.99 (Figure 4).

	Q1 Mass (Da)	Q3 Mass (Da)	Time (msec)	ID	DP (volts)	CE (volts)
1	75.100	43.000	20.0	NDMA 1	40.000	20.000
2	75.100	58.000	20.0	NDMA 2	40.000	16.000
3	89.100	61.000	20.0	NMEA 1	40.000	15.000
4	101.100	55.000	20.0	Npyr 1	40.000	21.000
5	103.000	75.100	20.0	NDEA 1	40.000	15.000
6	115.100	69.000	20.0	Npip 1	40.000	21.000
7	117.000	87.200	20.0	Nmor 1	40.000	16.000
8	131.000	89.100	20.0	NDPA 1	40.000	15.000
9	145.100	97.100	20.0	NDPA-d14	40.000	15.000
10	159.100	103.100	20.0	NDBA 1	40.000	14.000
11	81.000	46.000	20.0	NDMA-d6	40.000	16.000
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Figure 3: Eight Nitrosamine Compounds - Mass Spectrometry Parameters. MRM transitions and optimized voltages utilized for the target nitrosamines.

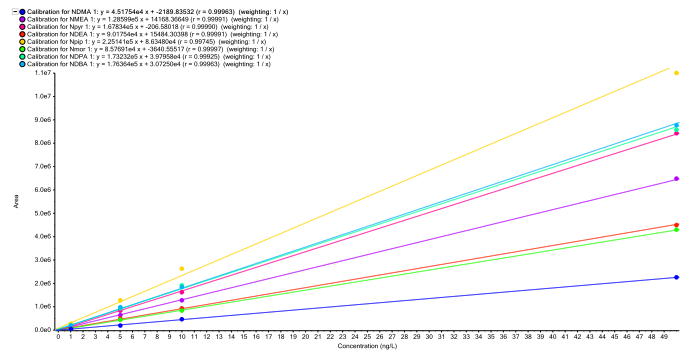


Figure 4: Linear Calibration Curves of 8 Nitrosamine Compounds in Water, Showing Good Linearity ($r > 0.99$).

Conclusions

This paper establishes a comprehensive method for the quantification of nitrosamine compounds, including sample preparation, data acquisition, and data processing using the 4500 QTRAP[®] system. This method offers clients a comprehensive solution that can be performed on SCIEX 3500, 4500, 5500, and 6500 systems, saving on method development time. The advantages of this method include simple sample pretreatment, brief analysis time, and high sensitivity, allowing accurate and quantitative analysis of nitrosamine disinfection byproducts in drinking water.

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