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Simple and sensitive determination of hydrazine in drinking water by ultra-high-performance liquid chromatography–tandem mass spectrometry after derivatization with naphthalene-2,3-dialdehyde

Jin-Aa Oh[a], Ho-Sang Shin[b,*]

[a] *Department of Environmental Science, Kongju National University, Kongju 314-701, Republic of Korea*
[b] *Department of Environmental Education, Kongju National University, Kongju 314-701, Republic of Korea*

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ABSTRACT

An ultra-performance liquid chromatography–tandem mass spectrometry (UPLC–MS/MS) method was developed to determine the level of hydrazine in drinking water. The method is based on the derivatization of hydrazine with naphthalene-2,3-dicarboxaldehyde (NDA) in water. The optimum conditions for UPLC–MS/MS detection were determined as follows: derivatization reagent dosage, 50 mg/L of NDA; pH 2; and reaction time, 1 min; room temperature. The formed derivative was injected into an LC system without extraction or purification procedures. Under the established conditions, the method was used to detect hydrazine in raw drinking water and chlorinated drinking water. The limits of detection and quantification for hydrazine in drinking water were 0.003 μg/L and 0.01 μg/L, respectively. The accuracy was in the range of 97–104%, and precision, expressed as relative standard deviation, was less than 9% in drinking water. Hydrazine was detected at a concentration of 0.13 μg/L in one sample among 24 raw drinking water samples and in a range of 0.04–0.45 μg/L in three samples among 24 chlorinated drinking water samples.

1. Introduction

Hydrazine is an inorganic compound with the formula N_2H_4, and it has a wide range of industrial and military applications [1,2]. This compound is primarily used in the manufacture of textile dyes, agricultural chemicals, pharmaceutical intermediates, and rocket fuels and polymerization of urethane as well as for the removal of halogens from wastewater and pharmaceutical intermediates [3–8].

Hydrazine is highly toxic [9–15] and can cause neurotoxicity, hepatotoxicity, and nephrotoxicity in rodents [11] as well as liver, kidney, and central nervous system problems in humans [13,14]. The United States Environmental Protection Agency (USEPA) has not classified hydrazine as a drinking water contaminant but as a probable human carcinogen (B2) [15]. The European Union has classified hydrazine as a substance of very high concern with restrictions on its usage [16]. Hydrazine is carcinogenic, mutagenic, and toxic for reproduction but specific legislation concerning its occurrence in drinking water does not exist [16].

Hydrazine drinking water contamination can originate from industrial waste, wastewater treatment plant effluents, and possible formation in drinking water disinfection processes and distribution systems. Hydrazine can be produced by the reaction of monochloramine with ammonia under chloramination [17–19] but it is not known if it can also be formed with conventional chlorination techniques. Due to these toxicological effects and its potential formation in drinking water under conventional chlorination, analytical approaches capable of detecting trace levels of hydrazine are required.

Hydrazine is difficult to detect in environmental water because it is completely soluble in water, slightly soluble in the low polarity media used for extraction and preconcentration, and prone to oxidation in the course of operations, such as steam distillation [20]. Currently, many analytical methods for the determination of hydrazine have been reported. Among these methods, the chromatographic methods are very specific and sensitive for coupling with derivatization, extraction, and concentration and are recommended for the detection of trace amounts of toxins in water. Specifically, gas chromatography (GC) and high performance liquid chromatography (HPLC) are typically used for the determination of hydrazine in water. GC methods for hydrazine have been developed using electron capture detection [21], nitrogen-selective detection

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* Corresponding author. Tel.: +82 41 850 8811; fax: +82 41 850 8998.
E-mail address: hshin@kongju.ac.kr (H.-S. Shin).

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[22,23], flame-ionization detection [24], mass spectrometry (MS) [23,25–27], and tandem mass spectrometry (MS/MS) [19,28]. HPLC methods have also been developed using diode array detection [20,29–31] and fluorescence detection [32–35]. Both the GC and LC methods require a derivatization step for the sensitive detection of hydrazine.

In GC, derivatization reagents, such as acetone [19], pentafluorobenzaldehyde [21,23], benzaldehyde [22], ethyl chloroformate [24], *n*-hexyl chloroformate [25], octafluoropentylchloroformate [26], *ortho*-phthalaldehyde (OPA) [27], and propyl chloroformate [28], have been used. However, these GC methods require additional extraction and concentration steps after derivatization. In particular, the reaction with propyl chloroformate [28] results in three products (i.e., bi-, tri-, and tetra-derivatives), which make the quantification of hydrazine challenging. HPLC methods also require derivatization reagents, such as 4-chloro-5,7-dinitrobenzofurazan [20,31], cinnamaldehyde [29], benzaldehyde [30], and naphthalene-2,3-dialdehyde (NDA) [32–35]. The most sensitive HPLC method for the determination of hydrazine in water involves the fluorescent derivatization of hydrazine with NDA [32–35], which yields a hydrazine detection limit of 0.05 μg/L.

LC–MS/MS has become a common technique that is used to analyze many types of compounds. In particular, the use of the multiple reaction monitoring (MRM) acquisition mode improves the analytical sensitivity by significantly decreasing the background while ensuring analyte identification. Several reports on the analysis of hydrazine using LC–MS/MS have been published [36,37], and comparable methods for use with drinking water are limited [37].

The aim of this study was to develop a rapid, selective, and sensitive hydrazine determination method using ultra performance (UP) LC–MS/MS after derivatization with NDA. Several derivatization parameters were studied to select parameters with high sensitivity and low interference with the derivative and to optimize the parameters of UPLC–MS/MS for analyzing hydrazine in drinking water. The new method was applied for the determination of hydrazine in drinking water.

2. Experimental

2.1. Reagents

Hydrazine (98%), *ortho*-phthalaldehyde (OPA) (≥99%), naphthalene-2,3-dialdehyde (NDA) (≥99%), anthracene-2,3-dialdehyde (ADA) (99%), sodium bicarbonate, potassium carbonate, potassium hydroxide, and hydrochloric acid (37%) were obtained from Sigma–Aldrich (St. Louis, MO, USA). The HCl was of analytical grade (Sigma–Aldrich). A stock standard solution of hydrazine was freshly prepared prior to use by dissolving 20.4 mg of hydrazine in 100 mL of reagent water. A 0.5 mL aliquot of this solution was diluted to 100 mL with pure water to provide a 1.0 mg/L hydrazine standard solution. This solution was used within 1 h of its preparation. The reagent water used in this study was obtained from Sigma–Aldrich.

2.2. Derivatization

Water sample of 1.0 mL was placed into a glass-stoppered test tube. Hydrochloric acid solution (0.1 M HCl) was added to maintain a pH of 2 for the water followed by agitation for 30 s.

To determine the optimal derivatization conditions, the reaction was performed for various amounts of OPA, NDA, and ADA (1.0, 2.0, 5.0, 10, 20, 30, and 40 mg/L in solution) and reaction times (1, 15, 30, 45, 60, 75, and 90 min) at room temperature in water. The derivatization efficiencies were calculated at various temperatures (25, 40, 50, 60, 70, 80, and 90 °C) and acidities (pH range between 1 and 7) at room temperature. The acidity of each sample was controlled adding 0.1 M HCl or 0.1 M KOH. The optimum conditions for hydrazine derivatization were determined using the area of the formed derivatives.

The solutions were passed through 0.20 μm PTFE syringe filters from Advantec (Tokyo, Japan). Then, the filtered solution was transferred into a V-shaped auto vial, and a 10.0 μL sample of the solution was injected into an LC–MS/MS system.

2.3. Water sampling

Raw drinking water and chlorinated drinking water samples were collected from water treatment plants without headspace in 40 mL brown glass bottles containing 1 drop of 2 M HCl.

2.4. Calibration and quantitation

The calibration curve for the linearity test was established by derivatization after adding 10, 20, 50, 100, 200, 500, and 1000 μL of the hydrazine standard (0.001 mg/L in reagent water) into a glass-stoppered test tube, and the total volume of the solution was adjusted to 1.0 mL using chlorinated drinking water in which the analyte was not detected. The peak areas of the hydrazine standards were used for the construction of the calibration curve.

2.5. Ultra performance liquid chromatography–mass spectrometry

UPLC was performed with an Agilent 1200 Series LC system (Agilent, Santa Clara, CA, USA) equipped with a binary pump, an on-line vacuum degassing system, and an autosampler. The analytes were separated by a 50 mm × 2.1 mm Eclipse Plus-C_{18} column with a 1.8 μm pore size (Agilent). A binary gradient with a flow rate of 0.2 mL/min was used. Eluent A contained 0.5 mM formic acid in water, and eluent B was acetonitrile. The mobile phase gradient was as follows: $A = 100\%$ at first, which was held for 0.5 min followed by a decrease to 85% by 1.5 min and to 0% by 9.0 min.

MS/MS detection was performed with an Agilent 6460 Series Triple Quadrupole instrument (Agilent). The mass spectrometer was operated with electrospray ionization in the positive ion mode (ESI+). The capillary voltage was set to 4.0 kV. The source temperature was 120 °C, and the desolvation temperature was 350 °C. Nitrogen was used as a desolvation gas (flow 600 L/h), and the detection was performed in the multiple reaction monitoring (MRM) mode. The fragment voltage and collision energy were optimized for hydrazine (Table 1).

3. Results and discussion

3.1. Derivatization

The authors of this study have previously published a derivatization method based on the Schiff reaction of hydrazine with OPA [27]. In this study, hydrazine was tested with three aromatic dicarbaldehydes to make it suitable for UPLC–MS/MS analysis. The two amino groups of hydrazine react with aromatic dicarbaldehydes to yield a single hydrazone product through a Schiff reaction and cyclization, as shown in Table 1. The formed derivative was injected into an LC system without a clean-up or concentration procedure.

To determine which aromatic dicarbaldehyde to employ, OPA, NDA, and ADA were compared with each other by analyzing the reactivity and sensitivity of the derivatives using UPLC–MS/MS. The reaction rates were determined through the detection of the substituted products at various reaction times (Fig. 1). The results indicated that NDA exhibited a very rapid reaction with hydrazine

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