Determination of trihalomethanes in drinking water by GC-ICP-MS using Compound Independent Calibration with Internal Standard.

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Abstract

Compound Independent Calibration with Internal Standard in combination with GC-ICP-MS allowed standardless determination of trihalomethanes ($CHCl_3$, $CHBrCl_2$, $CHBr_2Cl$ and $CHBr_3$) in drinking waters following European Norm ISO 10301. It was demonstrated that the ratio of peak areas (analyte to internal standard) is linear with the ratio of concentrations with slope of 1 and intercept of 0, both for chlorine and bromine, when the concentrations of analyte and internal standard are expressed in terms of elemental concentrations. Then, the use of $CBrCl_3$ as internal standard allowed the simultaneous determination of all four compounds in one single injection by detecting chlorine at mass 35 and bromine at mass 79. For the determination of trihalomethanes (THMs) in drinking waters the method required only the addition of a known amount of internal standard to 100 mL of sample, the extraction of the THMs using 4 mL of n-pentane and the direct injection of the extract in the GC-ICP-MS system. No additional injections were required for quantitation. Extraction recoveries were between 80 and 98%, reproducibility was below 3% and method detection limits were below 0.01 ng mL^{-1} for all compounds, meeting the requirements of international legislation for the routine determination of THMs in drinking waters.

Keywords

Compound Independent Calibration, trihalomethanes, GC-ICP-MS, drinking water.

Introduction

Compound Independent Calibration (CIC) for the determination of organic compounds after a chromatographic separation is a recurrent topic in modern analytical chemistry[1,2,3,4]. Traditionally, the coupling of Gas Chromatography with Microwave Induced Plasmas (GC-Atomic Emission Detector, AED) showed that CIC and molecular formula determination was possible under certain conditions[2]. For example, for split/splitless injection an apparent compound dependence of the AED response was observed due to compound discrimination at the injector[2]. Another GC detector showing compound independent capabilities is the Pulsed Flame Photometric Detector (PFPD)[5]. For both the AED and the PFPD quenching of the analyte signal by high concentrations of co-eluting compounds was detected pointing to one of the main drawbacks for universal CIC of GC detectors: matrix effects of co-eluting compounds. On the other hand, other most popular detectors for Gas Chromatography as Electron Impact-Mass Spectrometry (EI-MS) or Electron Capture Detector (ECD) show responses that are compound specific depending on the actual ionization efficiency or electron capture tendency for each analyte respectively.

The development of suitable interface systems for the coupling of the Inductively Coupled Plasma to Gas Chromatography[6,7,8] boosted the interest in compound independent sensitivity, particularly with the GC-ICP-MS coupling, due to the more robust plasma in comparison to the MIP. In this sense, the detection of non-metals (such as Si[9]; P, S, Cl, Br and I[10] and Br and I[11]) by GC-ICP-MS was shown to follow compound independent sensitivity which was predicted years before by Chong and Houk[12] for the GC-ICP-MS coupling. Additionally, compound independent sensitivity was also demonstrated for the HPLC-ICP-MS coupling in the field of phospho-peptide analysis[13], for selenium speciation[14] and for the determination of phospho-nucleotides[15]. In these cases, particular attention should be paid to gradient elution conditions when using organic modifiers[13].

Another field in which compound independent sensitivity is evaluated, or sometimes assumed, is for species-unspecific Isotope Dilution Analysis[16] using ICP-MS detection. Using this technique, an enriched isotope of the element to be determined is added post-column after the chromatographic separation in a chemical form which usually differs from that of the separated compounds. In general, no differences in elemental

sensitivity is found for different elemental species by ICP-MS but this fact can not always be assured; particularly when no standards of all elemental species detected are available. There are cases in which elemental sensitivity is demonstrated to be independent of the elemental species, such as for Se(IV), Se(VI) and selenomethionine[14], and others where the sensitivity, under certain conditions, is different for different species, such as for $(CH_3)_3Pb^+$ and Pb^{2+} in NaCl solutions[17] due to nebulisation effects.

The initial objective of this work was to check for compound independent sensitivity for different halogenated compounds using GC-ICP-MS as the first step to develop a post-column isotope dilution analysis procedure using ^{37}Cl and ^{79}Br enriched isotopes. Problems with the supply of the enriched isotopes prompted us to check the possibility of using a natural abundance internal standard for quantitation. As can be seen below, when compound independent sensitivity is assured, the use of an internal standard eliminates the need for any methodological calibration of the response of the instrument allowing for standarless determination of the analytes in a way which is similar to isotope dilution analysis.

The halogenated compounds selected in this work were the trihalomethanes (THMs). These compounds are the main disinfection-by-products formed during water chlorination by the reaction between natural organic matter and chlorine[18]. New regulations have been developed for the control of those substances in drinking water due to the adverse effects they can cause on human beings, so new methodologies for the quantification of THMs are needed. In this work we demonstrate that the elemental response for chlorine and bromine is linear and independent of the molecular structure for THMs ($CHCl_3$, $CHBrCl_2$, $CHBr_2Cl$ and $CHBr_3$) and the selected IS ($CBrCl_3$) when using GC-ICP-MS. The optimum operational conditions for the GC separation and the ICP-MS detection are presented. The CIC methodology has been applied and validated for the determination of THMs in drinking water showing adequate analytical characteristics in application of the European Legislation[19].

Experimental

Instrumentation

A Varian (Varian Inc., Walnut Creek, CA, USA) Model 3400 gas chromatograph fitted with a split/splitless injector was used. For the separation of the four THMs and the internal standard a low polarity capillary column DB-VRX (J&W Scientific, Folsom, CA, USA; 60 m x 0.32 mm x 1.8 μm film thickness) was selected as it provides optimum resolution for the separation of volatile compounds. The gas chromatograph was coupled to a HP-4500 inductively coupled plasma mass spectrometer (Yokogawa Analytical Systems Inc., Tokyo, Japan) using the transfer line described in detail previously[6]. Operating conditions are summarized in Table 1. The Liquid-Liquid Extraction of the THMs and the internal standard was carried out by means of a mechanical shaker (Heidolph REAX 2, Kelheim, Germany). All standard solutions and samples were prepared gravimetrically using an analytical balance (Mettler-Toledo GmbH, Im Langacher, Switzerland).

Reagents and materials

A certified standard mixture of THMs ($CHCl_3$, $CHBrCl_2$, $CHBr_2Cl$ and $CHBr_3$, 2000 μg mL^{-1} of each compound in methanol) was obtained from Supelco (Bellefonte, PA, USA). The internal standard used in this work ($CBrCl_3$, 99% purity) was obtained from Aldrich (Steinheim, Germany). Intermediate standard solutions of the THMs mixture and the internal standard were prepared in methyl *tert*-butyl ether (MTBE). Working standard solutions containing different concentrations of THMs and the same concentration of the internal standard were prepared in n-pentane daily. All the prepared solutions were stored in dark at -18 ºC until their use. MTBE (purity ≥ 99.0 %) and n-pentane (purity ≥ 99.0%) were both obtained from Fluka (Buchs SG, Switzerland).

A NIST certified reference material (SRM 1639) containing a mixture of halocarbons in methanol at different concentration levels ($CHCl_3$ 6235 ng μL^{-1}, $CHBrCl_2$ 389.9 ng μL^{-1}, $CHBr_2Cl$ 124.6 ng μL^{-1}, $CHBr_3$ 86.5 ng μL^{-1}, CCl_4 157.0 ng μL^{-1}, $CHCl=CCl_2$ 85.8 ng μL^{-1}, and $CCl_2=CCl_2$ 40.6 ng μL^{-1}) was obtained from LGC Promochem (Middlesex, United Kingdom). Ultrapure water was obtained from a Milli-Q water purification system (Millipore, Bedford, MA, USA).

Amber glass bottles of 500 mL with GL PTFE-lined screw caps were used for drinking water sampling. All the glass material was cleaned with detergent, rinsed with Milli-Q

water and oven dried at 80 ºC for at least 1 hour. Before its use glass material was brought to room temperature[20].

Analytical procedure

Five drinking water samples from different water supplies in Asturias (Spain) were collected in amber glass bottles. Before sampling, the tap was allowed to run for, at least, 10 minutes. After that, bottles were filled and sealed carefully in order to avoid analyte looses. Samples were transported and stored in the dark at 4 ºC. In all cases the THMs were extracted from the water samples within 24 hours and analyzed within 48 hours after collection[20].

For the determination of THMs in drinking water 100 mL of water sample were placed in a glass volumetric flask with glass stopper. A known amount of internal standard and 4 mL of n-pentane as extractant were added to the water sample (all by weight). The mixture was mechanically shaken for 10 minutes and then organic extract was removed into an amber glass vial. The organic extracts were stored in dark at -18 ºC until their analysis. Finally 1 μL of the organic extract was injected in the GC-ICP-MS system.

Results and discussion

Compound independent calibration with internal standard

Compound Independent Calibration (CIC) is a quantitative technique based on the capability of certain detectors of providing an elemental response independent of the chemical structure of the molecules which may contain the element. In this sense, the detector response would not be affected by the nature or the molecular structure of the analyte. If the detector is used in combination with a chromatographic separation the measured peak area should be proportional to the concentration of the element reaching the plasma regardless of the molecular structure of the compound.

If that is assumed, equations (1) and (2) must be fulfilled by both, the analyte and the internal standard:

$$[\text{Peak Area}]_{analyte} = k_x \times [X]_{analyte} \quad (1)$$

$$[\text{Peak Area}]_{IS} = k_x \times [X]_{IS} \quad (2)$$

being k_x the sensitivity constant (compound independent) for a given element X and $[X]_{analyte}$ and $[X]_{IS}$ the concentrations of the element X in the analyte and the internal standard respectively. If we divide equation (1) by equation (2):

$$\frac{[\text{Peak Area}]_{analyte}}{[\text{Peak Area}]_{IS}} = \frac{[X]_{analyte}}{[X]_{IS}} \quad (3)$$

In this way, equation (3) shows that the plot of peak area ratio between analyte and internal standard should follow a straight line with respect to the ratio of concentrations with slope 1 and intercept 0. This fact simplifies the calibration procedure for compounds containing the element X. As can be seen, equation (3) does not contain any sensitivity factor as it occurs in other calibration strategies (external calibration or standard additions). Therefore, once it is demonstrated that the elemental response of the ICP-MS is independent of the species measured, the determination of compounds containing this element is possible by means of a single chromatographic injection after the addition of a known amount of internal standard to the sample. Nevertheless, response is only truly compound independent if the response does not change for the duration of the chromatographic run. This may not be guaranteed if there are long run times or complexes matrices, which may affect plasma conditions.

In this work $CBrCl_3$ was selected as internal standard for the determination of both chlorinated and brominated trihalomethanes in drinking water, being X in equation (3) chlorine or bromine respectively.

Figure 1 shows the chromatographic separation of a standard solution mixture containing the four trihalomethanes and the internal standard. In this chromatogram isotopes ^{35}Cl, ^{37}Cl, ^{79}Br and ^{81}Br were monitored. As it can be observed, the chromatographic conditions listed in Table 1, provided a good separation for the four trihalomethanes, the internal standard and the two solvents used (MTBE and n-pentane), without band broadening and with a reasonable acquisition time of ca. 16 minutes.

In order to obtain the calibration curve, standard solutions containing different concentrations ranging from 0 to 2 μg mL^{-1} of each THM and CCl_4 and 1.5 μg mL^{-1} of internal standard in n-pentane were injected in the chromatographic system and the chlorine and bromine signal monitored in the ICP-MS instrument. In all cases the peak areas were integrated and divided by the peak area of the internal standard. Then, the concentrations of the analytes (as Cl or Br) were divided by the concentration of the internal standard (also as Cl or Br). Finally, the concentration ratios were plotted as a function of the peak area ratios for chlorine (Figure 2) and bromine (Figure 3).

Table 2 shows the slopes and intercepts obtained for calibration curves measured in different days. The uncertainties indicated in Table 2 correspond to the standard deviation of both the slope and intercept obtained from the regression line. As it can be observed, in both cases the calibration curve showed a slope and an intercept which are not statistically different from 1 and 0 respectively (P=0.05). These data suggest that the ICP-MS response for chlorine and bromine is independent of the chemical structure of the different trihalomethanes, CCl_4 and the internal standard used in this case and it allows to safely assume that compound independent calibration for chlorine and bromine can be obtained on a routine basis.

Analytical characteristics

Once demonstrated the capabilities of the ICP-MS to provide compound independent sensitivity for chlorine and bromine, the next step is to calculate the extraction yields when the THMs are extracted from water into n-pentane. In this sense, two experiments were performed. First, the absolute recovery of the extraction of THMs with n-pentane was calculated by adding different amounts of THMs to a tap water sample. After extraction, using the analytical procedure explained before, the internal standard was added to the n-pentane solution containing the extracted THMs. Finally, 1 μL of this organic solution was injected in the chromatographic system. The concentrations found using equation (3) were plotted against the expected concentrations. The slope of the curve obtained indicated the extraction recovery. As it can be seen in Table 3 the extraction recovery was different for each compound ranging from 70% to 95%. For the brominated THMs lower uncertainty was obtained

when bromine was used for quantitation instead of chlorine as can be observed in Table 3.

Secondly, the relative recovery of the procedure was calculated by adding both the internal standard and different amounts of THMs to a tap water sample. After that, samples were analysed using the analytical procedure explained before and the concentrations calculated using equation (3) were plotted against the expected concentrations. In this case, the slope of this curve indicated the method recovery as the internal standard was added to the sample instead of the n-pentane solvent. As it is shown in Table 3, all recoveries are now between 80% and 100%.

Alternatively, the recovery of the analytical method for each compound was also calculated by using a standard reference material (SRM 1639) which contains the four THMs at different concentration levels (see Table 3). For this purpose an adequate amount of standard reference material and internal standard were added to Milli-Q water in order to obtain a sample with the same concentrations of THMs as those expected in real tap waters samples. This spiked sample was analyzed using the proposed methodology. The accuracy of the method was calculated in this case dividing the concentration found by the expected concentration. The average recovery obtained for the THMs were also between 80 and 100% and very similar to those obtained by the standard addition method as can be seen in Table 3 (no statistical differences were found for P=0.05 for the most sensitive isotope).

The reproducibility of the analytical procedure was calculated by analysing 5 Milli-Q water samples spiked with the standard reference material at levels between: 54.62 ng mL^{-1} for $CHCl_3$ and 0.76 ng mL^{-1} for $CHBr_3$. The relative standard deviations obtained for the four THMs are listed in Table 3. As it can be observed the reproducibility was below 3% in all cases except for $CHBrCl_2$ and $CHBr_2Cl$ when monitoring the chlorine signal at mass 35. This can be explained when taking into account the low sensitivity of the ICP-MS instrument for chlorine and the low concentration of these compounds in the sample. Fortunately, these two compounds can be determined by monitoring the bromine signal at mass 79 with much better sensitivity.

Instrumental limits of detection for the most sensitive isotope were calculated from the compound independent calibration curves as three times the standard deviation of the intercept divided by the slope. Method detection limits were calculated as three times the standard deviation of the intercept of the standard addition experiments to milli-Q water taking into account the recoveries of the method and are also given in Table 3.

The main analytical characteristics (method recovery, reproducibility and method detection limits) are compared in Table 4 to other recently published procedures for the determination of THMs in drinking water.[21-27] As can be observed, all analytical procedures published include Gas Chromatography coupled to Electron Capture Detection (ECD)[21,23-27] or Mass Spectrometry (MS)[22,27] with a variety of sample preparation techniques including Liquid-Liquid Extraction (LLE)[27], Solid Phase Microextraction (SPME)[22,26], Liquid Phase Microextraction (LPME)[21,23,25] or Capillary Membrane Sampling (CMS)[24]. Overall, the performance of the method proposed here is equivalent or better than most methods published previously with the added advantage that no methodological calibration is required.

Analysis of drinking water samples

The method was applied to the determination of THMs in drinking water samples from Asturias (Spain). Figure 4 shows a typical chromatogram obtained for a drinking water sample spiked with the internal standard (sample 3 in Table 5). The concentrations of THMs in drinking water samples after recovery correction are given in Table 5 and were obtained by direct application of equation (3).

The uncertainty for each concentration was calculated as the total combined uncertainty (coverage factor k=2). The sources of uncertainty were the standard deviation of the compound independent calibration slope, the uncertainty in the recovery factors and the precision of the peak area ratio experimentally measured. To do that, the following equation was used:

$$\left[\frac{S_C}{C}\right]^2 = \left[\frac{S_{RA}}{RA}\right]^2 + \left[\frac{S_b}{b}\right]^2 + \left[\frac{S_R}{R}\right]^2 \qquad (4)$$

where, C is the concentration, RA is the peak area ratio, b is the calibration slope, R is the method recovery and S_C, S_{RA}, S_b, and S_R are the standard deviations of the concentration, the peak area ratio, the calibration slope and the method recovery, respectively. The influence of the standard deviation of the peak area ratio in the total uncertainty increases as the concentration of the compound decreases in the samples. Thus, the standard deviation of the peak area ratio is the main uncertainty factor in the cases of $CHBrCl_2$, $CHBr_2Cl$ when monitoring the chlorine signal and for $CHBr_3$, due to the low concentration of this compound in the water samples.

In the case of $CHBrCl_2$ and $CHBr_2Cl$ both elements, chlorine and bromine, can be monitored in order to quantify the concentration of these compounds in the samples as similar values were found (see table 5). However, the total uncertainty monitoring the chlorine signal was always worse than that found when monitoring the bromine signal, as it was explained before.

Results for corrected THMs concentrations and total THMs concentration (TTHMs expressed as the sum the four THMs in ng mL^{-1}) are also summarised in Table 5. As can be seen all water samples show TTHMs values below 150 ng mL^{-1} which is the parametric value set by the European Union for water intended for human consumption (100 ng mL^{-1} in 2008). In all cases the four THMs were detected and quantified. As expected, the abundance of these compounds decreases as the number of bromine atoms in the molecules increases.

Conclusions

As it has been demonstrated, the sensitivity factor of ICP-MS for chlorine and bromine is independent of the compound, at least for the THMs and the internal standard used in this work, using the conditions given in Table 1. Consequently, an internal standard can be used for the determination of these compounds in drinking waters avoiding other time-consuming calibration methodologies as external calibration or standard additions. In these sense, Compound Independent Calibration using ICP-MS could be considered an interesting alternative to the most popular ECD or MS detectors taking into account also the low limits of detection provided.

In CIC the internal standard plays a role similar to the isotopically enriched element used in post-column isotope dilution analysis. However, it must be remembered that CIC is only a quantification strategy that can not compete with species-specific isotope dilution analysis in terms of the control of the recovery of the analytical procedure. Unfortunately, isotopically enriched THMs with Cl or Br are not commercially available.

Acknowledgments

A. González-Gago is grateful to the Ministry of Education and Science (MEC, Madrid, Spain) for his pre-doctoral fellowship. Financial support from the Asturian Government (FICYT project PC-04-46) is gratefully acknowledged.

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Table 1. GC-ICP-MS operating conditions.

GC and interface parameters	
Column	DB-VRX (60 m × 0.32 mm ×1.8 □m)
Injection mode	Splitless
Injection volume	1 μL
Carrier gas / Inlet pressure	He / 15 psi
Injection temperature	175 ºC
Interface temperature	255 ºC
Oven programme	45 ºC (2 min) to 190 ºC at 12 ºC min^{-1} to 245 ºC (5 min) at 30 ºC min^{-1}
ICP-MS parameters	
Rf power	1280 - 1300 W
Sampling depth	5.5 - 6.0 mm
Carrier gas flow rate	1.37 - 1.45 L min^{-1}
Intermediate gas flow rate	1 L min^{-1}
Outer gas flow rate	15 L min^{-1}
Isotopes detected	^{35}Cl, ^{37}Cl, ^{79}Br, ^{81}Br
Integration time	0.05 s per m/z
Ion lens setting	Daily optimisation

Table 2. Slopes and intercepts of calibration curves obtained in different days.

Day	Cl (m/z = 35)		Br (m/z =79)	
	Slope	**Intercept**	**Slope**	**Intercept**
1	0.92 ± 0.01	0.01 ± 0.01	1.03 ± 0.02	-0.01 ± 0.02
2	0.993 ± 0.009	-0.005 ± 0.007	1.010 ± 0.008	-0.009 ± 0.009
3	1.04 ± 0.03	0.03 ± 0.02	1.09 ± 0.02	-0.04 ± 0.02
Average	**0.98 ± 0.03**	**0.01 ± 0.03**	**1.04 ± 0.02**	**-0.02 ± 0.03**

Table 3. Analytical characteristics.

		Absolute Extraction Recovery (%)	Relative Recovery (%)		Reproducibility* n = 5 (RSD%)	LOD (ng mL^{-1})	
			Standard Additions	Reference Material*		Instrumental	Method
$CHCl_3$	**m/z = 35**	69.4 ± 2.0	79.7 ± 4.9	81.4 ± 2.2	2.7	0.13	0.0063
	m/z = 79	--	--	--	--	--	--
$CHBrCl_2$	**m/z = 35**	72.2 ± 6.2	80.6 ± 1.4	92.2 ± 5.0	5.6	--	--
	m/z = 79	77.3 ± 2.5	84.6 ± 0.6	87.1 ± 2.7	2.9	0.12	0.0057
$CHBr_2Cl$	**m/z = 35**	92.6 ± 3.9	93.7 ± 2.2	84.2 ± 25.8	31	--	--
	m/z = 79	88.3 ± 1.8	94.7 ± 0.7	92.8 ± 2.4	2.5	0.077	0.0033
$CHBr_3$	**m/z = 35**	--	--	--	--	--	--
	m/z = 79	94.9 ± 2.5	100.7 ± 0.1	96.1 ± 3.0	2.8	0.062	0.0026

*NIST SRM 1639: $CHCl_3$ (54.62 ng mL^{-1}), $CHBrCl_2$ (3.41 ng mL^{-1}), $CHBr_2Cl$ (1.09 ng mL^{-1}) and $CHBr_3$ (0.76 ng mL^{-1}).

Table 4. Analytical characteristics compared to other published analytical methods.

a) Relative recovery (%)

	LLE-GC-ICP-MS	**LPME-GC-ECD**	**SPME-GC-MS**	**LPME-GC-ECD**	**CMS-GC-ECD**	**LPME-GC-ECD**	**SPME-GC-ECD**	**LLE-GC-ECD**	**LLE-GC-MS**
	This work	Ref 21	Ref 22	Ref 23	Ref 24	Ref 25	Ref 26	Ref 27	Ref 27
$CHCl_3$	80	74	98	98	100	101	107	100	95
$CHBrCl_2$	86	78	100	98	104	105	101	104	96
$CHBr_2Cl$	94	74	101	96	125	104	102	103	99
$CHBr_3$	98	73	96	97	124	102	106	102	100
b) Reproducibility (%)									
$CHCl_3$	2.7	3	3.8	7	4.5	11.3	3.2	1.0	3.4
$CHBrCl_2$	2.9	5	1.8	5	8.6	9.4	1.0	0.4	4.0
$CHBr_2Cl$	2.5	7	1.1	6	3.5	8.2	1.8	0.4	4.3
$CHBr_3$	2.8	2	0.6	6	4.3	8.7	2.1	1.2	4.1
c) Method detection limits (ng mL^{-1})									
$CHCl_3$	0.006	0.45	0.52	0.2	0.1	0.40	0.01	0.010	0.01
$CHBrCl_2$	0.006	0.23	0.21	0.01	0.1	0.15	0.005	0.005	0.02
$CHBr_2Cl$	0.003	0.32	0.13	0.01	0.1	0.15	0.005	0.007	0.02
$CHBr_3$	0.003	0.25	0.078	0.04	0.4	0.20	0.01	0.010	0.03

Table 5 Concentration of THMs (ng mL^{-1}) in drinking water samples, uncertainty expressed as total combined uncertainty (coverage factor k = 2).

	$CHCl_3$		**$CHBrCl_2$**		**$CHBr_2Cl$**		**$CHBr_3$**		**TTHMs***
	m/z = 35	m/z = 79	m/z = 35	m/z = 79	m/z = 35	m/z = 79	m/z = 35	m/z = 79	
Blank	0.3 ± 0.3	--	n.d.	0.03 ± 0.02	n.d.	n.d.	--	n.d.	**0.33**
Sample 1	10.1 ± 1.2	--	3.2 ± 0.4	3.3 ± 0.3	1.1 ± 0.9	1.1 ± 0.1	--	0.09 ± 0.02	**14.6**
Sample 2	20.1 ± 1.9	--	4.2 ± 0.6	4.5 ± 0.4	0.8 ± 0.6	0.50 ± 0.04	--	0.014 ± 0.001	**25.1**
Sample 3	17.9 ± 1.7	--	6.2 ± 1.3	6.4 ± 0.5	6.3 ± 13.7	2.2 ± 0.2	--	0.16 ± 0.02	**26.7**
Sample 4	3.4 ± 0.3	--	3.1 ± 0.6	3.1 ± 0.3	1.8 ± 2.0	1.6 ± 0.1	--	0.17 ± 0.02	**8.3**
Sample 5	22.1 ± 2.6	--	4.9 ± 1.2	4.4 ± 0.4	2.1 ± 4.3	1.06 ± 0.08	--	0.30 ± 0.03	**27.9**

* TTHMs = $CHCl_3$ (m/z =35) + $CHBrCl_2$ (m/z = 79) + $CHBr_2Cl$ (m/z = 79) + $CHBr_3$ (m/z = 79)

Legends of figures.

Figure 1. Chromatogram obtained using the instrumental conditions summarised in Table 1 for the four trihalomethanes and the internal standard ($CBrCl_3$).

Figure 2. Compound Independent Calibration curve obtained for chlorine.

Figure 3. Compound Independent Calibration curve obtained for bromine.

Figure 4. Chromatogram of a tap water sample.

Figure 1

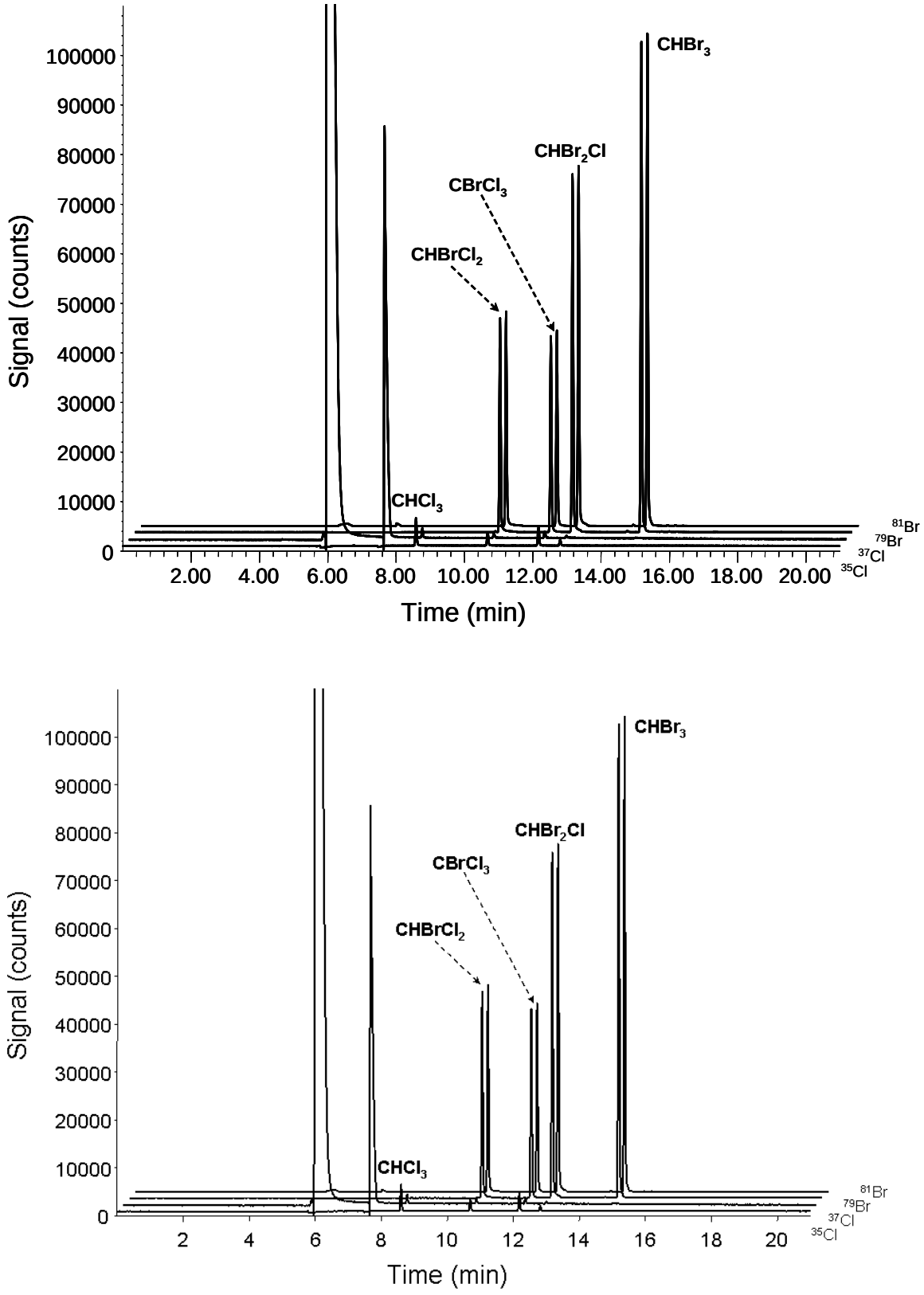
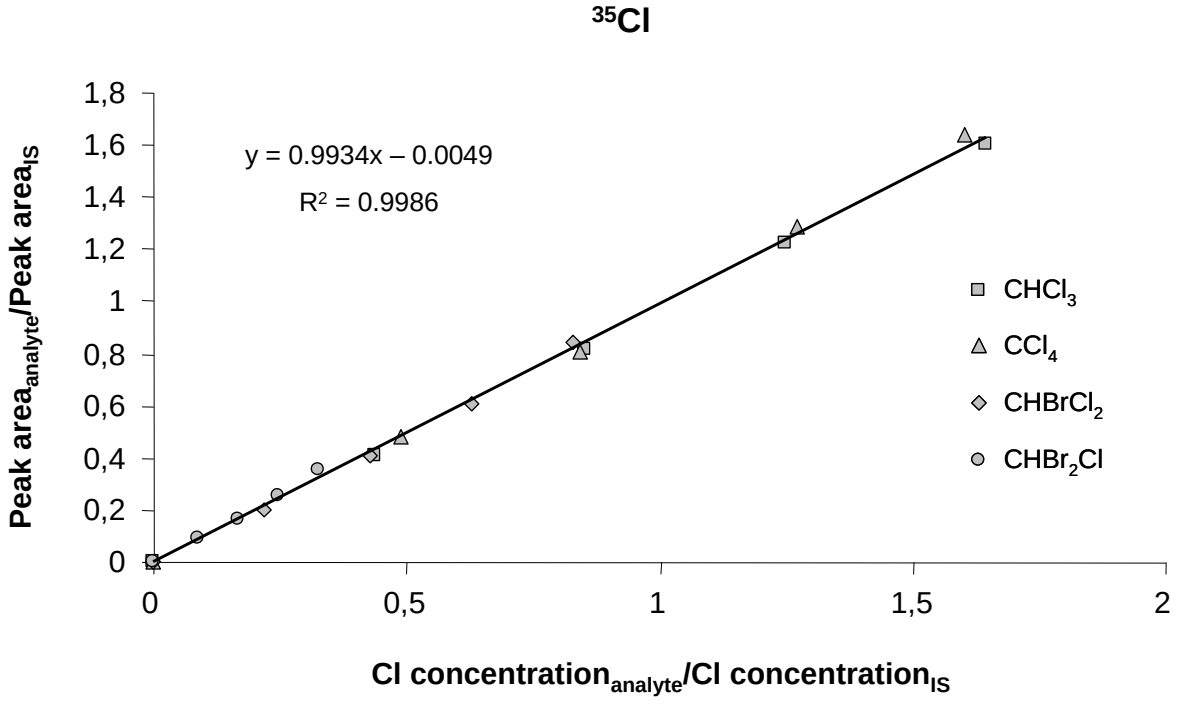

CHBr3
CHBr2Cl
CBrCl3
CHBrCl2
CHCl3
81Br
79Br
37Cl
35Cl
Signal (counts)
Time (min)

Figure 2


35Cl
y = 0.9934x – 0.0049
R2 = 0.9986
CHCl3
CCl4
CHBrCl2
CHBr2Cl
Peak areaanalyte/Peak areaIS
Cl concentrationanalyte/Cl concentrationIS
0
0,2
0,4
0,6
0,8
1
1,2
1,4
1,6
1,8
0,5
1,5
2

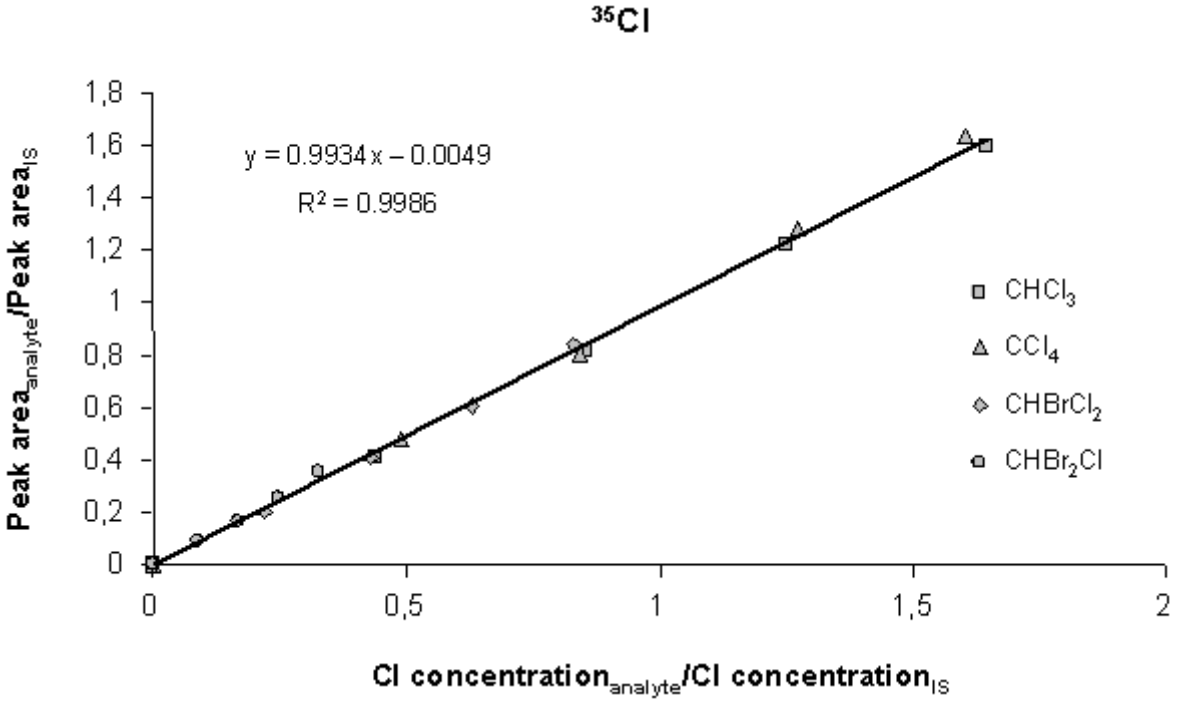
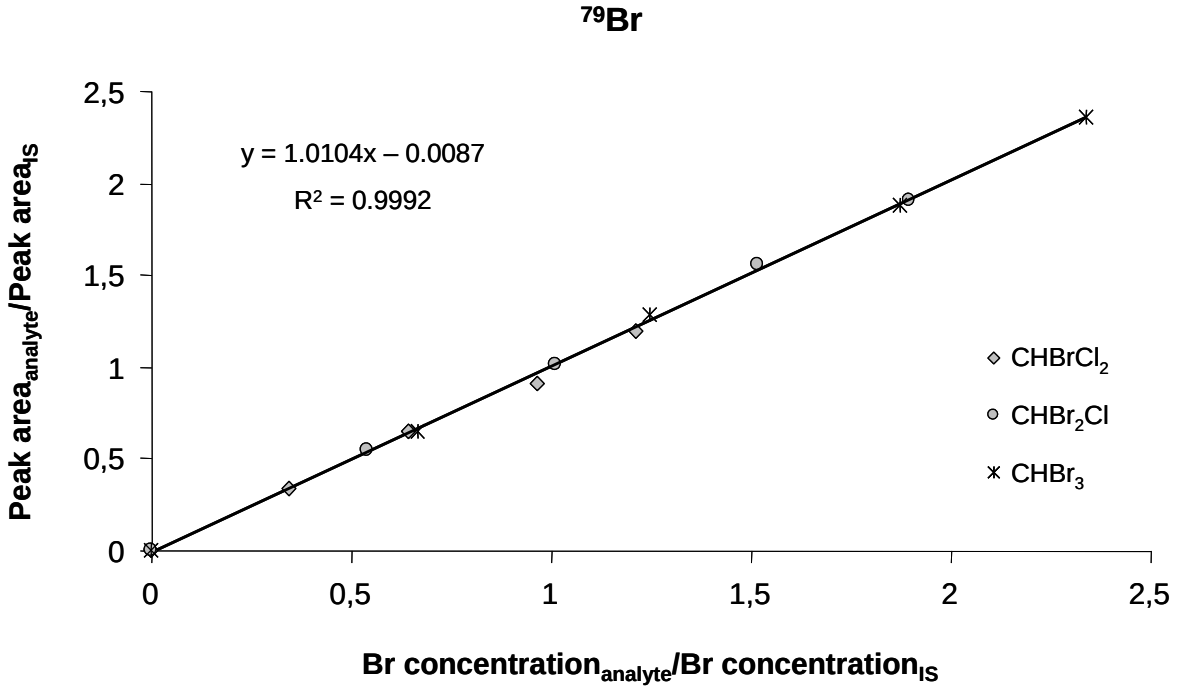

35Cl
y = 0.9934 x – 0.0049
R2 = 0.9986
CHCl3
CCl4
CHBrCl2
CHBr2Cl
Peak areaanalyte/Peak areaIS
Cl concentrationanalyte/Cl concentrationIS
0
0,2
0,4
0,6
0,8
1
1,2
1,4
1,6
1,8
0,5
1,5
2

Figure 3


79Br
y = 1.0104x – 0.0087
R² = 0.9992
Peak area analyte/Peak area IS
Br concentration analyte/Br concentration IS
CHBrCl2
CHBr2Cl
CHBr3
0
0,5
1
1,5
2
2,5

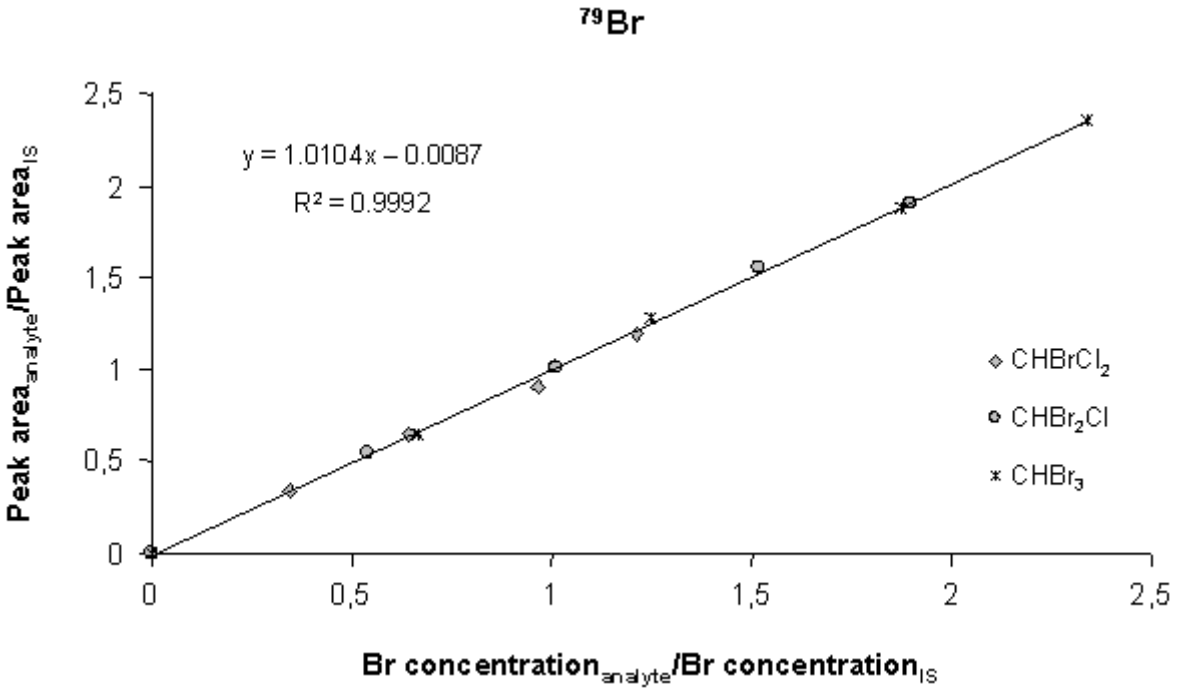
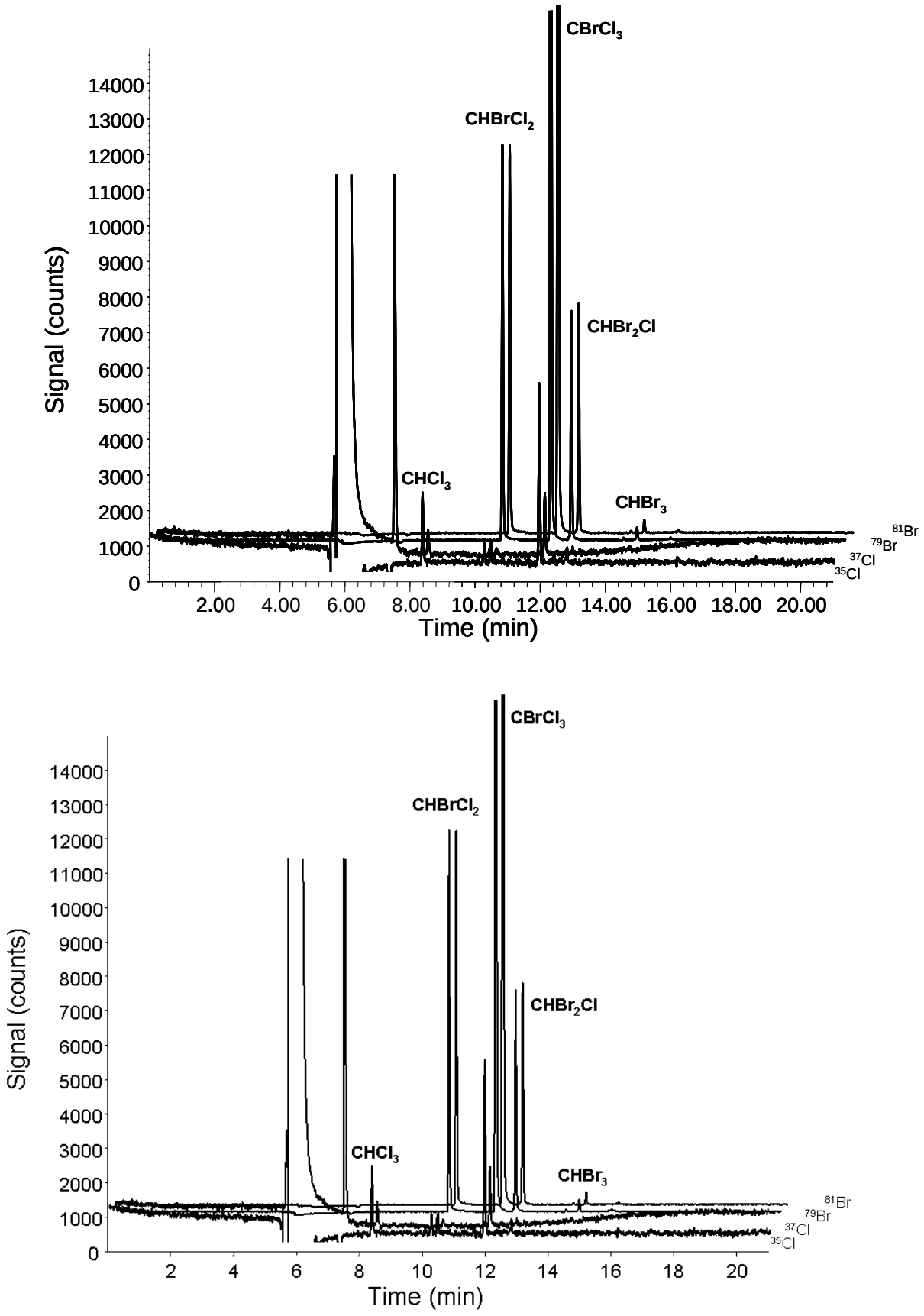

79Br
y = 1.0104x – 0.0087
R² = 0.9992
Peak area analyte/Peak area IS
Br concentration analyte/Br concentration IS
CHBrCl2
CHBr2Cl
CHBr3
0
0,5
1
1,5
2
2,5

Figure 4


CBrCl3
CHBrCl2
CHBr2Cl
CHCl3
CHBr3
81Br
79Br
37Cl
35Cl
Signal (counts)
Time (min)
0
1000
2000
3000
4000
5000
6000
7000
8000
9000
10000
11000
12000
13000
14000
2.00
4.00
6.00
8.00
10.00
12.00
14.00
16.00
18.00
20.00