Improved gas chromatography methods for micro-volume analysis of haloacetic acids in water and biological matrices

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A fast headspace solid-phase microextraction gas chromatography method for micro-volume (0.1 mL) samples was optimized for the analysis of haloacetic acids (HAAs) in aqueous and biological samples. It includes liquid–liquid microextraction (LLME), derivatization of the acids to their methyl esters using sulfuric acid and methanol after evaporation, followed by headspace solid-phase microextraction with gas chromatography and electron capture detection (SPME-GC-ECD). The derivatization procedure was optimized to achieve maximum sensitivity using the following conditions: esterification for 20 min at 80 °C in 10 μL methanol, 10 μL sulfuric acid and 0.1 g anhydrous sodium sulfate. Multi-point standard addition method was used to determine the effect of the sample matrix by comparing with internal standard method. It was shown that the effect of the matrix for urine and blood samples in this method is insignificant. The method detection limits are in the range of 1 μg L$^{-1}$ for most of the HAAs, except for monobromoacetic acid (MBAA) (3 μg L$^{-1}$) and for monochloroacetic acid (MCAA) (16 μg L$^{-1}$). The optimized procedure was applied to the analysis of HAAs in water, urine and blood samples. All nine HAAs can be separated in <13 min for biological samples and <7 min for drinking water samples, with total sample preparation and analysis time <50 min. Analytical uncertainty can increase dramatically as the sample volume decreases; however, similar precision was observed with our method using 0.1 mL samples as with a standard method using 40 mL samples.

Introduction

There is a continued need for development of improved analytical methods for halogenated acetic acids (HAAs) for human and environmental health investigations. Chronic, low-level human, animal and vegetation exposure to HAAs is prevalent because various combinations of HAAs are present as drinking water (and wastewater) disinfection by-products and as by-products of atmospheric oxidation of hydrochlorofluorocarbons. Clinicians and toxicologists are interested in the pharmacokinetic and toxicologic properties of haloacetic acids (HAAs), primarily as metabolites of trichloroethylene (TCE), trichloroethanol (TCE) and chloral hydrate (CH), which have been also used as therapeutic agents and anesthetics as well as industrial solvents and extractants. CH and a mixture of chlorinated and brominated HAAs are also formed as disinfection by-products (DBPs) through reactions between chemical disinfectants and dissolved organic matter during the treatment of drinking water. Together with trihalomethanes (THMs), they constitute the major mass fraction of DBPs. Animal studies have demonstrated the carcinogenic potential of dichloroacetic acid (DCAA), the peroxisome proliferation potential of tri- chloroacetic acid (TCAA) and other haloacetic acids, and the distinctly different pharmacokinetics and mechanisms of action between the di- and trihaloacetic acids. The United States Environmental Protection Agency (US EPA) Method 552.2 and Standard Methods 6251B are the drinking water and regulatory agency standardized methods that are used by most water utility laboratories across North America. Alternate techniques, such as high-performance liquid chromatography (HPLC), and capillary electrophoresis (CE) avoid the requirement for derivatization but are not applicable for drinking water analysis because of their high detection limits compared to GC methods. The most promising of the new techniques is electrospray ionization-high field asymmetric waveform ion mobility spectrometry-mass spectrometry (ESI-FAIMS-MS). While FAIMS provides extremely rapid and sensitive analysis of drinking water, there remain methodologic issues with regard to biological samples. Sample volume is limited for most biological fluids—for example, blood, plasma, urine, saliva and sweat—which also limits the sensitivity range that can be achieved. The dosages of HAAs in animal toxicological and pharmacokinetic studies has allowed adequate identification of HAAs in most cases; however, researchers are always faced with the issue of extrapolating high dose information to environmentally relevant chronic exposure scenarios. Developments of the past decade in trace analysis and capillary chromatography can be exploited to substantially improve our capability for the analysis of HAAs in biological samples. Solid-phase microextraction (SPME) integrates sampling, extraction, concentration and sample introduction in a single step. Recently Sarrion et al. used SPME coupled with GC-MS to analyze HAAs in water samples, but the volume of sample was relatively large and preconcentration was necessary; derivatization was done directly in 10 mL water samples.

In this paper, liquid–liquid microextraction (LLME) and SPME were combined with GC-ECD for the analysis of HAAs in micro-volume drinking water, rodent urine and blood samples with only 50–100 μL of sample volume. Potential matrix effects were investigated by comparing internal standard and standard addition quantification methods. This method is advantageous over those reported earlier because it does not use carcinogenic diazomethane for derivatization, has sensitivity at least an order of magnitude greater than shown previously for micro-volume samples, and is robust for all of the chloro- and bromoacetic acids.
Experimental section

Chemicals and materials

Monochloroacetic acid (MCAA, 99+%), monobromoacetic acid (MBAA 99+%), 2,3-dibromopropionic acid (2,3-DPBA 99+%), dichloroacetic acid (DCAA 99+%), bromochloroacetic acid (BCAA 97%) and tribromoacetic acid (TBAA 99%) were obtained from Aldrich Chem. Co. (Milwaukee, WI, USA). Trichloroacetic acid (TCAA >99.5%), dibromochloroacetic acid (DBBA 98%) and 2,3-dichloropropionic acid (2,3-DCPA >97%) were obtained from Fluka Chemie (Switzerland). Bromodichloroacetic acid (BDCAA) and chlorodibromoacetic acid (CDBAA) were obtained from Supelco Inc. (Bellefonte, PA, USA). Human serum was obtained from Sigma-Aldrich Inc. (St. Louis, MO, USA). All standards were used as received. 2,3-DCPA and 2,3-DBPA were used in the LLME and SPME methods as surrogate and internal standards. Methanol (HPLC grade), anhydrous sodium sulfate (certified ACS, suitable for pesticide residue analysis) and cupric sulfate pentahydrate (certified ACS) were purchased from Fisher Scientific (Nepean, Ontario, Canada). Sulfuric acid (ACS purity) was obtained from BDH Inc. (Toronto, Ontario, Canada). Methyl tert-butyl ether (MTBE) was obtained from Sigma-Aldrich Inc. (St. Louis, MO, USA). A Milli-Q water purification system (Millipore, Bedford, MA, USA) was used to prepare laboratory-grade water. Anhydrous sodium sulfate was heated to 400 °C for 4 h to remove phthalates and other interfering organic substances. It was stored at 110 °C, and cooled to room temperature before use. The individual stock standard solutions were prepared by weight in Milli-Q water. Standard mixes were prepared weekly and standard series were diluted before analysis. All solutions were stored frozen in the dark at −20°C and warmed to ambient temperature before use.

SPME experiments were performed using a Varian 8200/SPME autosampler (Varian Inc., Sugar Land, Texas, USA). A 100 µm polydimethylsiloxane (PDMS) coated fiber was purchased from Supelco (Belfonte, PA, USA). Before use, the fiber was conditioned in a heated GC split/splitless injection port under helium flow according to the manufacturer’s instructions. 1.5 mL polypropylene microcentrifuge vials were purchased from Rose Scientific Ltd. (Edmonton, Alberta, Canada). 2 mL autosampler vials were purchased from Supelco (Belfonte, PA, USA).

Chromatographic conditions

An HP6890 (Hewlett-Packard Co., Wilmington, DE, USA) capillary GC with micro-cell 63Ni electron capture detector and autosampler and a Varian CP3800 (Varian Inc., Walnut Creek, CA, USA) capillary GC with a 63Ni electron capture detector (ECD) and 8200/SPME autosampler were used for the LLME and LLME-SPME analyses, respectively. A DB-1 (20 m × 0.18 mm; 0.4 µm) fused silica capillary column (J&W Scientific, Folsom, CA, USA) was used for separation of HAAbs. Helium (99.999+%, Canadian Liquid Air Ltd., Edmonton, Alberta, Canada) was used as carrier gas at a flow rate of 0.8 mL min−1. The column temperature program was 40 °C, to 70 °C at 10 °C min−1 hold for 4 min, then to 220 °C at 15 °C min−1 hold for 3 min. The injector and detector temperatures were maintained at 230 °C and 300 °C, respectively. 2 µL liquid was injected in pressure pulse splitless mode at 30 psi for 0.1 min in the LLME method. The fiber was desorbed for 2 min in splitless mode in the LLME-SPME method.

Sample preparation for liquid–liquid microextraction (LLME) GC-ECD

The LLME method was adapted and modified from that reported by Schulz et al.20 for rodent fluids. Urine (0.1 mL) or blood (25–50 µL) and 0.1 M acetate buffer (0.2 mL, pH 5.2) were combined and vortex mixed in a 1.5 mL polypropylene microcentrifuge vial. 10 µL of 2,3-DCPA and 2,3-DBPA water solution were added as surrogate and internal standards. The solution was acidified with 25 µL of 50% sulfuric acid and HAAbs were extracted with 0.6 mL MTBE. After extraction, the water phase was removed and 0.2 mL of acidified methanol (10% H2SO4) was added. The mixture was vortexed and incubated for 1 h at 50 °C in order to derivatize HAAs. After cooling to room temperature, 0.4 mL of saturated sodium bicarbonate solution was carefully added to neutralize the solution. The water phase was removed and 0.2 g Na2SO4 was added to absorb residual water. The MTBE fraction was transferred to a 2 mL autosampler vial and analyzed by GC-ECD. US EPA Method 552.2 was also used to analyze water samples and compared with the LLME-GC-ECD method.

Sample preparation for LLME-SPME-GC-ECD

In the LLME-SPME-GC-ECD method, the extraction procedure was the same as in the LLME-GC-ECD method, with further adaptation of the method reported by Sarrion et al.22 After extraction, MTBE was placed in a 2 mL autosampler vial and evaporated just to dryness under a gentle stream of N2 (99.999% pure). Sodium sulfate (0.16 g), methanol (10 µL) and sulfuric acid (30 µL) were added to the dried residue in the vial, after which the vial was sealed using a Teflon-lined crimp-cap. The solution was vortex mixed and the HAAs were derivatized at 80 °C for 20 min. After derivatization, the sample was cooled down to room temperature. The sample components were absorbed from the headspace by the 100 µm PDMS fiber for 10 min at room temperature (25 °C), desorbed for 2 min in the injection port of the GC and detected with ECD detector. 2,3-DCPA and 2,3-DBPA were used as surrogate and internal standards for LLME and SPME methods.

The linear range, method detection limits (MDLs) and limits of detection (LOD) are shown in Table 1. The MDLs were calculated as SD × 3.143, where SD is the standard deviation of the concentration obtained from a replicate standard (n = 7) fortified with HAAs at concentrations that produced peak intensities approximately five times the intensity of the background noise. The value of 3.143 represents the Student’s t value for 99% confidence with 6 degrees of freedom.23 The MDL is almost the same as the LOD, which is arbitrarily defined as 3sLOD,26 where sLOD is the standard deviation, with at least 6 degrees of freedom, at concentrations near 0, obtained by extrapolation from the calibration curve. The limit of quantification is defined arbitrarily as 10sLOD. The estimated detection limit (LOD) and the method detection limit (MDL) were calculated as the quantitation limit (QLD) divided by the estimated sLOD. The LOD and MDL are shown in Table 1.

Table 1 Linear range, estimated detection limits and MDLs for LLME-GC-ECD and LLME-SPME-GC-ECD methods for HAA standards in water (µg L−1)

<table>
<thead>
<tr>
<th>Name</th>
<th>Linear range Low</th>
<th>Linear range High</th>
<th>LLME-GC-ECD Estimated DL</th>
<th>LLME-SPME-GC-ECD Estimated DL</th>
<th>MDL</th>
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<tr>
<td>MCAA</td>
<td>40</td>
<td>20000</td>
<td>15</td>
<td>16</td>
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<tr>
<td>MMBA</td>
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<td>12000</td>
<td>2</td>
<td>3.0</td>
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<tr>
<td>DCAA</td>
<td>5</td>
<td>4500</td>
<td>1</td>
<td>1.0</td>
<td>0.6</td>
</tr>
<tr>
<td>BCAA</td>
<td>10</td>
<td>4000</td>
<td>2</td>
<td>0.2</td>
<td>0.9</td>
</tr>
<tr>
<td>TCAA</td>
<td>5</td>
<td>600</td>
<td>1</td>
<td>0.2</td>
<td>0.6</td>
</tr>
<tr>
<td>DBAA</td>
<td>15</td>
<td>3500</td>
<td>5</td>
<td>0.3</td>
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</tr>
<tr>
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<td>5</td>
<td>0.3</td>
<td>1.2</td>
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<tr>
<td>CDBAA</td>
<td>35</td>
<td>2000</td>
<td>10</td>
<td>0.3</td>
<td>1.2</td>
</tr>
<tr>
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<td>70</td>
<td>3500</td>
<td>25</td>
<td>0.5</td>
<td>3.1</td>
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</table>
Results and discussion

Separation time

In Method 552.2, a DB-5.625 (30 m × 0.25 mm; 0.25 μm) column was used to analyze 9 HAAs. The separation time for 9 HAAs is about 40 min. The strongly retained trihaloacetic acids (BDCA, CDBA, TBA) have low response for this separation because of band-broadening. In order to shorten the separation time and increase the detection sensitivity for HAAs, a narrow, short column (DB-1: 20 m × 0.18 mm; 0.4 μm) was used. After optimization of conditions, the separation of all 9 HAAs was achieved in 7 min (Fig. 1). These conditions can be used for the analysis of water samples, but there are two peaks whose retention times are almost the same as DBAA and TBA in the human urine sample. In order to separate them, the separation time was increased to 13 min (Fig. 2). This new separation method is much faster than the previous one used in our laboratory. Additionally, the response for all HAAs is enhanced, particularly for trihaloacetic acids including BCAA and DBAA.

Selection of internal standard

In capillary GC, internal standard calibration is the most commonly used method. Variability in the procedure of sample pre-treatment and injection can be minimized by using appropriate internal standards. 1,2,3-trichloropropane is commonly added to the solvent as an internal standard in the extraction procedure. It compensates for changes in solvent volume, but it cannot account for variability caused by differences in the extraction and derivatization procedures. 2,3-DCPA and 2,3-DBPA were selected as surrogate and internal standards, because they were not detected in actual drinking water and laboratory studies of DBPs. Good calibration curves were obtained with these internal standards.

Optimization

Milli-Q water and human urine were used to optimize the derivatization parameters for these methods.

Optimization of LLME-GC-ECD method

When the concentration of sulfuric acid was increased, the detected amounts of mono- and dihaloacetic acids and trichloroacetic acid increased, whereas DBAA, BDCAA, CDBAA, and TBA decreased due to decomposition at high sulfuric acid concentrations. 25 μL 50% H₂SO₄ was selected to acidify the sample solution. The acidified methanol can mix with MTBE homogeneously when the concentration of sulfuric acid is ≤10%, which may increase the efficiency of the derivatization of HAAs. There are some unidentified broad peaks in the chromatogram that interfere with the separation of HAAs when a higher concentration of sulfuric acid is used. Therefore, acidified methanol with 10% sulfuric acid was selected as the derivatising reagent for HAAs.

Optimization of LLME-SPME-GC-ECD method

Two derivatization methods were tested, both of which rely on the alkylation of HAAs. Methanol or ethanol was used as an esterification reagent. The difference of the response for the majority of methyl esters and ethyl esters of HAAs was found to be insignificant. The retention times of ethyl esters of HAAs were several minutes longer than those of methyl esters under the same separation conditions. However, ethyl esters of BCAA and TCAA could not be separated on the DB-1 column. In order to maximize the benefit of rapid separation with resolution of all
components, methanol was used for derivatization. Headspace SPME reduced the number of unidentified peaks and gave a smoother baseline signal (Fig. 3) compared to liquid injection (Figs. 1, 2). Chromatography remained consistently cleaner because fewer matrix substituents, including residual H₂SO₄ and H₂O, were sampled from the headspace, resulting in fewer low volatility components that contributed to peak tailing and increasing baseline signals. H₂SO₄ and H₂O will degrade particularly the trihalogenated acid esters and will also degrade the stationary phase of the column. The former will contribute to decreased signal intensity for the trihaloacids whereas the latter will contribute to increased baseline signals and unidentified and interfering peaks.

**Effect of derivatization time and temperature**

The derivatization temperature was set initially at 50 °C for 10 min, based on the derivatization conditions reported by Sarrion et al. The volumes of sulfuric acid, methanol and the amount of anhydrous sodium sulfate were 30 μL, 10 μL and 160 mg, respectively. The responses of most HAAs increased with

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*Fig. 2* Liquid injection GC-ECD chromatograms of all 9 HAAs and samples. The conditions were as follows: HP 6890 GC; J & W DB-1 (20 m × 0.18 mm; 0.4 μm) column; inj. temp.: 230 °C; ECD temp.: 300 °C; col. temp.: 40 °C, to 70 °C at 10 °C min⁻¹ hold 4 min, to 220 °C at 15 °C min⁻¹ hold 3 min. Carrier gas: He 0.8 mL min⁻¹; Make up gas: argon (5% methane) 60 mL min⁻¹; inj. mode: 2 μL pulse splitless at 30 psi for 0.1 min. Concentrations in HAA standard and spiked urine (μg L⁻¹): MCAA 320, MBAA 58, DCAA 46, TCAA 30, BCAA 56, DBAA 120, BDCAA 64, CDBAA 94, TBAA 180.

*Fig. 3* Headspace SPME GC-ECD chromatograms of all 9 HAAs and samples. The conditions were as follows: Varian CP 3800 GC; J & W DB-1 (20 m × 0.18 mm; 0.4 μm) column; inj. temp.: 230 °C; ECD temp.: 300 °C; col. temp.: 40 °C, to 70 °C at 10 °C min⁻¹ hold 4 min, to 220 °C at 15 °C min⁻¹ hold 3 min. Carrier gas: He 0.8 mL min⁻¹; Make up gas: argon (5% methane) 25 mL min⁻¹; inj. mode: splitless 2 min. Concentrations in HAA standard and spiked urine (μg L⁻¹): MCAA 64, MBAA 12, DCAA 9.2, TCAA 5.9, BCAA 11, DBAA 23, BDCAA 13, CDBAA 19, TBAA 36.
increased holding time between derivatization and analysis, suggesting that derivatization was not complete after 10 min incubation. The derivatization temperature was increased while other conditions were held constant, which resulted in increased responses of HAAs, particularly for MCAA, MBAA, DCAA, 2,3-DCPA and 2,3-DDBPA. Ultimately, the derivatization temperature and time were optimized at 80 °C for 20 min. There was little change in the signal for HAAs for several hours after derivatization at these conditions.

Effect of sulfuric acid and methanol

The effects of sulfuric acid and methanol volume at 80 °C/20 min were studied. The results obtained with sulfuric acid volume from 10–90 μL showed that 10 μL is optimum. The responses of HAAs decreased with increasing volume of sulfuric acid. This could be due to dilution of HAAs in the solution when the volume was increased. Additionally, the responses of 9 HAAs and 2 internal standards decreased with increasing volume of methanol, similar to the effect of sulfuric acid volume. The optimum volume of methanol was set at 10 μL.

Effect of sodium sulfate

The effect of ionic strength on the SPME sensitivity was also studied. Anhydrous Na2SO4 (0 to 0.2 g) was introduced into the 2 mL vial before the addition of 10 μL methanol and 10 μL sulfuric acid. The addition of salt improved the effective absorption efficiency onto the fiber for all the compounds by shifting the equilibrium of the volatile organics towards the gas phase. Another effect of the Na2SO4 is the dehydration of the sample residue. In the esterification reaction, the presence of water will influence the equilibrium towards the left (i.e. towards the reagents), thereby reducing the efficiency of the derivatization reaction. A plateau in the response of HAAs appeared by 0.08 g with little response differences beyond that concentration; 0.1 g was chosen for all subsequent experiments. The sodium sulfate, which is stored at 110 °C, should be cooled down to room temperature before it is added to the samples. The signal of brominated acids decreased significantly, especially for TBA, when warm sodium sulfate was added to the vial. This is likely because the warm sodium sulfate causes decomposition of the acids.

Comparison of methods

In the LLME-GC-ECD method (Figs. 1, 2), the responses of trihaloacetic acids are lower than those in the SPME method with the same concentration (Fig. 3). The sensitivities for mono- and dihaloacetic acids in the two methods are similar, but the sensitivities for trihaloacetic acids in the SPME method are greater than in the liquid injection method. In the headspace SPME method, absorption of H2SO4 is unlikely, whereas coinjection of H2SO4 in the LLME method is probable. Complete neutralization of all of the sulfuric acid is not likely with NaHCO3, thereby allowing some residual H2SO4 to be injected with the sample. The acid, together with residual H2O, will result in degradation of the capillary column stationary phase and in acid-catalyzed hydrolysis of the HAA-methyl esters, particularly of the trihalogenated acids, resulting in reduced sensitivity for the analytes and higher, more variable background signals in the chromatographic runs. The esters of trihaloacetic acids may also be more efficiently sampled by the PDMS fiber. The estimated detection limits and the linear range of the two methods are listed in Table 1. Method 552.2 with LLME-GC and LLME-SPME-GC for municipal drinking water samples were compared (Table 2). The precision of the three methods at the observed concentrations were highly comparable, with the SPME method showing the best median precision. The exception to this observation is sample 4, whose DCAA value had an RSD of 19%. The average relative differences between the LLME methods and Method 552.2 ranged from 5.8% to 28%. In general, agreement within 20% between laboratories analyzing the same samples even when employing the same method is considered acceptable. Variability among analysts for trace analysis methods is often seen depending on their level of experience and the experience of the laboratory in which the method is run.

Application to water and biological samples

LLME-SPME-GC-ECD was used to determine HAAs in urine and blood samples of rats fed with a solution containing a mixture of THMs and HAAs. Internal standard calibration curves were generated using Milli-Q water as the standard matrix. Standard addition calibration curves were constructed by adding three different amounts of HAA standards to aliquots of the same rat urine samples. The equation of calibration curve for DCAA in rat urine is y = 0.03227 + 1.4057x. The correlation coefficient (r) is 0.9989. The concentration in the sample was estimated by the intercept on the x-axis of peak area ratio vs added amount ratio curve. The error of the results between internal standard method and standard addition method is less than 12%. Thus, it appears that the urine matrix is not a substantial influence on the method. Rat blood was analyzed similarly. Once again, the relative error of the results between internal standard method and standard addition method was less than 16%. Results of replicate rat urine analyses using LLME-GC and LLME-SPME-GC are listed in Table 3. Very good

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### Table 2

<table>
<thead>
<tr>
<th>Sample</th>
<th>TCAA</th>
<th>DCAA</th>
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<tr>
<td>552.2</td>
<td>56</td>
<td>64</td>
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<tr>
<td>LLME</td>
<td>9.0%</td>
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<tr>
<td>SPME</td>
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<td>13</td>
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</table>

* n = 2, therefore number denotes % deviation from the mean.

### Table 3

<table>
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<tr>
<th>TCAA</th>
<th>LLME-GC</th>
<th>LLME-SPME-GC</th>
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<tr>
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<td>RSD(%)</td>
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* Rat urine sample from pharmacokinetic study.
Substantial analyte preconcentration, either via solvent extraction of DCAA and TCAA in rodent urine were 86 to 110% and 82 to 110% (Table 1). This is an important factor in this method: precision can be generally maintained down to sub-mg L\(^{-1}\) concentrations even with the inherently greater level of imprecision that is probable when working with very small sample volumes.

Precision and recovery results for DCAA and TCAA in water with different concentrations on different days were as follows: the RSDs for DCAA at concentrations ranging from 10 to 4600 \(\mu\)g L\(^{-1}\) were 1.1 to 14%. The RSDs for TCAA at concentrations ranging from 6 to 600 \(\mu\)g L\(^{-1}\) were 0.5 to 13%. Recoveries of DCAA and TCAA in rodent urine were 86 to 110% and 82 to 110% in rodent blood.

Advantages over current and reported methods

Substantial analyte preconcentration, either via solvent extraction or direct evaporation of the sample can also result in concentration of the sample matrix, which is most problematic when using liquid injection and GC-MS analysis, since MS does not discriminate against non-electron negative compounds as does ECD. MS techniques still require further development for ultra-trace analysis of haloacid compounds in order to routinely achieve ECD-level sensitivity. Headspace sampling substantially reduces such matrix influences. For biological samples, non-carcinogenic acidic methanol was used instead of diazomethane, with a small tradeoff in throughput efficiency due to increased derivatization time. Using micro-bore capillary chromatography, all nine HAAs were analyzed in 7 min in water and < 13 min in biological samples, at greater sensitivity than using methods reported previously for microvolume samples. MDLs for six of the nine HAAs were between 0.6 and 1.2 \(\mu\)g L\(^{-1}\), 7.2 \(\mu\)g L\(^{-1}\) for MBAA, 6.3 \(\mu\)g L\(^{-1}\) for MCAA and 3.1 \(\mu\)g L\(^{-1}\) for TBAA; Schultz et al. reported MDLs of 0.8 to 130 \(\mu\)g L\(^{-1}\), with 0.8 \(\mu\)g L\(^{-1}\) for DCAA and all others above 3 \(\mu\)g L\(^{-1}\). A major advantage of our methods is that they achieve comparable sensitivity to the standard method that uses 40 mL of sample (Method 552.2) with no substantial loss of precision.

As mentioned above, it was found that the SPME method was more suitable for the biological samples because it virtually eliminated the effect of the sample matrix. It was also suitable for the trihaloacetic acids because they appeared to be readily absorbed on the fiber and have greater sensitivity compared to the liquid-liquid extraction method.

Acknowledgements

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