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# Ultra-sensitive determination of cyanide in surface water by gas chromatography–tandem mass spectrometry after derivatization with 2-(dimethylamino)ethanethiol

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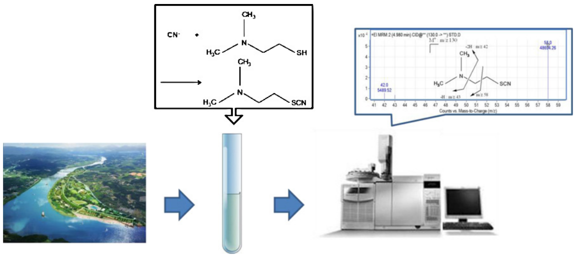
## HIGHLIGHTS

- New novel derivatization method of cyanide with 2-(dimethylamino) ethanethiol in water.
- A new gas chromatograph–tandem mass spectrometric method.
- A cyanide detection method with ultra-sensitivity and low interference.

## GRAPHICAL ABSTRACT



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## ABSTRACT

A gas chromatography–tandem mass spectrometric (GC–MS/MS) method has been established for the determination of cyanide in surface water. This method is based on the derivatization of cyanide with 2-(dimethylamino)ethanethiol in surface water. The following optimum reaction conditions were established: reagent dosage, 0.7 g $L^{-1}$ of 2-(dimethylamino)ethanethiol; pH 6; reaction carried out for 20 min at 60 °C. The organic derivative was extracted with 3 mL of ethyl acetate, and then measured by using GC–MS/MS. Under the established conditions, the detection and quantification limits were 0.02 $\mu g\,L^{-1}$ and 0.07 $\mu g\,L^{-1}$ in 10-mL of surface water, respectively. The calibration curve had a linear relationship relationship with $y = 0.7140x + 0.1997$ and $r^2 = 0.9963$ (for a working range of 0.07–10 $\mu g\,L^{-1}$) and the accuracy was in a range of 98–102%; the precision of the assay was less than 7% in surface water. The common ions $Cl^-$, $F^-$, $Br^-$, $NO_3^-$, $SO_4^{2-}$, $PO_4^{3-}$, $K^+$, $Na^+$, $NH_4^+$, $Ca^{2+}$, $Mg^{2+}$, $Ba^{2+}$, $Mn^{4+}$, $Mn^{2+}$, $Fe^{3+}$, $Fe^{2+}$ and sea water did not interfere in cyanide detection, even when present in 1000-fold excess over the species. Cyanide was detected in a concentration range of 0.07–0.11 $\mu g\,L^{-1}$ in 6 of 10 surface water samples.

## 1. Introduction

The cyanide ion consists of a carbon atom triply bonded to a nitrogen atom; it is a highly toxic chemical that is utilized in many industries, including gold and silver mining, pesticide production, and chemical manufacturing. Free cyanide is defined as the sum of the cyanide present as either HCN or $CN^-$ and may be released into the aquatic environment through waste effluents from numerous industries and processes [1]. Exposure to cyanide is also possible through the ingestion of certain foods (e.g., almonds or cassava root) [2,3], and the exposure to smoke from cigarettes or fires [4,5].

Acute cyanide exposure can cause histotoxic hypoxia through the inhibition of cytochrome C oxidase, coma with seizures, apnea, or cardiac arrest, and can result in death [6]. A fatal dose for

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humans can be as low as 1.5 mg $kg^{-1}$ of body weight [7]. Chronic exposure to cyanide can also lead to weakness and a variety of symptoms, including permanent paralysis, nervous lesions, hypothyroidism, and miscarriages [8,9]. Other effects include mild liver and kidney damage [8,9].

The Republic of Korea [10], the World Health Organization (WHO) [11], the EU 98/83/EC Drinking Water Directive [12] and the US Environmental Protection Agency (EPA) [13] have set the maximum concentration for cyanide in drinking water at 0.01, 0.07, 0.05, and 0.2 mg $L^{-1}$, respectively. The US EPA [14] has also established water quality criteria for aquatic life of 5.2 $\mu g\,L^{-1}$ for fresh water.

Although cyanide appears in surface-water quality criteria in Korea, its concentration has not yet been established. It may be necessary to review water such quality criteria after satisfactory monitoring techniques and risk assessments have been developed. Establishing safe cyanide-related water quality criteria for human health and aquatic life through monitoring requires a sensitive analytical method, with a detection limit lower than the water quality criteria established in other nations.

Many analytical methods based on different chemical principles have been proposed for the determination of cyanide. Spectrophotometry has been widely employed in the determination of cyanide through the use of many types of dye [15–19]. Electrochemical methods using sensors have been routinely used for cyanide analysis [20–22]. Flow injection analysis [23], atomic absorption spectrometry [24], electrophoresis [25–27], and ion chromatography [28] have also been used for the determination of cyanide, but their sensitivities are not adequate to detect below $\mu g\,L^{-1}$ levels in environmental water.

Chromatography is a highly convenient analytical technique when employed in combination with pretreatment techniques of derivatization, extraction, and concentration to detect toxicants in trace amounts in water. High performance liquid chromatography (HPLC) methods [29–35], liquid chromatography–tandem mass spectrometry (LC–MS/MS) [36–41], and direct injection MS/MS [42,43] have previously been reported in the analysis of cyanide. In these methods, cyanide was derivatized with reagents including 2,3-naphthalenedialdehyde [29–38,41], *o*-phthalaldehyde [32,33], quinoline and benzoyl chloride [32], and metal-ligand reagents [35,39,40].

Gas chromatography (GC) has also been reported in cyanide determination studies [44–50]. Cyanide can also be derivatized to cyanogen chloride [45], hydrogen cyanide [46,47], and pentafluorobenzyl cyanide [48,49] in biological samples or aqueous phases. GC coupled with mass spectrometry (MS) was utilized for the selective and sensitive determination of cyanide in biological samples [51–55]. These methods have disadvantages, including the use of complex derivatization steps [51] and high detection limits [51–54]. Moreover, most of the methods reported are for cyanide determination in biological samples [51–55], and comparable methods in environmental water are limited in number [49]. One of the most sensitive determination methods for cyanide in water was accomplished by fluorescent derivatization of cyanide with *o*-phthalaldehyde [33], in which the detection limit of cyanide was determined to be at trace levels to 0.1 $\mu g\,L^{-1}$. However, it is hard to discriminate against the potential interferences occurring after derivatization when the injection volume was as large as 200 μL.

This study aimed to develop a new cyanide derivatization method using 2-(dimethylamino)ethanethiol in surface water with a sensitive gas chromatography–tandem mass spectrometry (GC–MS/MS). This article focuses on the establishment of the optimum reaction conditions of cyanide with 2-(dimethylamino) ethanethiol, the optimum extraction conditions, and the optimum operating conditions of the GC–MS/MS instrument.

## 2. Experimental

### 2.1. Reagents

Potassium cyanide (97%), 2-(dimethylamino)ethanethiol hydrochloride (95%), and sodium acetate (99%) were obtained from Sigma–Aldrich (St. Louis, MO, USA). Potassium cyanide-$C^{13}N^{15}$ ($^{13}C$: 99%, $^{15}N$: >98%) was purchased from Cambridge Isotope Laboratories (Andover, MA, USA). Sodium hydroxide (97%), acetic acid (99.7%) and anhydrous sodium sulfate (99%) were obtained from Junsei chemical (Tokyo, Japan). Hexane, diethyl ether, ethyl acetate, methyl-*tert*-butyl ether (MTBE), and methylene chloride were used as solvents. A standard stock solution of cyanide (1000 mg $L^{-1}$) was freshly prepared before use by dissolving of 25.8 mg of cyanide to 10 mL with NaOH solution (0.2% in pure water). A working solution was used after more dilutions with 0.2% NaOH solution. Acetate buffer solution was made with 0.5 M sodium acetate and acetic acid. This solution was used within 1 h of its preparation. The reagent water used in this study was obtained from Sigma–Aldrich (St. Louis, MO, USA).

### 2.2. Derivatization and extraction

Ten milliliters of the water sample were transferred into a 20 mL test tube. 2.0 mL of acetate buffer solution were added to control the pH to pH 6.0 and agitated for 1–2 min. 0.35 mL of 2-(dimethylamino)ethanethiol solution (2.0% in water) and 20 μL of 2.5 mg $L^{-1}$ cyanide-$C^{13}N^{15}$ as an internal standard were added to the solution, which was reacted for 20 min at 60 °C. After the reaction, the aqueous solution was extracted with 3.0 mL of ethyl acetate by mechanical shaking for 10 min. The organic layer was dried by passage through anhydrous sodium sulfate, and then concentrated under a nitrogen stream to 100 μL. A 1.0 μL sample of the solution was injected in GC–MS/MS system.

### 2.3. Water sampling

Surface water samples were collected from 10 basins in the Gum River, Korea without headspace in 100 mL brown glass bottles containing 0.1 mL of 0.5 M NaOH. The sampling sites were selected to uniformly represent all streams of the River. All samples were stored at 4 °C before further analysis and the analysis was finished within 2 weeks after sampling.

### 2.4. Calibration and quantization

The calibration curve for the linearity test was established by adding 14.0, 20.0, 100, and 200 μL of cyanide standard (0.05 mg $L^{-1}$ in 0.2% NaOH solution), 10.0, 20.0 μL of cyanide standard (5.0 mg$L^{-1}$ in 0.2% NaOH solution) and 20 μL of 2.5 mg $L^{-1}$ $C^{13}N^{15}$ as an internal standard in 10.0 mL of surface water, in which the analyte was not detected. The following procedures were performed according to the derivatization and extraction method described before. A calibration curve was obtained from the regression line of peak area ratios of cyanide to the internal standard on concentration using a least-squares fit method.

### 2.5. Gas chromatography–tandem mass spectrometry

The analytical instruments used were an Agilent 7890A gas chromatograph with a split/splitless injector (Agilent Technologies, Santa Clara, CA, USA). The analytical column was a 30 m HP InnoWax capillary column (30 m × 0.25 mm id × 0.25 μm film thickness). Samples were injected in the pulse splitless mode. The flow rate of helium as carrier gas was 1.0 mL $min^{-1}$. The oven temperature program began at 60 °C, was raised to 100 °C at