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A new method for quantifying *N*-nitrosamines in wastewater samples by gas chromatography—triple quadrupole mass spectrometry

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ABSTRACT

We developed a methodology for the separation, identification, and quantification of eight *N*-nitrosamines. For a range of wastewater samples, including raw sewage and final-discharge wastewater, the methodology, which was based on solid-phase extraction (SPE) and a purification technique followed by analysis using a gas chromatograph equipped with a triple-quadrupole mass spectrometer, gave effective separation of the targeted compounds. The limits of detection of this method for *N*-nitrosamines in wastewaters ranged from 0.1 to 1.0 ng L^{-1} and the limits of quantification ranged from 0.4 to 3.3 ng L^{-1}. As a result of preliminary recovery testing, we decided on a combination of two types of sorbent cartridges for SPE—one was aminoprophyl for sample purification and the other was activated charcoal for analyte concentration—that gave excellent recovery rates (98% to 152%) of three deuterided nitrosamines (surrogates). Using this combination of SPE, internal surrogates, and an injection surrogate, we obtained good recovery rates (80% to 131%) with low relative standard deviations (1% to 14%, $n=3$) for eight *N*-nitrosamines in all samples of influent, secondary effluent, and final discharge. We applied the newly developed pre-treatment method to an influent wastewater samples. All of the *N*-nitrosamines except two (NMEA and NDPA) were detected in the influent sample, at 1 to 1057 ng L^{-1}.

1. Introduction

Nitrosamines are mutagenic and carcinogenic compounds widely present in the environment [1–4]. *N*-nitrosamines are produced by reaction of amines or their derivatives with nitrosating agents such as nitrous acid, nitrites, or nitrogen oxides [5–7]. Recommendations about the presence of *N*-nitrosodimethylamine (NDMA) and other nitrosamines in drinking water have been recently adopted in various countries [8,9]. The California Department of Health Services has established a notification level of 10 ng L^{-1} for NDMA, *N*-nitrosodiethylamine (NDEA), and *N*-nitrosodipropylamine (NDPA). On the basis of a 10^{-4} cancer risk, it has also established response levels of 200, 100, and 500 ng L^{-1} for NDMA, NDEA and NDPA, respectively. A provisional guide value of 12 ng L^{-1} was proposed for NDMA in the Netherlands in 2004, and a guide value of 10 ng L^{-1} for NDMA and *N*-nitrosomorpholine (NMOR) in drinking water has been recommended in Germany. In 2003, Ontario issued an interim maximum acceptable concentration of 9 ng L^{-1} for NDMA [10,11]. The U.S. Environmental Protection Agency has added several nitrosamines to the list of non-regulated pollutants [12]. For wastewater, in the early 1990 s a regulatory level of 200 ng L^{-1} in effluents was established for NDMA by the Ontario Ministry of Environment and Energy [13].

N-nitrosamines [NDMA, NDEA, NMOR, NDPA, *N*-nitrosopyrrolidine (NPYR), *N*-nitrosopiperidine (NPIP), and *N*-nitrosodibutylamine (NDBA)] have been detected in wastewater [2,8,14–16]. NDMA and NMOR in surface waters [3,8] and NDMA, NDEA, NMOR, NPYR, NPIP, and *N*-nitrosodiphenylamine have been detected in drinking water [1,4,9,17].

The need to detect nitrosamines in the low-nanogram-per-liter range in water samples is challenged by the fact that enrichment of these very polar but uncharged compounds from water and selective detection of the small molecules are both difficult. However, several sensitive methods based on solid-phase extraction (SPE) with carbonaceous adsorbents and gas chromatography—mass spectrometry (GC–MS) has been developed [1,13,18–20]. On the other hand, The applicability of liquid chromatography (LC) coupled to MS to detect nitrosamines has so far mainly been shown for tobacco-specific nitrosamines [21,22]. Only recently, 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

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samples from five water treatment plants in South China [23]. When starting our own studies on nitrosamines in wastewater, it turned out that LC coupled to low-resolution tandem mass spectrometry was not sufficiently selective for the detection of several of the nitrosamines of interest in this complex matrix. This encouraged us to explore the suitability of high resolution tandem mass spectrometry using the recently developed LTQ Orbitrap MS [24]. Concerning the extraction of nitrosamines from water samples, liquid–liquid extraction (LLE) [25], SPE with carbonaceous adsorbents such as Ambersorb 572 [13, 10 and 25] and coconut charcoal [26,27], and solid-phase microextraction (SPME) [28] and [25] have been used. In spite of the highly variable and low recoveries obtained for NDMA when using LLE and SPE with Ambersorb 572, relative low detection limits were obtained with GC/LRMS analysis (2–5 ng L^{-1}) [27]. On the contrary, the methods based in SPME and GC/LRMS analysis showed a limited sensitivity for nitrosamines, with detection limits of 30–138 ng L^{-1} [27]. In 2004, the EPA created a method to measure nitrosamines (EPA Method 521) based on SPE with coconut charcoal cartridges EPA 521 and GC/MS/MS, using large volume injection, an ion trap mass spectrometer and chemical ionization with methanol or acetonitrile [26]. On the other hand, the method from the Ontario Ministry of the Environment is based on SPE with Ambersorb 572 and GC/HRMS analysis [10]. Both methods achieve low detection limits for nitrosamines in water samples (0.26–0.66 and 0.4–0.8 ng L^{-1}, respectively).

In general, electron ionization coupled with low-resolution MS lacks the selectivity to be applied to complex matrixes and yields low numbers of rather unspecific fragments. This can be overcome in parts by high-resolution mass spectrometry [13]. The use of positive chemical ionization with ammonia or isobutane as a reagent gas results in more selective ionization, less fragmentation, and the formation of higher molecular weight adduct ions along with the molecular ions [1]. The use of tandem-MS further increases selectivity [18,19]. The goal of this study was to develop a methodology for the separation, identification, and quantification of eight *N*-nitrosamines in wastewater samples. The new methodology was applied to the quantification of these analytes in wastewater samples.

2. Materials and methods

2.1. Chemicals

N-nitrosodimethylamine (NDMA), *N*-nitroso-n-methylethylamine (NMEA), *N*-nitrodiethylamine (NDEA), *N*-nitrosodi-n-propylamine (NDPA), *N*-nitrosopyrrolidine (NPYR), *N*-nitrosopiperidine (NPIP), *N*-nitrosomorpholine (NMOR), and *N*-nitrosodi-n-butylamine (NDBA) were purchased from Supelco (Bellefonte, PA). Deuterated *N*-nitrosodimethylamine-d_6 (NDMA-d_6), *N*-nitrosodi-n-propylamine-d_{14} (NDPA-d_{14}), and *N*-nitrosopyrrolidine-d_8 (NPYR-d_8) were used as internal standards, and toluene-d_8 was used an injection internal standard; these chemicals were purchased from Cambridge Isotope Laboratories (Pointe-Claire, PQ, Canada). As the corresponding isotope-labeled analogs were not available for all of the compounds, we used NDPA-d_{14} as an internal standard for quantification of NDBA and NPYR-d_8 for NMEA, NDEA, NPIP, and NMOR. Individual stock solutions of the standards were prepared at 1 mg L^{-1} in dichloromethane (DCM) and stored at low temperature (−20 °C). Working standard mixtures (10 to 250 μg L^{-1}) of the compounds were prepared daily and used in standard curve preparation. GC–MS-grade DCM was obtained from Wako (Tokyo, Japan). Ultra pure water (Milli-Q) was obtained from Milli-Q-Plus (Millipore, USA).

2.2. Sample collection and preservation for method optimization

For analytical method development and optimization, several types of wastewater samples, namely influent, secondary effluent, and final discharge, were collected from a wastewater treatment plant (WWTP) located in a residential area of city O in Japan. All the samples were collected as grab samples and were filtered with a glass fiber filter (GF/B, pore size: 1.0 μm, Whatman, Osaka, Japan), which was washed with acetone before use. Sodium thiosulfate ($Na_2S_2O_3$ at 10 mg 1000 mL^{-1}) was added to all final discharge samples to quench residual chlorine. All samples were

Table 1
Characteristics of target *N*-nitrosamines, and optimized analytical parameters.

No.	*N*-nitrosamine	CAS number	Molecular weight	Corresponding internal standard	MS parameters		
					PI[a] (m/z)	DI[b] (m/z)	CE[c] (eV)
1	*N*-nitrosodimethylamine (NDMA)	62-75–9	74.08	NDMA-d_6	75	43	−15
						58	−10
2	NDMA-d_6 - internal standard		80.12		80	46	−20
						64	−10
3	*N*-nitroso-n-methylethylamine(NMEA)	10595-95–6	88.11	NPYR-d_8	89	43	−10
						61	−5
4	*N*-nitrosodiethylamine (NDEA)	55-18–5	102.14	NPYR-d_8	103	56	−20
						75	−5
5	*N*-nitrosodi-n-propylamine (NDPA)	621-64–7	130.22	NDPA-d_{14}	131	43	−10
						89	−5
6	NDPA-d_{14} - internal standard		145.20		145	97	−5
7	*N*-nitrosopyrrolidine (NPYR)	930- 55–2	100.11	NPYR-d_8	101	55	−10
						70	−5
8	NPYR-d_8 - internal standard		109.12		109	62	−10
9	*N*-nitrosopiperidine (NPIP)	100-75–4	114.15	NPYR-d_8	115	41	−15
						69	−10
10	*N*-nitrosomorpholine (NMOR)	59-89–2	116.10	NPYR-d_8	117	57	−10
						87	−5
11	*N*-nitrosodi-n-butylamine (NDBA)	924-16–3	158.24	NDPA-d_{14}	159	57	−10
						103	−5

CAS, Chemical Abstracts Service.

[a] Parent ion.
[b] Daughter ion.
[c] Collision energy.

collected in 1-L amber glass bottles, held in the dark at 4 °C, and analyzed within 10 h (Table 1).

2.3. Optimization of SPE

The wastewater matrix presents several challenges for analytical chemists, including unwanted chemical interference and low or enhanced ionization of targeted chemicals. To optimize the method of SPE, we performed pre-treatment using various sequences of cartridges containing sorbent. Other previous studies, SPE with carbonaceous adsorbents such as Ambersorb 572 [13, 10 and 25] and coconut charcoal [26] have been used. However, our previous study [16], we used the AC-2 (400 ± 20 mg, Activated Carbon, Waters, Osaka) cartridge to extract the NDMA (high recovery rate; 81–89%). Therefore, we also choose the AC-2 cartridge for extraction in this study for other *N*-nitrosamines. Furthermore, we also used NH2 cartridge (silica-based polar-bonded phase with basic character) to reduce the amount of co-extracted acidic interferences in wastewater, substantially. We used five sequences of cartridge and three types of cartridge, namely AC-2, NH2 (360 mg, Aminopropyl, 55 to 105 μm partial size, Waters), and PS-2 (265 mg, Styrene-divinylbenzene copolymer, Waters). To optimize the method of SPE, we compared the different sequences of cartridges in detecting analytes (Table 2).

2.4. Pre-treatment procedure

To validate the analytical method, we analyzed several types of wastewater samples by using the method shown in Section 2.2. First, 200 mL of each corrected sample was filtered with a GF/B glass fiber filter. Then the deuterated forms of NDMA (NDMA-d_6; CDN Isotopes, Pointe-Claire, Canada), NDPA (NDPA-d_{14}; CDN Isotopes), and NPYR (NPYR-d_8; CDN Isotopes) were added to all filtrate samples as internal standards and the *N*-nitrosamines in the filtrate were concentrated in a Sep-Pak NH2 cartridge (as a sample clean-up step) and an AC-2 cartridge (Mode 3) at a rate of 10 mL min^{-1}. Use of the NH2 cartridge (silica-based polar-bonded phase with basic character) substantially reduces the amount of co-extracted acidic interferences. The cartridges were conditioned in advance with 5 mL of DCM, 5 mL of methanol, and 5 mL of Milli-Q water. After concentration, only the AC-2 cartridge was dehydrated, using a pneumatic pump (Ulvac, DA-6-S, Osaka, Japan), for 2 h, in order to remove the remaining water in the cartridge. *N*-nitrosamines were eluted from the dehydrated cartridge with 2 mL of DCM. The eluate was further concentrated with a gentle stream of N_2 gas at 35 °C just before dryness. The residue was reconstituted in 200 μL of DCM and subjected to *N*-nitrosamine quantification by GC–MS/MS. To correct for fluctuations in the GC–MS/MS apparatus, an injection internal standard (toluene-d_8: CDN Isotopes) was added just before injection of the samples into the system.

Table 2
Optimization of SPE by using different sequences of cartridges for *N*-nitrosamine detection.

Cartridge	Mode				
	1	2	3	4	5
A[a]	Single AC-2	Double AC-2	NH2	AC-2	PS-2
B[b]			AC-2	NH2[c]	AC-2

[a] Top cartridge.
[b] Bottom cartridge.
[c] Attached below the dried AC-2 cartridge.

2.5. Measurement by GC–MS/MS

The eight *N*-nitrosamines, their three internal standards, and the injection internal standard were analyzed on a Varian 300 triple-quadrupole mass spectrometer (Varian, Tokyo, Japan) coupled to a Varian 450 gas chromatograph (Varian). Chromatographic separation was achieved in a FactorFour VF-17 ms capillary column (Varian; 30 m length, 0.25 mm ID, and 0.25 μm film thickness). Specific information details of GC–MS/MS are given in Table 3.

An optimization process was performed for each analyte to optimize data acquisition under multiple reaction monitoring (MRM) mode. This process was performed by injecting 1 mg L^{-1} of individual standard solutions without using a column. Collision energy and ionization mode were optimized for each analyte in order to obtain maximum sensitivity with the greatest amount of product ions available, and the most sensitive MRM transitions were determined for each analyte. NDMA was quantified by using the m/z 75 parent ion and 43 and 58 daughter ions, and NDMA-d_6 was quantified by using the m/z 80 parent ion and 46 and 64 daughter ions. NMEA was quantified by using the m/z 89 parent ion and 43 and 61 daughter ions, and NDEA was quantified by using the m/z 103 parent ion and 56 and 75 daughter ions. NDPA was quantified by using the m/z 131 parent ion and 43 and 89 daughter ions, and NDPA-d_{14} was quantified by using the m/z 145 parent ion and 97 daughter ions. NPYR was quantified by using the m/z 101 parent ion and 55 and 70 daughter ions, and NPYR-d_8 was quantified by using the m/z 109 parent ion and 62 daughter ions. NPIP, NMOR, and NDBA were quantified by using the m/z 115 parent ion and 41 and 69 daughter ions for NPIP, the m/z 117 parent ion and 57 and 87 daughter ions for NMOR, and the m/z 159 parent ion and 57 and 103 daughter ions for NDBA. The MS parameters are summarized in Table 1. Fig. 1

Separation of the eight *N*-nitrosamines, their three internal standards, and the injection standard (toluene-d_8) was performed in less than 15 min. The chromatograms of the eight *N*-nitrosamines (250 μg L^{-1} spiked Milli-Q water extract) are shown in Fig. 2.

3. Results and discussion

3.1. Limit of detection (LOD) and limit of quantification (LOQ)

The LOD and LOQ of this method were determined by measuring standard solutions with *N*-nitrosamine concentrations of 5, 10, 20, 50, and 100 μg L^{-1} by GC–MS/MS. From five measurements of each

Table 3
Detailed analytical parameters for GC–MS/MS.

GC chromatograph (Varian 450-GC)	
Column	VF-17 ms, 30 m × 0.25 mm ID
Flow rate	1 mL min^{-1}
Oven program	40 °C, hold 1 min, To 80 °C at 5 °C min^{-1}, To 280 °C at 20 °C min^{-1}, hold 3 min
Injector temperature	250 °C
Injection mode	Splitless, hold 1 min
Injection volume	2 μL
Mass spectrometer (Varian 300-MS)	
Ionization mode	Positive chemical ionization
Detector range	600 to 2000 V
Source temperature	220 °C
Transfer line temperature	250 °C
Carrier gas	Helium at 1.5 mL min^{-1}
CI gas	Methane
Filament Current	50 μA
Electron energy	70 eV

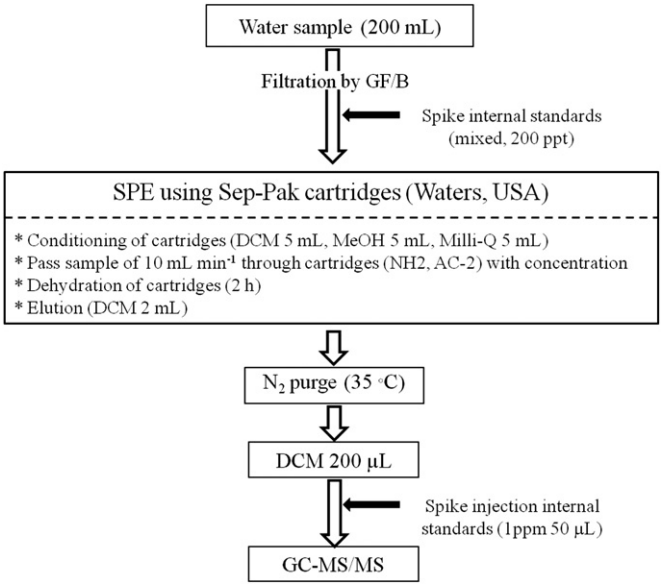

Fig. 1. Pre-treatment process flow chart for the eight *N*-nitrosamines and their three internal standards.

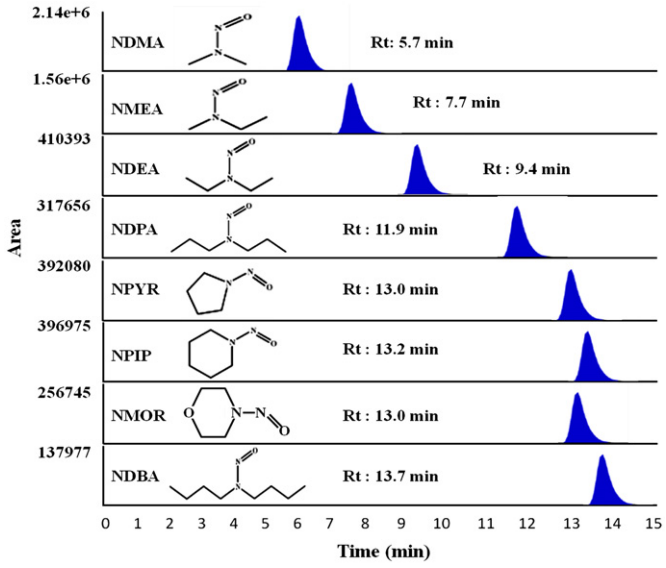

Fig. 2. Compound structures and GC–MS/MS chromatograms for the eight *N*-nitrosamines (250 µg L^{-1} standard solution; Rt: retention time).

solution, the mean, SD, and RSD were calculated. Using the SD (σ) of the solution with the lowest concentration and an RSD of $<20\%$, the LOD of the eight *N*-nitrosamines was in the range of 0.1 to 1.0 ng L^{-1} and the LOQ was in the range of 0.4 to 3.3 ng L^{-1}. Detail information on the LODs and LOQs of the eight *N*-nitrosamines is given in the Supplementary material (Table S1). Other previous studies, detection limits were in the range of 2 to 5 ng L^{-1} for NDMA with GC/LRMS analysis using SPE with Ambersorb 572 [25], and 30–138 ng L^{-1} using SPME and GC/LRMS analysis for NDMA and other six *N*- nitrosamines [27].

3.2. Method validation and recovery analysis

The recovery rates of eight *N*-nitrosamines and the three internal standards were investigated by adding a standard solution (200 ng L^{-1}) of each of the eight *N*-nitrosamines and three internal standards into the influent, secondary effluent, final discharge, and Milli-Q ($n=5$). Furthermore, the rates of recovery of the eight *N*-nitrosamines were compared with and without the addition of internal standards. The rates of recovery were calculated as:

$$\text{Recovery}(\%) = (\text{Ca}-\text{c})/\alpha \times 100 \quad (1)$$

where Ca is the concentration of each of the eight *N*-nitrosamines in the sample with standard solution added (ng L^{-1}), *C* is the concentration in the original sample, and α is the concentration in the standard solution.

The recovery rates of internal standards from WWTPs and Milli-Q water using five different cartridge sequences (Table 2) are shown in the Supplementary material (Table S2). The recovery rates using mode 5 (PS-2 cartridge connected AC-2 cartridge) ranged from 60% to 148%, except in the case of for NDPA-d_{14}. Because NDPA-d_{14} was not detected, NDPA-d_{14} was concentrated into the PS-2 cartridge. From our results, we decided that mode 3 (NH2 cartridge connected with an AC-2 cartridge) was the optimum for SPE.

Absolute recoveries of the internal standards in mode 3 ranged from 98% to 152%, with 2% to 10% reproducibility (RSD; n=5), even in wastewater samples (Table S2); these are higher than the reported values (e.g. 20% to 119% in wastewater and 38% to 118% in drinking water samples; [29,30]). Other previous studies for using different SPE material, it was initially reported as an SPE material for the analysis of NDMA by Taguchi et al. [13]. Initial recoveries were 40%, although subsequent work by Cheng et al. [20] reported recoveries of 62% for NDMA and 74–89% for 7 additional *N*-nitrosamines. Cheng et al. [20] also reported 59% recovery of NDMA and 76–95% recovery of 7 additional *N*-nitrosamines using a combination of Ambersorb 572 and graphitic carbon [20]. Charrois et al. [31], which combined Ambersorb 572 with an ethylvinylbenzene-divinylbenzene sorbent, increased recoveries to 98% for NDMA and 78–94% for 7 additional *N*-nitrosamines. Prior to the publication of Method 521, the highest reported recoveries of NDMA and *N*-nitrosodiethylamine (NDEA) on carbon sorbents were reported by Kawata et al. [32] and Kadokami et al. [33], in which studies both chemicals were recovered at greater than 90%. However, the carbon SPE materials used by these researchers are not readily available in the United States, and the methodology is not readily amenable to automation. Carbon SPE disks used by Tomkins and Griest [34] demonstrated only 64% recovery for NDMA, while the coconut charcoal column SPE method reported by Greene et al. [35] had a more promising recovery of 84% for NDMA.

3.3. Comparison of recovery rates with and without the use of internal standards

As the corresponding internal standard was not available for all compounds, we used NDPA-d_{14} as an alternative internal standard for quantification of NDBA and NPYR-d_8 for quantification of NMEA, NDEA, NPIP, and NMOR. We determined the recovery rates with (R2) and without (R1) corresponding internal standards. For all samples of influent, secondary effluent, and final discharge, R2 ranged from 80% to 131%, with 1% to 14% reproducibility (RSD; n=3), whereas R1 ranged from 55% to 370% (Table 4). We therefore considered that NDPA-d_{14} was an appropriate alternative internal standard for quantification of NDBA, and that NPYR-d_8 was appropriate for NMEA, NDEA, NPIP, and NMOR.

3.4. Application to wastewater analysis

We applied the newly developed pre-treatment method to an influent sample. Fig. 3 shows a segment of the extracted MRM chromatograms of six *N*-nitrosamines and three internal standards

Table 4
Recovery rates of *N*-nitrosamines from influent, secondary effluent, final discharge, and Milli-Q water.

N-nitrosamine	Recovery rate ± relative SD (%, $n = 3$)							
	Wastewater						Milli-Q water	
	Influent		Secondary effluent		Final discharge			
	R1[a]	R2[b]	R1	R2	R1	R2	R1	R2
NDMA	78 ± 1	104 ± 4	176 ± 2	90 ± 4	59 ± 13	95 ± 9	90 ± 5	98 ± 5
NMEA	81 ± 2	107 ± 2	176 ± 6	97 ± 9	61 ± 14	100 ± 5	92 ± 5	100 ± 5
NDEA	136 ± 1	110 ± 1	213 ± 6	118 ± 7	162 ± 4	122 ± 12	100 ± 4	109 ± 7
NDPA	191 ± 7	91 ± 12	240 ± 5	97 ± 2	231 ± 13	111 ± 4	104 ± 3	104 ± 3
NPYR	288 ± 3	92 ± 6	370 ± 11	130 ± 8	236 ± 14	95 ± 5	131 ± 8	131 ± 8
NPIP	60 ± 3	102 ± 3	280 ± 10	112 ± 6	231 ± 14	111 ± 2	105 ± 4	105 ± 4
NMOR	170 ± 1	81 ± 14	307 ± 8	124 ± 6	222 ± 14	106 ± 8	111 ± 3	111 ± 3
NDBA	168 ± 6	80 ± 9	235 ± 10	95 ± 5	55 ± 7	91 ± 12	91 ± 3	91 ± 3

[a] Recovery rates without internal standards.
[b] Recovery rates with internal standards.

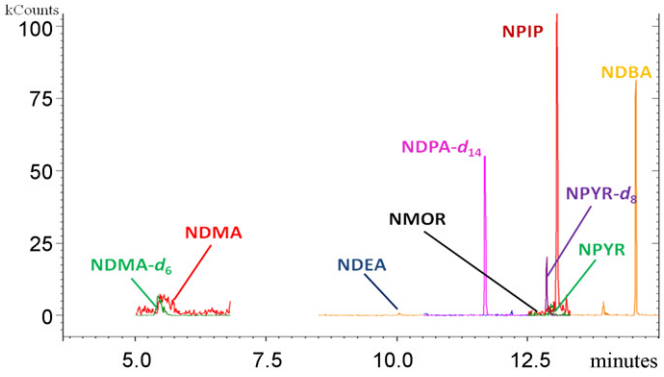

Fig. 3. MRM chromatograms of six *N*-nitrosamines and three internal standards in an influent sample.

Table 5
Concentrations and recovery rates of *N*-nitrosamines from influent in WWTP.

N-nitrosamine	Concentration (ng L^{-1}) with recovery rate ± relative SD (%, $n=5$)
NDMA	84 with 104 ± 4
NDMA-d_6	198 with 99 ± 12
NMEA	ND
NDEA	5 with 110 ± 1
NDPA	ND
NDPA-d_{14}	237 with 123 ± 12
NPYR	52 with 92 ± 6
NPYR-d_8	241 with 137 ± 12
NPIP	320 with 102 ± 3
NMOR	1057 with 81 ± 14
NDBA	5 with 80 ± 9

ND, Not Detected.

in an influent sample. And Table 5 shows that the concentrations and recovery rates of *N*-nitrosamines from influent in WWTP. Two *N*-nitrosamines (NMEA and NDPA) were not detected in the sample.

4. Conclusions

We developed a new pre-treatment and GC–MS/MS method for simultaneous analysis of eight *N*-nitrosamines and three internal standards. Our findings were as follows:

(1) To optimize the pre-treatment method, five different sequences of cartridge were studied. The combination of NH2 cartridge connected to an AC-2 cartridge gave relatively high recoveries of the three internal standards for eight N-nitrosamines, with a recovery range from 98% to 152% and 2% to 10% reproducibility (RSD; n=5), even in wastewater samples.
(2) For samples of influent, secondary effluent, and final discharge, the recovery rates with internal standards ranged from 80% to 131%, whereas the recovery rates without internal standards ranged from 55% to 370%. As a result, we considered that NDPA-d_{14} was an appropriate alternative internal standard for quantification of NDBA, and that NPYR-d_8 was appropriate for NMEA, NDEA, NPIP, and NMOR.
(3) The newly developed method of pre-treatment was applied to an influent sample and yielded *N*-nitrosamine concentrations ranging from not detected to 1057 ng L^{-1}. Recently, NDMA has been discharged from drinking and wastewater treatment plants as a disinfection by-product; levels of NDMA in reclaimed water supplied for reuse will therefore need to be managed carefully. Our new method will be helpful in the analysis of wastewater samples in this context.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.talanta.2012.04.027.

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