



Determination of N-nitrosodimethylamine in drinking water by UPLC-MS/MS

Wanfeng Wang¹, Jianying Hu², Jianwei Yu¹, Min Yang^{1,*}

1. State Key Lab of Environmental Aquatic Chemistry, Research Center for Eco-Environmental Sciences, Chinese Academy of Sciences, Beijing 100085, China. E-mail: fengmanlou2005@gmail.com

2. College of Environmental Science, Peking University, Beijing 100871, China

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Abstract

The method for detecting N-nitrosodimethylamine (NDMA) in drinking water using ultra performance liquid chromatography (UPLC) coupled with tandem mass spectrometry (MS/MS) was improved by optimizing the clean-up procedure to remove the matrix interference in pretreatment process, and was then applied to a survey of NDMA in both raw and finished water samples from five water treatment plants in South China. The NDMA concentrations ranged from 4.7 to 15.1 ng/L in raw water samples, and from 4.68 to 46.9 ng/L in finished water. The NDMA concentration in raw water was found to be related with nitrite concentration, and during the treatment, the NDMA concentration increased following ozonation but decreased after subsequent activated carbon treatment.

Key words: drinking water; N-nitrosodimethylamine; UPLC-MS/MS; the matrix interference

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Introduction

N-Nitrosodimethylamine (NDMA) is one of the family members of extremely potent carcinogens, teratogens, mutagens known as N-nitrosamines (IARC, 1978), which was estimated to have an excess lifetime cancer risk of 10^{-6} at a concentration of 0.7 ng/L in drinking water by the US Environmental Protection Agency (US EPA, 2009). Because of its high carcinogenic potency, NDMA has become one of the most focused DBPs in drinking water industry since it was first detected as a new disinfection byproduct in drinking water in Ontario, Canada in 1989 (Jobb et al., 1992). It is now listed among the Unregulated Contaminant Monitoring Rule2 (UCMR2) (US EPA, 2006). Although the maximum contaminant level (MCL) for NDMA in drinking water has not yet been established in the USA, limits have been set at 10 ng/L in California (OMOE, 2003) and at 9 ng/L in Ontario (SDWA, 2002).

The occurrence of NDMA in drinking water treatment processes has been investigated throughout Canada and the USA, and NDMA was found to be existed with the highest concentration of 100 ng/L in some drinking water distribution systems in Alberta of Canada (Barrett et al., 2003), and 30 ng/L in twenty-one finished water samples in USA (Charrois et al., 2007). The NDMA concentration in Japan is relatively low: the highest concentration was 10 ng/L in five plants of twenty-one drinking water treatment plants (DWTPs) (Mari et al., 2009). Up to now, in China, there is no report regarding the occurrence of NDMA in

drinking water systems. However, it is easy to speculate that NDMA should exist in some urban water systems, considering the fact that source water pollution problem is still serious and chloramine disinfection is adopted in many waterworks.

Due to the low concentration of NDMA in drinking water, a sensitive and specific analytical method of NDMA in drinking water is necessary. With the rapid development of analytical methods, some high resolution instruments like GC-MS/MS, GC-HRMS and LC/MS/MS combined with sample pre-concentration method has been applied to the analysis (William et al., 2003; Mari et al., 2009). Currently both liquid-liquid and solid-phase extraction (SPE) methods have been utilized for the extraction of NDMA from water samples (Charrois et al., 2004; US EPA, 2004). Liquid-liquid extraction (LLE) required the use of large organic solvents and the processes were labor-intensive and time-consuming since NDMA is hydrophilic, polar compound. Compared with LLE for sample preparation, SPE has the advantages of shorter processing time and less solvent requirement. But the matrix interference could not be removed easily in analyzing NDMA by SPE-LC-MS/MS. Therefore, in this study, the clean-up procedure was optimized to remove the matrix interference during the analysis of NDMA using an UPLC-MS/MS system. A survey of NDMA in both raw water and finished water samples from five waterworks in South China was conducted using the improved method. This study will provide valuable information regarding the occurrence of NDMA in drinking water in China.

* Corresponding author. E-mail: yangmin@rcees.ac.cn

jesc.ac.cn

1 Materials and methods

1.1 Chemicals and materials

Standard solution of NDMA (200 µg/mL) and isotopically labeled standard [6-²H₂] NDMA (NDMA-d₆, 0.1 g) were obtained from Supelco (USA). Methanol, dichloromethane, diethylether, acetonitrile and hexane of HPLC grade, were obtained from Fisher Chemical Co., (USA). Sodium bicarbonate was obtained from Beijing Chemical Co., (China) and ammonium bicarbonate from Fluka (USA). Solid phase extraction cartridges (Sep-Pak[®] plus AC-2, 400 mg and Sep-Pak[®] Vac florisisil, 1 g/6 mL) were obtained from Waters (Milford, USA) and glass fiber pads (GF/C, 1.2 µm) were obtained from Whatman Co. (Maidstone, UK). Stock solutions (10 mg/L in methanol) for all standard substances were prepared, and stored at –20°C.

1.2 UPLC-MS/MS analysis.

Separation was performed on an ACQUITY UPLC system with a BEH C18 column (2.1 mm × 150 mm i.d., 1.7 µm; Waters, USA). The mobile phase was composed of 10 mmol/L ammonium bicarbonate aqueous solution and acetonitrile. The ratio of solvent acetonitrile was changed as follows: increased from 5% to 55% from 0 to 3.5 min, then increased to 95% over 0.35 min, maintained at 95% for 2.2 min, and returned back to 5% over 0.35 min, followed by a 2 min re-equilibration prior to the next sample injection. The flow rate was 0.2 mL/min for all stages and the sample injection volume was 20 µL. Source temperature, desolvation temperature, the rate of desolvation gas, and the cone gas are 110°C, 350°C, 850 L/hr, and 50 L/hr, respectively. Detection was performed using an ACQUITY TQD tandem mass spectrometer (Waters, USA) operated in the electrospray ionization (ESI) positive-ion mode. The MRM transitions were *m/z* 74.9/43.1 and *m/z* 74.9/57.9 for NDMA and *m/z* 81.0/46.0 for NDMA-d₆.

1.3 Sample collection and preparation

Samples were collected from five waterworks, which were all supplied with inland river water, in South China in March 2009. The water quality parameters of samples are shown in Table 1. Plants A and B adopt the conventional treatment process including coagulation, sedimentation and sand filtration. Plants C, D and E adopt ozone-BAC (biological activated carbon) in addition to the conventional process. Of the five waterworks, only plant A adopts pre-chlorination (2 mg/L). Samples of raw water and

finished water were collected from plants C, D and E, and samples of each major treatment steps were collected from plants A and B.

Sodium thiosulfate (100 mg/500 mL) was added to the finished water samples to quench chlorine residue, followed by filtration with glass fiber pads (1.2 µm, Whatman GF/C). After filtration, water samples (500 mL) were basified to pH 8.0 using sodium bicarbonate and added 20 ng/L of surrogate standard (NDMA-d₆) and then extracted with two activated carbon cartridges in series at a flow rate of 3–5 mL/min under vacuum, which were previously conditioned with 20 mL of dichloromethane/diethylether (50:50, V/V), followed in sequence by 20 mL of methanol and 20 mL of pure water. The cartridges were then dried under a slow flow of nitrogen and eluted with 10 mL of dichloromethane/diethylether solution (50:50, V/V) at a flow rate of 2 to 3 mL/min. The eluent was then purified by passing through a florisisil cartridge, which was rinsed with 20 mL methanol and then preconditioned with 10 mL of hexane and 10 mL dichloromethane/diethylether (50:50, V/V) in series. The eluate was concentrated to around 50 µL residues, which was then diluted to 200 µL with dichloromethane for UPLC-MS/MS analysis.

1.4 Method detection limit (MDL) and recovery

The average absolute recovery rates of NDMA in ultrapure water, river water, and finished water samples were 65%, 62%, and 61%, respectively (number of replicates, *n* = 3) (Table 2). The relative recovery obtained using NDMA-d₆ ranged from 96% to 108%. The MDL for NDMA was calculated to be 1.2 ng/L based on a signal-noise ratio of 3:1 using standard solutions in the SIM mode, according to the regulation of the limits of quantification (LOQ)/the method detecting limits (MDL) ratio of 3.3:1 regulated by the International Union of Pure and Applied Chemistry (IUPAC), and the LOQ for NDMA was 3.96 ng/L.

Table 2 Recovery of NDMA in pure, river, and drinking water

	NDMA concentration (ng/L)	Absolute recovery (%) ^a	Relative recovery (%) ^b
Ultrapure water	20	65 (10.2)	108 (13)
River water	20	62 (4.7)	96 (6.2)
Finished water	20	61 (6.3)	103 (4.1)

^a Values shown in parenthesis are relative standard deviation; ^b recovery adjusted relative to NDMA-d₆.

Table 1 Water quality parameters for water samples from drinking water treatment plants (DWTPs)

DWTPs	NH ₃ -N (mg/L)		COD (mg/L)		NO ₂ ⁻ -N (mg/L)		Cl ₂ (mg/L)
	RW	FW	RW	FW	RW	FW	
A	0.67	1.08	5.92	3.76	0.227	< 0.001	1.8
B	0.2	0.21	2.3	1.5	0.022	< 0.001	1.35
C	2.33	< 0.02	7.03	1.93	0.11	< 0.001	1.0
D	2.54	–	–	–	0.104	< 0.003	0.55
E	2.19	0.46	5.04	1.87	0.1	< 0.001	0.56

RW: raw water; FW: finished water.

–: no detection.

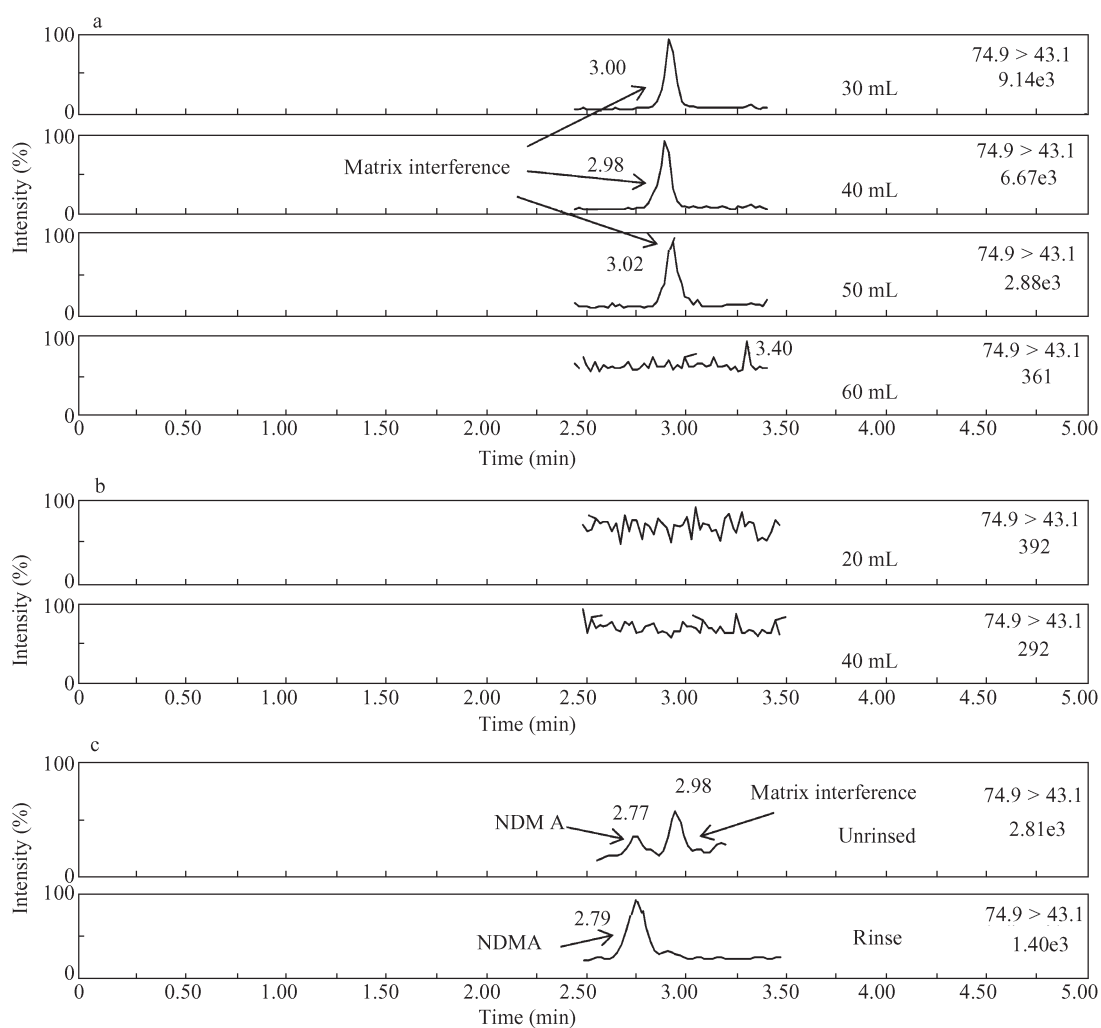


Fig. 1 Optimization of sample preparation. (a) chromatograms of rinsed floril by dichloromethane/diethylether (50:50, V/V); (b) chromatograms of rinsed floril by methanol; (c) comparison between rinsed and unrinsed water samples.

2 Results and discussion

2.1 Optimization of sample preparation

The floril cartridge was reported to be effective in removing the matrix interference in water samples (Mari et al., 2009). However, we found that some materials released from floril cartridges could disturb the NDMA detection, leading to the overestimation of NDMA concentration, even varying with different batches. In order to remove the matrix interference, different solvents were tried for rinsing the floril cartridges. The results are shown in Fig. 1. If the dichloromethane/diethylether (50:50, V/V) solution was used, a volume of 60 mL was required to completely remove the matrix interference released from floril cartridges (Fig. 1a). However, methanol was more effective, which only required 20 mL to completely remove the matrix interference (Fig. 1b). Figure 1c compares the chromatograms acquired with and without methanol rinsing. It is clear that the NDMA peak without the matrix interference was obtained through methanol rinsing.

2.2 Selection of mobile phase

The optimal UPLC-MS/MS conditions are important for the unequivocal identification of NDMA at very low levels in environmental samples. Since the ESI is largely dependent on the solvent conditions, the mobile phase and the additive were investigated. In comparison with acetonitrile/water containing 10 mmol/L ammonium bicarbonate, the mobile phase of acetonitrile/water containing 0.1% formic acid showed a 33% increase in the signal intensity. However, the matrix interference released from floril cartridge could not be eliminated when the latter mobile phase was used for analyzing environmental samples. Thus, acetonitrile/water containing 10 mmol/L ammonium bicarbonate was selected as mobile phase.

2.3 Analysis of NDMA in waterworks

NDMA was detected in both raw water and finished water samples from the five waterworks as listed in Table 3. Figure 2 shows the typical LC-MS/MS chromatograms obtained for raw water, sedimentation effluent, filtration

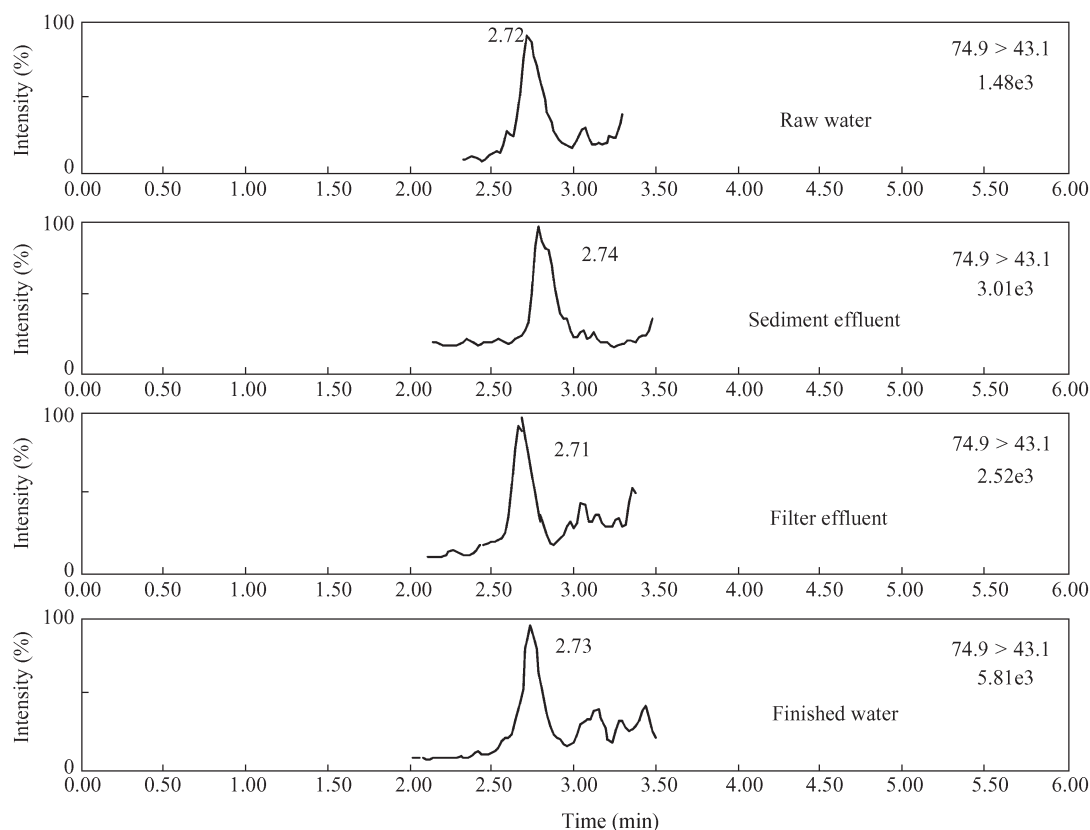


Fig. 2 LC-MS/MS chromatograms of NDMA in water samples from plant A.

effluent, and finished water samples from plant A. The NDMA concentrations in raw water and finished water samples ranged from 4.7 to 15.1 ng/L, and from 4.68 to 46.9 ng/L, respectively, which were comparable to reported results. The concentrations of NDMA in raw water and finished water were 0–2.6 ng/L and 10 ng/L, respectively, in Japan (Mari et al., 2009), 8–9.4 ng/L and 24–30 ng/L in the United States (Barrett et al., 2003), and as high as 66–100 ng/L of NDMA was detected in drinking water distribution systems in Canada (Charrois and Hrudey, 2007). In plant E, the NDMA concentration increased after ozonation, which is also reported previously (Mari et al., 2009; Carles et al., 2008). Among the five waterworks, plant A shows the highest NDMA concentrations in each step. Table 3 also shows that prechlorination could produce significant amount of NDMA in plant A. The NDMA concentrations were very different between plant A and plant B, although they adopt the same water treatment process, showing that the water quality is an important factor for NDMA formation. The COD and ammonia

values of raw water (Table 1) showed that all of the source waters were heavily polluted except for plant B. Especially for plant A, its water intake is located downstream of a river that was contaminated by the discharging of industrial and domestic wastewater, and therefore leading to high concentrations of COD (5.92 mg/L), ammonia (0.67 mg/L) and nitrite (0.227 mg/L), which may be the reason for high NDMA concentration in the raw water. The low NDMA level for plant B might be attributed to its relatively good water quality. The correlations between the water quality indices including total organic carbon (TOC), ultraviolet absorbance, etc. and NDMA concentration were analyzed in previous publications (Zhao et al., 2008; Mari et al., 2009). However, no clear relationship was obtained between the NDMA concentration in the finished water samples and the concentrations of water quality indices in raw water samples. It is interesting that a good relationship was observed between nitrite concentrations and NDMA concentrations in raw water samples (Fig. 3). However, the values of other parameters (residual chlorine, ammonia, COD) have no relationship with NDMA concentrations in both raw water and finished water samples.

On the other hand, the relatively low NDMA concentrations in plants C, D and E might be attributed to the adoption of ozone-BAC process. It is obvious in plant E that after ozonation, the NDMA concentration increased from 4.7 to 14.3 ng/L as shown in Table 3, but it decreased markedly (from 14.3 to 4.48 ng/L) after activated carbon filtration treatment with a removal of more than 68%. The removal was in accordance with the results previously

Table 3 NDMA concentration in water samples from waterworks

DWTPs	NDMA concentration (ng/L)				
	RW	SE	OE	FE	FW
A	15.1	28.8	–	22.6	46.9
B	5.12	6.61	–	4.69	5.97
C	8.9	nd	nd	nd	5.8
D	8.1	nd	nd	nd	nd
E	4.7	nd	14.3	nd	4.48

SE: sedimentation effluent; OE: ozonation effluent; FE: filtration effluent. nd: no detection ; –: no process in the waterworks.

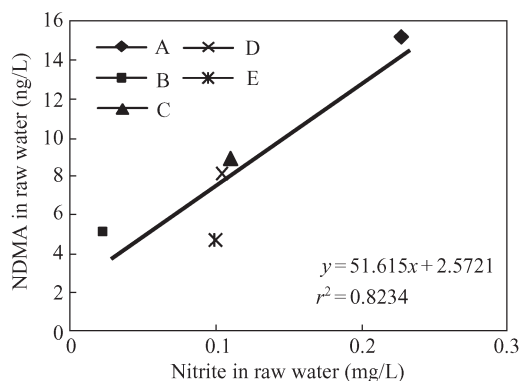


Fig. 3 Correlation between NDMA formation and the water quality.

reported (Mari et al., 2009; Carles et al., 2008).

3 Conclusions

Methanol can be considered an effective solvent to remove the matrix interference from florisil cartridges in analyzing NDMA in water samples. A survey on five waterworks in South China showed that all the five raw water samples contained NDMA (4.7–15.1 ng/L), which was related with the nitrite concentrations in raw water. Among the five waterworks, only plant A showed a significant increase of NDMA in finished water. The relatively low NDMA concentrations in other plants might be attributed to the adoption of ozone-BAC process or relatively good raw water quality. This primary study regarding the occurrence of NDMA in drinking water in China could provide the first information on the potential risk of NDMA from waterworks in China.

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