

Improved Analysis of N-Nitrosamines by Atmospheric Pressure Chemical Ionization Liquid

Lihini Tharanga Mendis¹; Ethan R Hain¹; Sarah Monti¹; Valeria Zerda-Pinto¹; Ruth Marfil-Vega¹; Landon A Wiest¹; Christopher Gilles¹; Samantha A. Olendorff¹; William Lipps¹

1. Shimadzu Scientific Instruments, Columbia, MD

1. Introduction

N-nitrosamines are carcinogenic contaminants that are disinfection by-products formed when chloramines react with organic matter dissolved in water. N-nitrosamines are notoriously difficult to analyze due to their low environmental concentrations, low molecular weight, and volatility. ASTM method D8456-22 was designed for the analysis of thirteen N-nitrosamines by LC-MS/MS by direct injection for analysis of groundwater, surface water, and wastewater. LCMS settings, including CID gas pressure, interface temperature, nebulizing/drying gas flows, and interface voltage were optimized to improve sensitivity for the analysis of these N-nitrosamines. These improvements resulted in accurate, reproducible quantitation for these compounds as low as 0.05 ppb in reagent water, dechlorinated tap water, 500 ppm total dissolved solids (TDS) water, and 3000 ppm TDS water.

2. Methods

The thirteen N-nitrosamines and two internal standards were separated by a Nexera LC and quantified by a Shimadzu LCMS-8060RX by APCI according to ASTM D8456-22 (Table 1). The LC stream was diverted to waste at 3 and 11.75 minutes to ensure no loss of analysis, but adequate protection of the LCMS. Standards were prepared in reagent water from 0.05 to 10 ppb. Spiked samples were prepared at concentrations ranging from 0.05 to 6 ppb in reagent water, dechlorinated tap water, 500 ppm TDS water, and 3000 ppm TDS water. Samples were filtered by 0.2 µm nylon filters before being analyzed.

Table 1. LC and MS parameters

LC		MS	
Column	Shim-pack GIST C18, 5 µm, 4.6×150 mm	Temperature Settings	
Mobile Phase		Interface Temp.	250 °C
A		DL Temp.	180 °C
B		Heat Block Temp.	200 °C
Flow Rate		Gas Flow	
Injection Volume		Nebulizing	4 L/min
Column Oven Temp.		Drying	5 L/min
		CID Gas Pressure	210 kPa

LC Gradient

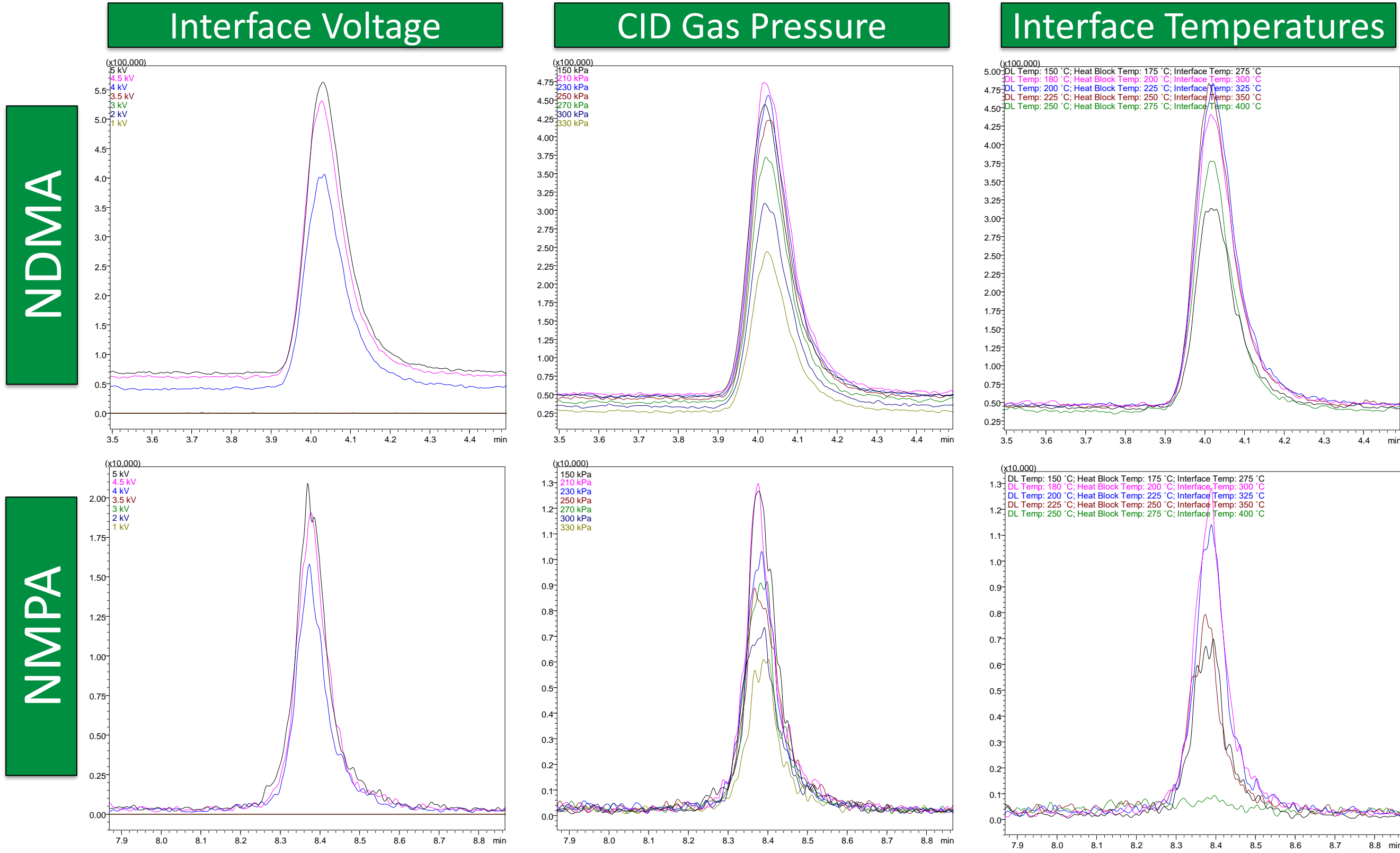
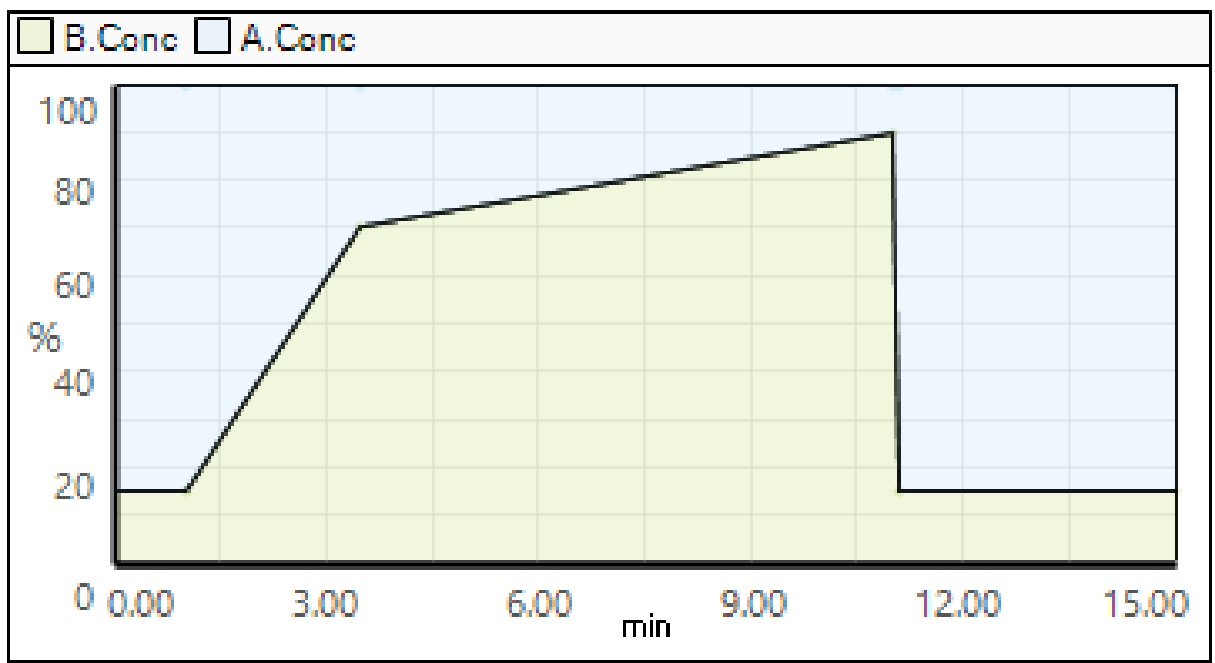


Figure 2. Calibration curves (0.05-10 ppb) for the 13 N-nitrosamine targets and 2 internal standards (2 ppb) in reagent water. Blue squares show repeated points and red dots show the average.

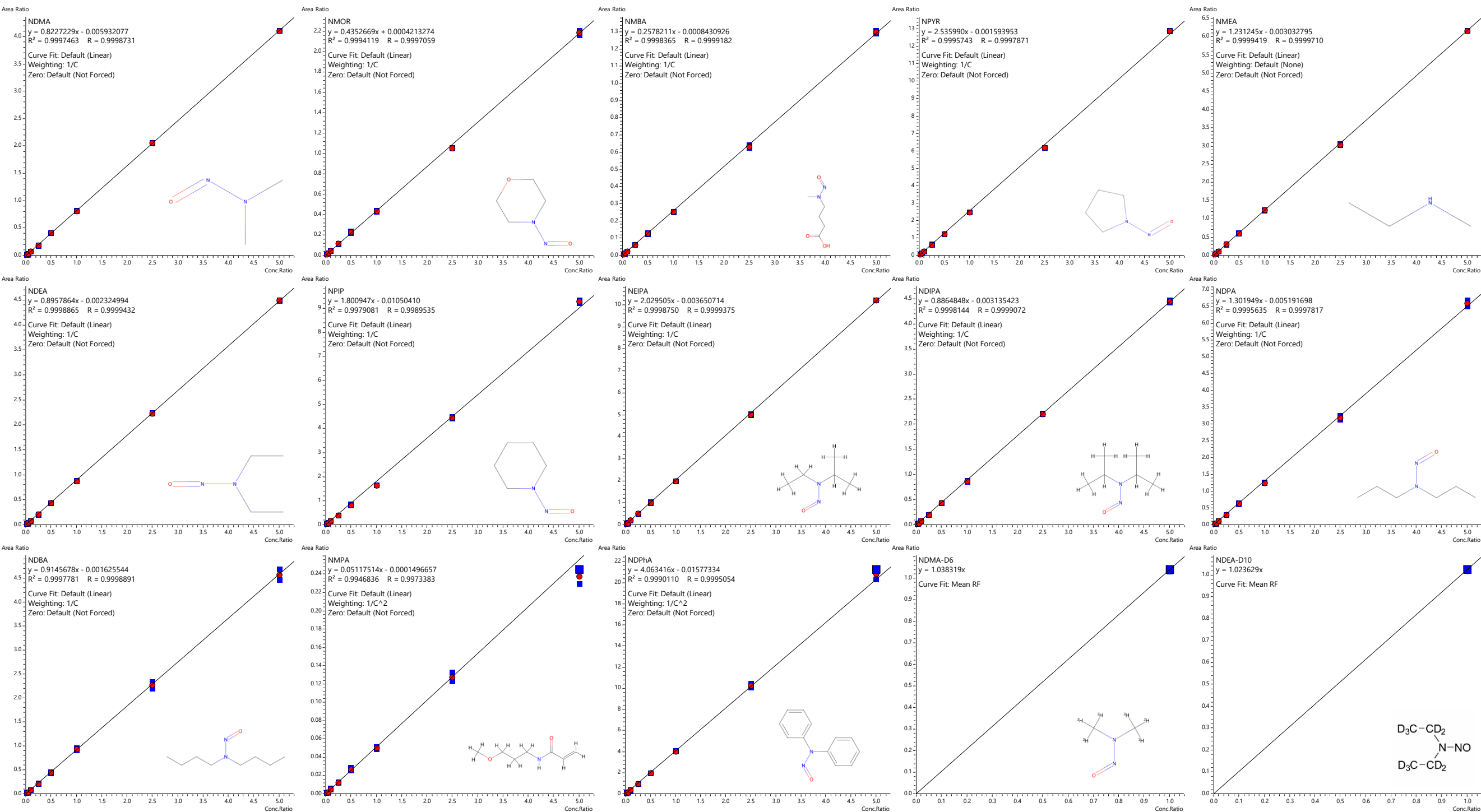
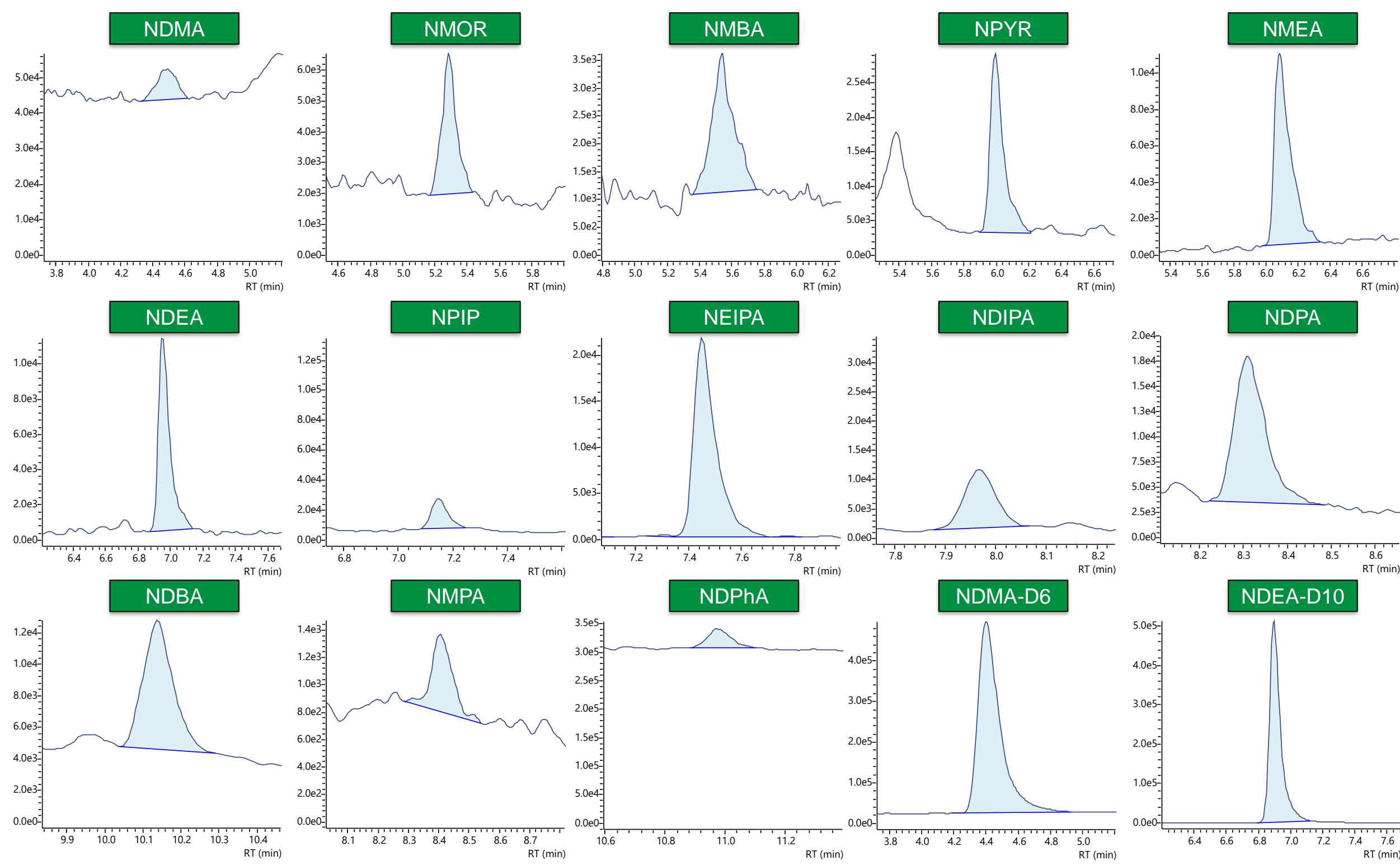


Figure 1 (left). Optimization of method parameters for the two most challenging compounds, NDMA and NMPA. Most compounds ionized best at the highest interface voltage. CID gas pressure was generally better at lower pressures, but interface temperature was optimized primarily for NMPA

Figure 3 (right). Chromatograms of the 15 N-nitrosamines analyzed at 0.05 ppb in 3000 ppm TDS water.



Compound	Transitions	Internal Standard Group	RT (min)	R ²	Accuracy Range (%)	Average Accuracy (%)	%RSD Concentration (0.05 ppb)
NDMA	75 > 43; 75>58	1	4.47	0.99975	86.9-118.9	101.8	7.67
NMOR	TIC (117>87; 117>45; 117> 28)	2	5.27	0.99941	84.2-116.5	100.9	9.69
NMBA	147>117; 147>44	1	5.54	0.99984	89.1-118.2	101.7	5.35
NPYR	101>55; 101>41	2	6.00	0.99957	84.1-106.7	98.8	5.18
NMEA	89>61; 89>43	2	6.08	0.99994	84.8-117.0	100.9	7.49
NDEA	103>29; 103>45	2	6.95	0.99989	83.7-116.7	100.8	5.47
NPIP	115>69; 115>41	2	7.15	0.99791	88.7-118.6	101.7	7.14
NEIPA	117>45; 117>27	2	7.45	0.99988	83.4-113.3	99.1	5.77
NDIPA	131>89; 131>43	2	7.96	0.99981	84.1-115.1	100.1	6.49
NDPA	131>89; 131>43	2	8.35	0.99956	81.7-116.6	100.8	4.33
NDBA	159>41; 159>29	2	10.13	0.99978	86.9-116.4	100.5	9.73
NMPA	137>107; 137>66	2	8.41	0.99468	80.6-117.5	97.5	9.19
NDPhA	170>93; 170>65	2	10.97	0.99901	88.4-117.8	103.7	8.12
NDMA-D6	81>46	1	4.40	NA	99.4-113.3	101.8	3.64
NDEA-D10	113>34	2	6.95	NA	94.4-104.5	98.5	0.58

3. Results and Conclusion

◆ All fifteen N-nitrosamines were separated and analyzed within 15 minutes with a linear range of 0.05-10 ppb with sufficient accuracy and precision (e.g., %RSD < 10%).

◆ The analysis of nitrosamines by APCI-LC-MS/MS was improved through systematic optimization of LCMS parameters and demonstrated to function effectively in four environmentally relevant matrices.

Reference:

• "Standard Test Method for Determination of Nitrosamines in Water by Liquid Chromatography Tandem Mass Spectrometry (LC-MS/MS)," ASTM D8456-22, ASTM International, 2022.

Disclaimer:

The products and applications in this presentation are intended for Research Use Only (RUO). Not for use in diagnostic procedures. ¹The authors are affiliated and funded by Shimadzu Corporation. ²The named authors declare no competing financial interest.