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Optimization of a Novel Procedure for Determination of VOCs in Water and Human Urine Samples Based on SBSE Coupled with TD-GC–HRMS

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Abstract

In this study, stir-bar sorptive extraction and thermal desorption followed by gas chromatography coupled with high resolution mass spectrometry was applied for determination of halo-organic compounds (bromodichloromethane, dibromochloromethane, bromoform, and tetrachloroethylene) in water and human urine samples. Time of extraction and stirring speed were optimized. The results show that the optimum extraction time is 30 min with 600 rpm of stirring speed with Twister of 20 mm in length and 1.0-mm film thickness of PDMS (126 µL). The calibration curves, limits of detection and quantification for all compounds were calculated. This procedure is characterized by very low limits of detection and quantitation: lower than 0.0017 µg/L and good repeatability for all four volatile compounds. This new analytical procedure was identified to be easy, reliable, sensitive, and requires only small amounts of sample. It can constitute a good alternative to well-known procedures based on application of head space and gas chromatography coupled with electron capture detection.

Introduction

Volatile halogenated compounds [VOXs, also known as halogenated volatile organic compounds (HVOCs)] such as bromodichloromethane ($CHCl_2Br$), dibromochloromethane ($CHClBr_2$), tribromomethane (bromoform, $CHBr_3$), and tetrachloroethene (tetrachloroethylene, perchloroetylene, C_2Cl_4) belong to the most important pollutants of indoor and workplace air. People are exposed to these compounds in their homes and workplaces during varying activities of everyday life. These compounds are present in drinking water and water of swimming pools due to chlorination for disinfection purposes. They are also widely employed in industry as degreasing agents (1) and even more commonly are used for the dry-cleaning of clothes (2–4). C_2Cl_4has been classified as group 2A carcinogen by the International Cancer Research Institution and $CHCl_2Br$ as group 2B carcinogen, which means that they are possibly carcinogenic to humans (5).

Halogenated compounds can enter the human body by many different routes; for example, by inhalation, dermal contact, or inadvertent ingestion from hand-to-mouth contact. After intake, the chemicals may enter the bloodstream, and in the body they can be accumulated or are excreted, usually via urine (in non-metabolised form) (6,7).

Liquid samples usually require special treatment prior to the final analysis [e.g., by gas chromatography (GC)]. The sample preparation techniques commonly used in water analysis for the content of HVOCs are gas, sorbent, solvent, and membrane extraction. To prepare liquid biological samples for GC analysis, one must take into consideration the nature of the matrix, the method of sample introduction into a GC column, and the limited quantity of the sample. Due to these facts, urine samples have become of great interest for analysts. Special attention has recently been paid to the use of so-called solvent-free analyte isolation and/or enrichment techniques, which can be attributed to the widespread use of green analytical chemistry (8). In practice, various implementations of the headspace (HS) technique are most often used for this purpose, with static HS being the most popular. However, HS technique is non-selective towards volatile compounds and can require long sampling times. Still, analytical chemists feel the need to search for a new methodological and instrumental approach. Stir-bar sorptive extraction (SBSE) can constitute the technique of choice for this task (9,10). SBSE is a novel technique based on the same principles as the well-known SPME technique. Partitioning coefficient of the solutes between the silicone phase and the aqueous phase has been evaluated for the enrichment of volatile organic compounds from water and biological fluid samples. In the case of SBSE technique, stir-bars were coated with a 50–250 times larger amount of polidimethylosiloxane (PDMS) layer than in SPME technique,

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which increases the preconcentration capacity and recovery, and decreases the limit of detection (LOD). Another advantage offered by this technique is the fact that the stir-bar does not have to be extensively dried before the desorption process, thus less of the volatile compounds are lost during this step (11–21).

The aim of this study was to evaluate SBSE technique, followed by thermal desorption and GC-HRMS analysis, for the determination of $CHCl_2Br$, $CHClBr_2$, $CHBr_3$, and C_2Cl_4 in water and human urine samples. Stirring rate and time of extraction were optimized. Basic metrological parameters such as linearity, LOD, and limit of quantification (LOQ) were calculated. Isotope dilution was used for the analysis of all samples, quality controls (QC), and standards. The use of the isotope dilution technique increased the precision and accuracy of the analysis.

Experimental

Reagents and analytical standards

Standards for optimization and calibration of the SBSE-TD-GC–HRMS procedure are as follows: $CDBr_3$ was purchased from Sigma-Aldrich (Steinheim, Germany); $CHCl_2Br$, $CHClBr_2$, $CHBr_3$, and C_2Cl_4 (200.00 mg/dm^3, 5000.00 mg/dm^3) were purchased from Supelco (Bellefonte, PA).

CH_3OH for chromatography was obtained from Merck (Darmstadt, Germany). "Zero water" (level of total organic carbon 1–4 µg/L C) was produced by a Milli-Q Millipore system (Molsheim, France).

Theoretical recovery of VOX

Table I shows the log $K_{o/w}$ and theoretical recovery values of four halo-organic compounds investigated in this work. The theoretical recovery (TR) was calculated by applying the following formula:

$$TR = (K_{o/w}/\beta)/(1 + K_{o/w}/\beta) = 1/(\beta/K_{o/w} + 1) \qquad \text{Eq. 1}$$

where $\beta = V_s/V_{PDMS}$, V_{PDMS} is the volume of PDMS (V_{PDMS} = 126 µL), and V_s is the volume of the sample (water or urine).

Table I. Values of log $K_{o/w}$ and Theoretical Recoveries of $CHCl_2Br$, $CHClBr_2$, $CHBr_3$, and C_2Cl_4

Compound	log $K_{o/w}$	Sample volume (mL)	Theoretical recovery (%)
$CHCl_2Br$	2.00	2	86.3
		5	71.6
		10	55.8
		20	38.7
C_2Cl_4	3.40	2	99.37
		5	98.45
		10	96.94
		20	94.06
$CHClBr_2$	2.16	2	90.1
		5	78.5
		10	64.6
		20	47.7
$CHBr_3$	2.38	2	93.8
		5	85.8
		10	75.1
		20	60.2

Water and human urine samples

In the sampling of water, the basic rule is to fill up a container fully (no HS) and to keep it at about 4ºC, protected from possible contamination. The isotope dilution method was used for the water samples. Various quantities of the analytes (0.5, 1, 2, 5, and 10 µg/L) and an equal amount of deuterated bromoform (2 µg/L) were added to each sample of millipore water (10 mL), followed by the analysis using the SBSE-TD-GC–HRMS procedure.

Urine samples should be collected without HS stored at ~ 4ºC and analyzed within 24 h. One urine sample was collected from a volunteer and divided into five aliquots of equal volume. One of them was used as a blank, spiked with the $CDBr_3$ standard only, and analyzed directly for the content of organohalogen compounds. The other four aliquots were spiked with the same quantities of the analytes (2 µg/L) and the same amount of deuterated bromoform (2 µg/L), respectively. Every urine sample was analyzed using the SBSE-TD-GC–HRMS procedure.

Conditioning of the coated stir bars

The coated stir-bars (Twisters) for sorptive extraction were obtained from Gerstel (Gerstel GmbH, Mulheim an der Ruhr, Germany). Twisters of 20 mm of length and coated with a 1.0-mm thick film of PDMS (126 µL) were conditioned prior to the first and after each analysis as follows: used Twisters were placed into a clean 100-mL flask containing a 1:1 mixture of dichloromethane and methanol and shaken for 30 min on a rotating shaking machine to clean the PDMS phase. After 30 min, the solvent mixture was changed for a fresh one and shaken for another 30 min. The Twisters were removed from the solvent and dried for a short time on a clean surface at room temperature; afterwards, they were placed into clean TDS tubes and conditioned in a Gerstel tube conditioner at 300ºC at a flow rate of helium of 100 mL/min for 1 h. After cooling down, the Twisters were placed into clean screw cap vials. After the stir bars were conditioned, no memory effect was observed.

Instrumentation

All analyses were performed by thermodesorption GC–MS. An Agilent GC 5890 Series II (Santa Clara, CA) was equipped with an autosampler Gerstel MPS 2 (Mulheim, Germany), a tray for 98 desorption tubes Gerstel VT98t, and a desorption unit Gerstel TDU which was coupled to a cold injection system Gerstel CIS 3. The Gerstel MASter software was used to control and set the parameters for the autosampler, desorption unit, and the injection system. The desorption (TDU to CIS) and the injection (CIS to column) were both performed in splitless mode at a helium flow of 70 mL/min. A liner filled with glass wool was installed in the CIS.

The temperature for desorption of the analytes was programmed from 30°C to 200°C at 60°C/min and a final hold of 5 min. The desorbed analytes were trapped in the CIS 3 at –100°C and afterwards heated to 200°C at 12°C/s for injection onto the GC column.

The GC system was connected to a high resolution mass spectrometer Thermo Scientific MAT 95 (Bremen, Germany) and a Restek Rtx-CL Pesticides 2 capillary column (Bellefone, PA)(30 m × 0.25 mm i.d., 0.20-µm film thickness) was used for the chromatographic separation. The GC temperature program was as follows: 30°C, 5 min; 12°C/min to 95°C, 2 min; 25°C/min to 200°C, 5 min. Helium served as carrier gas at a head pressure of 16 psi.

The MS was operated in SIM mode at a resolution of > 7000. The temperature of the ion source was 260°C. The two most intense ions of the molecular ion cluster or a high abundant fragment ion cluster for each compound were monitored, as summarized in Table II.

SBSE-TD-HRGC-HRMS procedure for determination of VOX in liquid samples

10 mL of sample (water or urine) and the standard solutions were pipetted into a special 10-mL THM flask from Supelco (Bellefonte, PA). A Twister was placed into the sample and stirred for 30 min at 600 rpm. After sampling, the stir-bar was taken out of the vial with tweezers and shortly dipped on a clean paper tissue to remove residual water droplets. The Twister was finally placed into an empty desorption liner of 60 mm length and 6 mm i.d. The desorbed analytes were detected as described earlier. In Figure 1, the general scheme of the whole procedure is depicted.

Results

Instrumental operating conditions

In a first approach, the GC–HRMS conditions including oven temperature, thermal desorption program, and retention time characteristic were evaluated. Instrumental optimization was performed with $CHCl_2Br$, $CHClBr_2$, $CHBr_3$, and C_2Cl_4 standard solutions, which were directly spiked onto the stir bar by use of a zero dead-volume syringe (1 µL of a 200 mg/L solution).

Table II. Identification and Quantification Conditions for $CHCl_2Br$, C_2Cl_4, $CHClBr_2$, and $CHBr_3$ in Water and Human Urine Samples

Compound	RT* (min)	Selected ions for identification (m/z)†	
$CHCl_2Br$	4.4	M^+-Br	**82.9455,** 84.9426
C_2Cl_4	6.7	M^+	**163.8754**, 165.8725
$CHClBr_2$	7.1	M^+-Br	**126.8950**, 128.8927
$CHBr_3$	9.4	M^+-Br	170.8445, **172.8425**
Deuterated $CHBr_3$	9.4	M^+-Br	171.8508, **173.8487**

* RT = retention time

† Ion chosen for quantification in bold.

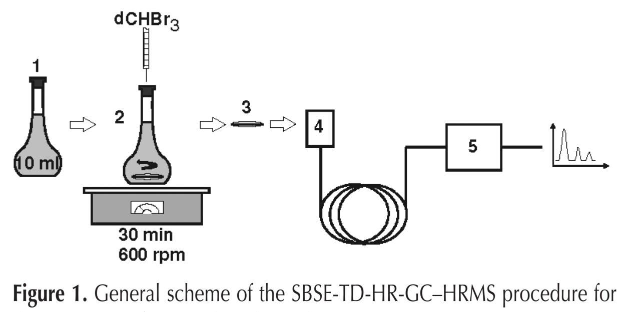

Figure 1. General scheme of the SBSE-TD-HR-GC–HRMS procedure for determination of VOX in liquid samples.

Optimization of the SBSE

Sample volume, time of SBSE extraction, and stirring speed were evaluated to achieve the best overall analytical conditions.

All extraction experiments were carried out in special 10-mL screw cap vials, which can be filled up to a minimum of HS and provide a diameter wide enough to stir the coated bars in it. With a sample volume of 10 mL, a total recovery of the analytes of at minimum 56% is expected (Table I), resulting in a good performance of the method.

Optimization studies were carried out in water samples spiked at the 10 µg/L level. The important parameters extraction time (30, 60, and 90 min) and stirring speed (500, 600, 800, and 1000 rpm) were optimized. Additionally, stir-bars having a PDMS phase volume of 126 µL were chosen because a higher extraction capacity is attained.

The ideal enrichment time is the one in which the amount of compounds detected reaches a maximum, and any subsequent increment in time does not result in a higher compound signal. When an application involves a mixture of compounds with multiple functionalities, different maxima are expected and a compromise is needed for choosing the enrichment time. For these experiments, 30, 45, and 60 min and 500, 600, 800, and 1000 rpm were evaluated. The results demonstrated that at 30 min a good detection capability was obtained for all four compounds and the deuterated $CHBr_3$. It was observed that the peak area for each compound was relatively the same with increasing time, and at 600 rpm the best response for the standard was observed. (results for $CHCl_2Br$ are shown in Figure 2).

Calibration and linearity

Five levels of concentration were tested in triplicate; these concentrations covered the concentration ranges expected for four halo-organic compounds in water samples (22). Calibration curves were evaluated as:

$$Y = f(x)$$

$$P_{vox}/P_{CDBr3} = f(C_{VOX}/C_{CDBr3}) \qquad \text{Eq. 2}$$

where P_{vox} is the peak height of the compound, P_{CDBr3} is the peak height of the deuterated $CHBr_3$, C_{VOX} is the concentration of the compound added to the sample (0.5, 1, 2, and 5 µg/L), and C_{CDBr3}

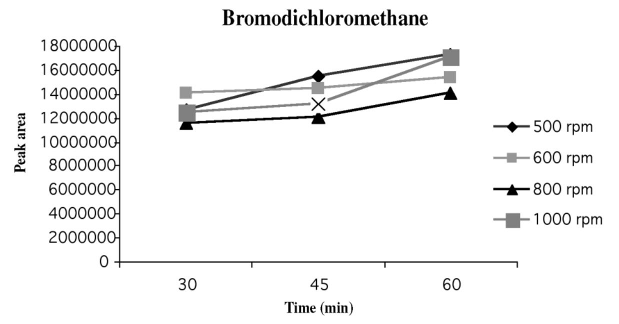

Figure 2. Relation between extraction time and stirring speed for $CHCl_2Br$.

is the constant concentration of the deuterated $CHBr_3$ (2 µg/L).

The range of concentration, regression line equation, and correlation coefficient appears in Table III. In general, the linearity was very good in the concentration range examined (0.5–5 µg/L) with correlation coefficients greater than 0.979.

LOD and LOQ

The LOD and LOQ were established by considering the mean noise levels on the mass traces chosen for quantification, respectively (Table II). The LOD was set at a signal-to-noise (S/N) ratio of 3 and the LOQ at a S/N of 10, respectively. The LOD and LOQ values obtained in spiked water samples are listed in Table IV. These LOD values are theoretical and show the great potential of this procedure to determine VOC concentrations at very low ppt levels. However, it is necessary to prepare new calibration curves for lower concentration range. Even with a less sensitive benchtop MS, the performance of the method is likely to meet the typical requirements.

Table III. Parameters of the Calibration Curves Obtained for Standard Solutions of Four Halo-organic Compounds

Compound	Matrix	Concentration range (µg/L)	Regression line equation	Correlation coefficient
$CHBrCl_2$	Water	0.5–5.0	y = 0.1721x – 0.0289	0.9792
C_2Cl_4	Water	0.5–5.0	y = 0.4521x – 0.0683	0.9861
$CHBr_2Cl$	Water	0.5–5.0	y = 0.3174x – 0.0395	0.9926
$CHBr_3$	Water	0.5–5.0	y = 0.9352x + 0.0366	0.9940

Table IV. LOD and LOQ Values Obtained for Four Halo-organic Compounds in Water Samples in the Application of SBSE-TD-HRGC–HRMS

Compound	LOD (µg/L)	LOQ (µg/L)
$CHClBr_2$	0.0017	0.0057
C_2Cl_4	0.00023	0.00076
$CHCl_2Br$	0.000094	0.00031
$CHBr_3$	0.000030	0.000099

Table V. Values of Average P_{vox}/P_{CHBr3} and Repeatability for all Four Compounds Analyzed in Both Matrices

Compound	Matrix	No. of results	Average P_{vox} / P_{CDBr3} (for C_{vox} / C_{CDBr3} = 1)	Repeatability (%)
$CHCl_2Br$	water	5	0.111	8.6
	urine	4	0.104	6.2
C_2Cl_4	water	5	0.321	7.4
	urine	4	0.313	5.1
$CHClBr_2$	water	5	0.223	9.1
	urine	4	0.286	6.3
$CHBr_3$	water	5	0.905	10.5
	urine	4	1.05	6.4

Determination of halo-organic compounds in human urine samples

Five urine samples obtained from one volunteer were analyzed using the SBSE-TD-GC–HRMS procedure. One sample was analyzed as a blank sample; the other four were spiked with the same volume of all compounds investigated (to get a concentration of 2 µg/L) and the same volume of the deuterated $CHBr_3$. The repeatability was evaluated on relative P_{vox}/P_{CDBr3} values using replicates of spiked urine sample, which were analyzed on the same day and by the same analyst. The repeatability for water matrix was evaluated using replicates of five samples. The results show that the obtained P_{vox}/P_{CDBr3} values did not differ significantly in between the analyses of the urine and water samples (Table V). Values for the repeatability of equal to or lower than 10% allowed the assumption of a good precision for this method.

By applying the isotope dilution technique the concentration of the analytes in the sample (C_{VOX}) are calculated by applying the following equation:

$$C_{VOX} = (C_{CDBr3,} \times P_{vox}) / (rrf_{vox} \times P_{CDBr3}) \qquad \text{Eq. 3}$$

where P_{vox} is the peak height of each VOX presented in the sample, C_{CDBr3} and P_{CDBr3} are the concentration of the spiked

Table VI. Determined Mean Concentrations (µg/L) of Halo-organic Compounds in Spiked Urine Samples

Compound	Determined C_{VOX}	Theoretical C_{VOX}
$CHCl_2Br$	1.80	2.0
C_2Cl_4	1.97	2.0
$CHClBr_2$	1.80	2.0
CHBr3	1.97	2.0

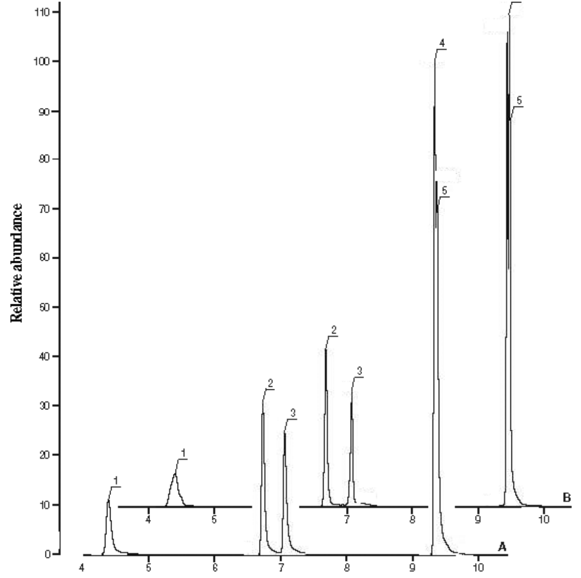

Figure 3. Examples of chromatograms obtained during the analysis of water, (A), and urine samples, (B), with standard solution of volatile halo-organic compounds (2 µg/L): $CHCl_2Br$, 1; C_2Cl_4, 2; $CHClBr_2$, 3; $CDBr_3$, 4; $CHBr_3$, 5.

labeled standard in the sample and its resulting peak height, and rrf_{vox} is the relative response factor of the analyte in relation to the labeled standard. Rrf_{vox} is calculated from the data of the calibration and linearity experiments by applying the previously rearranged equation. If equation 3 was applied to the spiked urine samples, the results minus the amounts detected in the blank sample should be equal to the spiked concentrations. Concentrations for all compounds presented in blank urine sample (except $CDBr_3$, which was added to the urine sample) are below the evaluated concentration range.

The data in Table VI illustrate that the calculated C_{VOX} are close to the theoretical spiked concentrations, which confirm that the analytical procedure is performing correctly and the response factors, which were determined in the water matrix, are also valid for the urine matrix. All P_{vox}/P_{CDBr3} values for water and urine standard solutions were statistically compared for all analytes. It shows that little or no matrix effect is observed.

In Figure 3, the chromatogram of a water and a urine sample are shown. Also, no matrix effect on the chromatographic performance could be detected, except a slight peak broadening for $CHClBr_2$ (little matrix effect).

Conclusion

The procedure of simultaneous determination of four volatile organohalogen compounds ($CHCl_2Br$, $CHClBr_2$, $CHBr_3$, and C_2Cl_4) in small samples of water and human urine based on application of SBSE-TD-GC–HRMS has been developed and validated. The key parameters (time, stirring speed) of the extraction step have been optimized to obtain an isolation and concentration method adequate for compounds of high volatility. The results show that the optimum extraction time is 30 min with 600 rpm of stirring speed with a Twister (20 mm in length × 1.0-mm film thickness) of PDMS (126 µL). The SBSE-TD-GC–HRMS procedure is sensitive and shows a good linearity between 0.5 and 10 µg/L for all compounds tested. This procedure is characterized by very low LOD and LOQ: lower than 0.0017 µg/L and good repeatability for all four volatile compounds. No significant or little matrix effects were observed.

The examined analytical procedure is easy to handle, solvent-free, fast, and was successfully applied for the simultaneous determination of volatile trace compounds in very low volumes of water and human urine samples. Results show the great potential of the SBSE-TD-GC–HRMS procedure with isotope dilution technique used on sampling preparation step can be an excellent alternative to standard HS-GC–ECD–MS procedure.

Acknowledgments

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