Towards the revision of the drinking water directive 98/83/EC. Development of a direct injection ion chromatographic-tandem mass spectrometric method for the monitoring of fifteen common and emerging disinfection by-products along the drinking water supply chain

Towards the revision of the Drinking Water Directive 98/83/EC. Development of a direct injection ion chromatographic-tandem mass spectrometric method for the monitoring of fifteen common and emerging disinfection by-products along the drinking water supply chain

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Abstract

According to the recent proposal released by the European Commission for the revision of the 98/83/EC Directive, water suppliers will be requested to monitor the nine bromine- and chlorine congeners of haloacetic acids, HAAs, as well as the oxyhalides chlorite and chlorate, as disinfection by-products (DBPs) originated during the potabilization process.

In this work, we propose a direct-injection method based on ion chromatography and mass spectrometric detection for the determination of the mentioned DBPs as well as bromate (already included in the 98/83/EC), implemented also for the following emerging HAAs monoiodo-, chloroiodo- and diiodo-acetic acids. The method was optimized to include the fifteen compounds in the same analytical run, tuning the chromatographic (column and gradient) and detection conditions (suppression current, transitions, RF lens settings and collision energies). To avoid matrix effect and to manage the instrumental conditions, optimization was performed directly in drinking water matrix. The method quantitation limits satisfy the new limits imposed by the future directive and range from 0.08 µg/L (monobromoacetic acid) to 0.34 µg/L (trichloroacetic acid). The performance of the method was checked along different strategic sampling points of three potabilization plants serving the city of Turin (Italy), including intermediate treatments and finished waters. Recovery was checked according to the ±30% limit of acceptability set by EPA regulations. The effect of disproportionate concentrations of chlorite and chlorate in respect to HAAs on HAA signals was studied; this aspect is underestimated in literature. The method is routinely applied by the potabilization plant of the city of Turin to confirm the effectiveness of all control measures in abstraction, treatment, distribution and storage. This study represents the first example in Italy of development and use of a cutting-edge technique for HAAs analysis along the potabilization processes.

Keywords: drinking water directive, haloacetic acids, ion-chromatography, mass spectrometry, plant monitoring

1. Introduction

Within the European Community, the quality and safety of water intended for human consumption is currently disciplined by the so-called 98/83/EC Drinking Water Directive [1].

As a result of the Regulatory Fitness and Performance programme (REFIT) evaluation and of the follow up actions to the European Citizens' Initiative (ECI) Right2Water, the European Commission adopted on 1 February 2018 a proposal for the revision of the Drinking Water Directive [2]. In the upcoming proposal for the revision of the 98/83/EC Directive, attention is devoted to the disinfection by-products (DBPs) originated during potabilization process. More in detail, the directive requires the monitoring of the nine bromine- and chlorine congeners of haloacetic acids, HAAs, (monochloro-, dichloro-, and trichloro-acetic acid, mono- and dibromo-acetic acid, bromochloroacetic acid, bromodichloroacetic acid, dibromochloroacetic acid and tribromoacetic acid), which must not be present at concentrations higher than 80 μg/L as a sum. After trihalomethanes, HAAs are the second most prevalent DBP class generated in disinfected waters, and their toxicological effects are well ascertained [3].

The upcoming revision of the 98/83/EC Directive is also going to regulate the presence of chlorate and chlorite, which are predominantly formed when the disinfectants used are hypochlorite and/or chlorine dioxide solutions. According to WHO recommendations, the guideline value allowed for chlorite and chlorate in drinking water is 0.7 mg/L. According to indications provided by the European Food Safety Authority (EFSA) on toxicological reference value for chronic risk assessment provided for chlorate, the EU Commission is going to regulate the presence of both chlorate and chlorite at the stricter level of 0.25 mg/L, overcoming the fact that current EU drinking water directive does not set any specific limits in drinking water.

For those regions whose drinking water sources are impacted by sea water intrusion and thus contain relatively high concentrations of Br^- and I^- ions, besides brominated compounds, the presence of iodinated (emerging) DBPs in finished drinking waters could also be observed [4]. Monoiodoacetic acid

inhibits glyceraldehyde-3phosphate dehydrogenase (GAPDH) activity in a greater extent than bromo- and chloro-analogous [5].

Bromate occurrence in drinking water is ascribed to the oxidation of Br^- naturally occurring in water during ozonation process, even if bromate could be present, as a contaminant, in commercial solutions of sodium hypochlorite used for disinfection of drinking water [6]. Bromate is considered a probable human carcinogen, it was listed in B2 Group by IARC and its presence is regulated in drinking waters by US EPA and 98/83/EC Directive which both set a limit of 10 µg/L.

Regarding the analytical determination of DBPs, the methods most used for this purpose are based on gas (GC) and liquid chromatographic (LC) techniques. GC is employed for HAA analysis after a preliminary derivatization step [7], as recommended by EPA 552.2 method [8]. Detection can be accomplished with ECD or MS [9] detectors at µg/L levels.

LC methods are mainly based on the anion-exchange methods, exploiting, if possible, the ionic nature of the DBPs. Ion chromatography coupled to MS-MS detection allows to achieve detection limits for selected HAAs at fractions of µg/L without sample pretreatment [10, 11]. Hundreds ng/L detection limits levels can be achieved for HAAs enriching acidified sample onto functionalized graphene/alumina nanocomposites [12]. So far, only few emerging iodinated HAAs have been monitored in waters, using GC-MS [13] and LC-MS [4] methods after sample pretreatment or direct large volume injection [14]. Oxyhalide DBPs (chlorite, chlorate, perchlorate and bromate) are easily determined in drinking water using ion chromatography with suppressed conductivity as recommended by EPA methods 300.1 [15] and 314.0 [16], colorimetry [17] and in few cases by mass or mass tandem spectrometry [18].

In view of the upcoming revision of the Drinking Water Directive 98/83/EC, water suppliers that treat and supply drinking water as well as institutions in charge to control safety of the distributed water must be ready to measure all the above-mentioned compounds in a routine basis, to meet future legislative requirements.

The aim of this work is to develop a sensitive, accurate method without sample pretreatment for the determination of DBPs, including emerging iodinated HAAs, in one chromatographic run, to be used

by the water supplier laboratories for the routine controls required for the upcoming Drinking Water Directive.

With the aim of satisfying currently accepted EPA standards [10] in an analytical method of wider applicability, an ion chromatographic method with tandem mass spectrometry was here optimized for the simultaneous determination of the DBPs subjected to the attention of the future legislation, i.e. monochloro-, dichloro-, and trichloro-acetic acid, mono- and dibromo-acetic acid, bromochloroacetic acid, bromodichloroacetic acid, dibromochloroacetic acid and tribromoacetic acid, chlorite, chlorate, as well as bromate (already included in the 98/83/EC), and monoiodo-, chloroiodo- and diiodo-acetic acids as emerging HAAs.

Before applying the developed method to real samples of different provenience, the robustness of the method was checked evaluating the recovery of analytes in samples withdrawn from different points of three potabilization plants, characterized by matrix composition at different complexity. Quantitation limits and acceptance criteria of the method fully comply future regulatory requirements. The method is currently routinely applied for the analysis of fifteen DBPs by the laboratory in charge of supplying and monitoring drinking water in the Italian city of Torino.

This study represents the first example of simultaneous analysis of the DBPs included in the forthcoming Drinking Water Directive revision and a rare example in Italy of development and application of direct injection IC/MS-MS technique for the analysis of organic and inorganic disinfection by-products along the drinking water supply chain (raw, treated and distributed waters).

2. Materials and methods

2.1 Chemical standards and reagents

Acetonitrile, ammonium chloride, monoiodoacetic acid (MIAA), as well as the following isotopically enriched internal standards monobromoacetic acid-1-^{13}C (MBAA-^{13}C), dichloroacetic acid-2-^{13}C (DCAA-^{13}C), trichloroacetic acid-2-^{13}C (TCAA-^{13}C), were from Sigma Aldrich (St. Louis, MO, USA). Iodoacetic acid-D3 (MIAA-D3), diiodoacetic acid (DIAA) and chloroiodoacetic acid (CIAA),

were from Chemical Research (Rome, Italy). Inorganic anions were purchased in a standard mixture of 1000 mg/L from Ultra Scientific (Bologna, Italy). The nine bromo- chloro- HAA congeners (monochloro- MCAA, dichloro-DCAA, and trichloro-acetic acid TCAA, mono- MBAA and dibromo-acetic acid DBAA, bromochloroacetic acid BCAA, bromodichloroacetic acid BDCAA, dibromochloroacetic acid DBCAA and tribromoacetic acid TBAA) were purchased from Restek (Bellefonte, PA, USA) in a mixture containing 1000 mg/L of each HAA in MTBE. Deionized water (18.2 MΩcm resistivity) for eluent preparation and for dilution of stock standard solutions was obtained by an EMD Millipore Milli-Q Direct Water Purification System (Millipore, Bedford, MA, USA).

2.2 Instrumental equipment and operating conditions

A Thermo Fisher Scientific (Waltham, MA USA) ICS-5000 IC system was used throughout this work. The system includes a DP dual pump module for analytical and capillary applications, a CD conductivity detector, an AS autosampler, and a Reagent-Free (RFIC) eluent generator EG-5000 with ECG III cartridges KOH to provide the gradient of KOH (mobile phase) using deionized water from an AXP-MS pump (Thermo Fisher Scientific). For sample injections (120 µL), two autosamplers without (AS-DV) and with sample tray temperature control (AS-AP) set at 9±1 °C were used; both were from Thermo Fisher Scientific. Separations were performed on an IonPac AS24 (250x2 mm i.d.) coupled with a guard column IonPac AG24 (50x2 mm i.d.) both from Thermo Fisher Scientific, thermostatted at 15 °C in order to minimize the degradation at high pH values for MBAA, CDBAA and TBAA. Eluent gradient (0.3 mL/min) was set as follows, 7 mM KOH: t=0-15.1 min; 7-15.5 mM KOH: t=15.1-25.8 min; 60 mM KOH: t=25.9 min, keep until 46 min; 7 mM KOH; t=47-58 min.

To remove trace anion contaminants from hydroxide eluent and to minimize base line shifts during gradient operation, an electrolytically continuously regenerated trap column (CR-ATC, 8% DVB crosslinking, 55 µm particle size) was installed in the eluent line after the pump prior to the sample injection. After eluent generation and before the separation column, Electrolytic suppression was accomplished using an ASRS 500 (2-mm) from Thermo Fisher Scientific.

A TSQ Endura triple-stage quadrupole mass spectrometer with ESI interface (HESI-II) was employed for detection. A diverter valve was used to waste the anion interfering species from matrix, thus preventing inorganic anions to enter the MS equipment. After the IC suppressor and before the ESI inlet, acetonitrile (CH_3CN) was added to the eluate at 0.3 mL/min through an additional AXP-MS pump. The addition of CH_3CN leads to higher efficiency in gas phase ion generation during the ESI process [19], enhancing analyte sensitivity [20]. The MS spectrometer was tuned and calibrated through the software TSQ Endurance Tune Application 2.1 (Thermo Fisher Scientific) by direct infusion of polytyrosine-1,3,6 (Thermo Fisher Scientific). Performance was checked every two weeks using the same polytyrosine-1,3,6 solution.

2.3 Preparation of standard solutions and water samples

Standard solutions were prepared in 5-mL vials directly in the autosampler. Ten levels of standard solutions were used for the construction of the calibration curve which was comprised between 0.25 and 20 µg/L starting from a 1 mg/L standard mixture of DBPs in water. To each standard solution, 500 µL of 1000 mg/L NH_4Cl were added to reach a final concentration of 100 mg/L NH_4Cl as well as and 50 µL of internal standard solution (0.4 mg/L) to reach a final concentration of 4 µg/L.

Water samples were withdrawn from the treatment train of the water plant and filtered in Millex Gv filters (0.22-µm, Millipore). Water was sampled into 100 mL glass flasks containing 10 mg NH_4Cl and immediately analysed.

3. Results and Discussion

3.1 Optimization of MS/MS conditions

Starting key MS/MS conditions were set as follows. Ion source polarity was in the negative ion mode, spray voltage: 3200 V, vaporizer gas pressure (N_2): 45 units, auxiliary gas pressure (N_2): 10 units, capillary temperature: 200 °C, vaporizer temperature: 200 °C, collision gas (Ar) pressure: 1.5 mTorr, ion

cycle time: 0.5 s. To maximise the peak response for the analytes, capillary and vaporizer temperatures were further optimized in the range 200-230 °C (capillary T) and 200-260 °C (vaporizer T) by the injection of analyte mixtures at 5 µg/L. Best conditions were achieved with capillary temperature of 220 °C and vaporizer temperature of 250 °C. Further increase of these values lead to decreased peak signals especially for HAAs due to analyte degradation [21].

RF lens settings and collision energies (CE) for each transition were specifically optimised for each analyte, by infusion of 500 µg/Lof each HAA and isotopically enriched internal standard (Table 1). According to literature data [22, 23], $[M-H]^-$, resulting from deprotonation of molecular ion, is the predominant precursor ion for haloacetic acids containing one or two halogen atoms, whereas $[M-COOH]^-$ precursor is preferred for haloacetic acids containing three halogen atoms. Dimer ions can even be formed increasing infusion concentration (>1 µg/L) [24]. In this work, each precursor ion was selected based on literature information on the most abundant species formed in ESI detection [10, 24]. In detail, for HAAs, the selected precursor ion is the one deriving from deprotonation ($[M-H]^-$) of molecular ion for MCAA, MIAA, DCAA, MBAA, BCAA, DBAA, CIAA, DIAA and TCAA of the acid, whereas for BDCAA, CDBAA and TBAA, the precursor ion selected is the one resulting from decarboxylation ($[M-COOH]^-$) of the acid. For TCAA, even if many authors suggest the selection of $[M-COOH]^-$ as the precursor ion [22, 23], it is not infrequent the selection of the $[M-H]^-$ species [10, 20]. In this work, the $[M-H]^-$ was preferred over the $[M-COOH]^-$ species due to the difference in signal response which was as high as 10^4 ($[M-H]^-$ /$[M-COOH]^-$).

For each precursor ion, the three most abundant product ions were monitored. Transitions to halide substituent were found to be the most abundant for HAAs containing one and three halogen atoms, i.e. MCAA, MBAA, MIAA, BDCAA, CDBAA, TBAA, except for TCA, for which transition to the $[M-COOH]^-$ ion is preferred. For HAAs containing two halogen atoms, except for CIAA, the $[M-COOH]^-$ ion is also preferred. These findings are coherent with literature reports [23]. CIAA exhibits the most abundant transition to the I^- ion in agreement with detection studies conducted in reversed phase liquid chromatography and tandem mass spectrometry [14].

Precursor ion was used as quantifier ion, whereas product ion was used as qualifier ion.

3.2 Optimization of ion chromatographic conditions

Separation column. The fifteen DBPs and the main common anions in drinking water are characterized by different chemical properties, hence their simultaneous separation in matrix is a challenging task. Gradient conditions are often required to provide elution in reasonable analysis time and baseline resolution for analytes belonging to different classes. The elution of chlorite, chlorate and bromate is usually accomplished with isocratic runs on high capacity carbonate selective columns, such as IonPac AS9-HC, and more recently IonPac AS23 [25] which ensure baseline resolution of oxyhalides even at high matrix ion content. However, carbonate selective columns are not recommended for gradient elution, since baseline drift is too severe, hence hydroxide selective columns are the election choice. Hydroxide selective column such as IonPac AS19 have shown improved sensitivity and allows the detection of chlorite, chlorate and bromate at lower concentrations in respect to the carbonate selective IonPac AS23 column [26].

On the other hand, hydroxide selective columns of even high capacity are best suited for HAAs monitoring in drinking waters where common ions can be present in concentrations as high as 250 mg/L Cl^- and SO_4^{2-} [20].

At the light of the above considerations, for the simultaneous elution of the fifteen DBPs, the column chosen was the IonPac AS24, which is as yet the best hydroxide selective high-capacity column available in the market for the elution of nine Cl-, Br- HAA congeners. The separation for all the fifteen DBPs in the presence of Cl^-, SO_4^{2-}, NO_3^- and CO_3^{2-} ions must be preliminarily checked with conductivity detection (see below). A good separation of matrix ions from analytes of interest is important to reduce matrix effects and to preserve the ESI source, through eluate diversion to the waste. In fact, it has been shown that in the absence of matrix diversion, recoveries for species eluting close to Cl^- ion can be reduced to 77±10% in finished drinking waters [23].

Elution conditions. Gradient profile proposed by column manufacturer (Eluent #1, Table 2) was initially tested in drinking water distributed in Turin, Italy (15 mg/L Cl^-, 20 mg/L NO_3^-, 35 mg/L SO_4^{2-}, 250 mg/L HCO_3^-), spiking 5 µg/L of each analyte. Although the fifteen analytes could be separated from matrix interferent, diversion to waste could not avoid the enhancement of chlorate signal by carbonate ion and the suppression of DIAA signal by sulfate ion. This suppression can be avoided changing the selectivity coefficient DIAA/sulfate ion. Taking advantages of the fact that changes in counter-ion eluent concentration (OH^-) have greater effects on divalent ions rather than on monovalent ions, as predicted by the ion-exchange mechanisms [27], the instantaneous eluent change to 60 mM KOH was anticipated just after the elution of DCAA (Eluent #2, Table 2), keeping constant the slope of gradient after the first 15 minutes of elution. As expected, the increase of eluent strength shifted the divalent SO_4^{2-} ion more than the monovalent DIAA, moving SO_4^{2-} ion close to carbonate ion which could be both diverted to waste (Table 2). Therefore, the following time intervals for eluate diversion to waste were set: 18-23 min (Cl^-), 28.3-28.8 min (CO_3^{2-}, SO_4^{2-}), 30.5-32.3 min (NO_3^-) which allow us to detect all the fifteen DBPs. The optimized diverter times eliminate the suppression effect on chlorate due to carbonate ion, which in drinking water samples was about 35%.

The optimized separation of the fifteen DBPs is shown in Fig. 1. Total analysis time is 60 minutes and includes the re-equilibration of the column to the starting gradient conditions.

3.3 Optimization of suppressor current

Factors known to favour ionization process at atmospheric pressure, besides organic solvents such as methanol or acetonitrile, are: (i) low ionic strength, (ii) the absence of inorganic non-volatile salts and (iii) the presence of the analyte as an ion in solution [28]. Chemical suppression is a necessary step to meet these conditions; the efficiency of eluent suppression affects the sensitivity of the MS detection, since excessive background conductivity causes MS signal suppression. The suppressor current value was optimized through the injection of HAA mixture and the evaluation of limits of detection (LODs) and quantitation (LOQs) according to Shrivastava and Gupta [29]. The current range explored was

252 varied between 45 mA and 70 mA, which corresponds to the recommended range for current setting at
253 the higher KOH concentration reached in the gradient. Data obtained show that the lowest quantitation
254 limits can be achieved setting the suppressor current at 50 mA; higher current values enhance the
255 background noise. The best improvements of quantitation limits were observed for DBAA, DCBAA e
256 DBCAA and in a less extent for TBAA. At this current value, total conductivity within the imposed
257 gradient conditions varies from 0.8 to 3.0 µS.
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259 *3.4 Figures of merit of the method*
260 *Linearity, limits of detection and quantitation.* Linearity was evaluated over two orders of
261 magnitude, correcting peak response of each analyte with the relative response factor of the internal
262 standard, as assigned in Table 1. Table 3 collects the results obtained, as well as the LOD and LOQ values
263 [29].
264 A comparison of LOD values with EPA 557 method is not possible for all the analytes, since this
265 study also includes oxyhalide DBPs (chlorite, chlorate) and emerging iodoacetic (monoiodo-,
266 chloroiodo- and diiodo-acetic) acids not included in the above-mentioned standard. However, the
267 optimization carried out allowed to get improved (from 2 to 3 times) detection limits for MCAA, MBAA,
268 BCAA and TBAA, but higher (from 2 to 3.5 times) for DBAA, BDCAA, DBCAA and bromate.
269 Comparable LODs were obtained for DCAA and TCAA.
270 As regards iodoacetic acids, when comparisons are possible, detection limits are improved in
271 respect to the IC-ICP/MS approach [30], and comparable or even better than IC-tandem mass
272 spectrometry methods [14].
273 As regards oxyhalides (chlorite, chlorate and bromate) our LODs are more than 20 times better
274 than conductivity detection in hydroxide selective columns [26] and comparable for chlorite and bromate
275 to those shown by the few studies based on IC-MS for oxyhalides [18]. The slightly better LOD obtained
276 for chlorate in respect to this work (0.045 vs 0.188 µg/L) is explained with the pretreatment of drinking
277 water samples with OnGuard cartridges for matrix removal, which is effective also for carbonate ions.

Effect of refrigeration. Current literature dealing with HAAs determination underline the possibility of degradation of MBAA, DBCAA and TBAA with temperature at high pH value, thus recommending the injection of samples at refrigerated conditions and elution at sub-ambient temperature. Differently from what expected, refrigeration was found also beneficial for the enhancement of signal intensity for TCAA (+73%) > DCAA (+62%) > BCAA (+58%) > DBAA (+41%) > bromate (40%). The easier degradation of tri-substituted haloacids agrees with the degradation studies presented by Lifongo et al. [31]. The limits of detections obtained within this work at controlled autosampler and elution temperature conditions (Table 3) were compared with those obtained by Wu et al. [23], who eluted HAAs at alkaline conditions, thermostatting the column at 45 °C, without any control of injection temperature. In this regard, the limits presented [23] for some analytes seem surprisingly low (MCAA: 0.041 µg/L, bromate: 0.0051 µg/L, TCAA: 0.03 µg/L) in consideration of the above-mentioned discussion on compound stabilities and of the limits obtained in this work and current literature [10].

Accuracy and precision. Recovery (R) for all analytes were determined at five concentration levels spiking known concentrations from 0.25 to 20 µg/L for each analyte in ultrapure water in the presence of 100 mg/L NH_4Cl. Each concentration level was analysed with 24 repetitions for each DBP and 57 repetitions for internal standards. The following equation was used [10]:

$$R = 100 \cdot \frac{(A - B)}{C}$$

where A= measured concentration in the fortified sample; B= measured concentration in the unfortified sample; C= fortification concentration.

According to the data obtained (Table 4), recovery is within ±50% of the true value for 0.25 µg/L (which corresponds to the lowest calibration level of the calibration curve) and within ±30% of the true value for the other levels, thus fulfilling the requirement set by EPA [10].

Precision ranged from 1.3% (MIAA) to 12% (MCAA) for the lowest calibration level and from 1% (MIAA) to 5.4% (chlorate) for the highest calibration level. These data fully satisfy precision

303 requirements set by EPA according to which seven replicates in the midrange of calibration curve should
304 be ≤20% [10]. Since a unique method for the determination of the disinfection by-products considered
305 in this work is not available in literature, comparisons are possible only for classes of analytes determined
306 with different analytical approach. For the nine Cl- and Br- congeners, mean recoveries for the same
307 fortification levels are comparable or even improved (DCAA, DCBAA) in respect to other IC-MS/MS
308 methods [10]. For iodinated DBPs, better mean recoveries were obtained within this work for MCAA in
309 respect to the ones obtained by reversed-phase LC-MS/MS with large volume injection [14]. It should
310 be remarked that the above-mentioned methods were tested for limited numbers of replicates (n=4-15)
311 in respect to our study.
312 Inter-day, evaluated in 4 different days by 57 replicates, and intra-day precision, evaluated within
313 the same day by 15 replicates, was studied using internal standards at 4 µg/L concentration. The
314 satisfactory data obtained (Table 4) indicate the robustness of the method developed.
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319 *3.5 Application to drinking water supply chain*
320 Before applying the developed method to the analysis of drinking water samples, the robustness
321 of the method was checked evaluating the recovery of analytes in samples withdrawn from different
322 points of the treatment train, characterized by matrix composition at different complexity.
323 Three drinking water plants (DW1, DW2, DW3) were considered and analysed. The first two,
324 DW1 and DW2, are conventional treatment plants, including dynamic separation basins (DSB) for the
325 removal of slurry from clarified waters, in which coagulant, hypochlorite and chlorine dioxide solutions
326 are dosed. The third, DW3, is an advanced treatment plant, dosing ozone as oxidant and performing
327 biological treatment and extended activated carbon filtration; samples were taken at the outlet of a

clarification basin (CB3) in which coagulant and hypochlorite solutions are added. Effluents from DW plants (E1, E2, E3), which represent distributed waters, were also analysed.

Due to the unbalanced amounts of HAAs and bromate in respect to chlorite and chlorate ions (which derive from reagent conversion), recoveries of analytes were determined in DSB1, DSB2, E1, E2 (for DW1 and DW2 plants), and in CB3 and E3 (for DW3 plant) for HAAs and bromate. The five samples withdrawn from each treatment stage (DSB1, DSB2, E1, E2, CB3 and E3), added with 100 mg/L NH_4Cl, were fortified with 5 µg/L HAAs and bromate and analysed. The data obtained (Table 5) clearly show that all HAAs (except MCAA) satisfy the ±30% requisite of the EPA regulation. MCAA is at the lower limit of acceptability of the above-mentioned requisite in DSB1-2 and in E1.

This behaviour is explained by the suppression effect of chlorite ion, which in DSB1-2 and in E1 samples is present in disproportionate concentrations (about 350 µg/L, respectively) in respect to MCAA (5 µg/L).

To this purpose, the effect of chlorite on MCAA signal suppression in drinking water samples is reported in Figure 2, where the continuous line represents the spiked MCAA concentration (5 µg/L) and the two dotted lines represent the ±30% requisite (3.5 and 6.5 µg/L).

Data show that the limit set for chlorite (250 µg/L) by the revision of the Drinking Water Directive 98/83/EC allows the determination of MCAA with the required accuracy. Concentrations of chlorite as high as 1 mg/L still allow the quantitation of MCAA with standard addition method (20% recovery for MCAA). It is worth mentioning that the effect of chlorite on MCAA detection is not investigated in current literature [14, 23], since only Cl^-, NO_3^-, SO_4^{2-}, HCO_3^- are considered in the matrix. Moreover, current EPA method [10] does not allow the determination of MCAA in waters containing chlorite.

The method developed was hence used to check the drinking water supply chain in the main stages of treatment for each DW plant on a daily basis (Table 6), as well as in domestic tap water samples of different provenience (Table 7).

As far as the plant is concerned, the presence of DBPs in DSB1-2 and CB3 is coherent with the addition of the hypochlorite solution. This intermediate disinfection stage is of low impact in HAAs

formation, since the sum of the compounds subjected to regulation is well below the limit established for finished waters (80 µg/L). The subsequent filtration stages are efficient in the reduction of HAA9 since these compounds are present in the distributed waters at concentrations below 6 µg/L. The frequency of occurrence of haloacetic DBPs roughly followed the order DCAA>TBAA>BCAA>TCAA>>DBAA>>DCBAA>>MBAA. Emerging iodinated compounds were not detected.

Regarding the domestic tap water samples, two of them were withdrawn from houses served by the plant here studied (samples A,B, Turin, Italy), one from a house located in Monte Carlo (sample C, Principality of Monaco) and one from a drinking fountain of the province of Imperia (sample D, Italy). Samples C and D were chosen since their sampling areas correspond to municipalities located in coastal zones and hence vulnerable to the presence of brominated and iodinated compounds.

The results on tap waters sampled in houses located in the plant area considered confirms the absence of any criticality. Waters sampled from the coastal area are not affected by the presence of iodinated HAAs, even if a signal below the quantitation limit could be ascribed to MIAA. In one case, the presence of brominated species (BCAA, DBAA) at very low concentration levels (sum 1 µg/L) was revealed.

4. Conclusions

This paper reports the first chromatographic method to fulfil the upcoming revision of the Drinking Water 98/83/EC Directive, allowing the simultaneous determination of the nine HAAs and the three oxyhalides ions listed in the regulation. The method already includes three additional emerging iodinated acids (not yet considered by the revision). The method, validated directly in waters withdrawn from strategic points of the potabilization plant, is a powerful tool for water suppliers which are asked to put in place operational, supply-specific monitoring programmes intended to confirm the effectiveness of all control measures in abstraction, treatment, distribution and storage.

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References

[1] European Commission, Council Directive 98/83/EC of 3 November 1998 on the quality of water intended for human consumption, available at https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:31998L0083, (1998).

[2] European Commission, Proposal for a Directive of the European Parliament and of the Council on the quality of water intended for human consumption, https://eur-lex.europa.eu/legal-content/EN/TXT/?qid=1519210589057&uri=CELEX:52017PC0753, (2018).

[3] S.D. Richardson, M.J. Plewa, E.D. Wagner, R. Schoeny, D.M. DeMarini, Occurrence, genotoxicity, and carcinogenicity of regulated and emerging disinfection by-products in drinking water: A review and roadmap for research, Mutation Research/Reviews in Mutation Research, 636 (2007) 178-242.

[4] Y. Pan, W. Li, H. An, H. Cui, Y. Wang, Formation and occurrence of new polar iodinated disinfection byproducts in drinking water, Chemosphere, 144 (2016) 2312-2320.

[5] J.A. Pals, J.K. Ang, E.D. Wagner, M.J. Plewa, Biological mechanism for the toxicity of haloacetic acid drinking water disinfection byproducts, Environmental science & technology, 45 (2011) 5791-5797.

[6] H.S. Weinberg, C.A. Delcomyn, V. Unnam, Bromate in Chlorinated Drinking Waters: Occurrence and Implications for Future Regulation, Environmental Science & Technology, 37 (2003) 3104-3110.

[7] D.W. Hawker, J.L. Cumming, A. Watkinson, M.E. Bartkow, The occurrence of the herbicide dalapon (2,2-dichloropropionate) in potable water as a disinfection by-product, Journal of Environmental Monitoring, 13 (2011) 252-256.

[8] US Environmental Protection Agency, Method 552.2: determination of haloacetic acids and dalapon in drinking water by liquid–liquid extraction, derivatization and gas chromatography with electron capture detection. Environmental Monitoring and System Laboratory, Cincinnati, OH., (1995).

[9] Y. Xie, Analyzing Haloacetic Acids Using Gas Chromatography/Mass Spectrometry, Water Research, 35 (2001) 1599-1602.

[10] US Environmental Protection Agency, Method 557: determination of haloacetic acids, bromate, and dalapon in drinking water by ion chromatography electrospray ionization tandem mass spectrometry (IC-ESI-MS/MS). EPA Document no. 815-B-09-012., (2009).

[11] R. Xue, A. Donovan, H. Shi, J. Yang, B. Hua, E. Inniss, T. Eichholz, Rapid simultaneous analysis of 17 haloacetic acids and related halogenated water contaminants by high-performance ion chromatography-tandem mass spectrometry, Analytical and Bioanalytical Chemistry, 408 (2016) 6613-6622.

[12] Z. Zhong, G. Li, Y. Shao, B. Zhu, Z. Liu, J. Deng, J. Mo, Amino-functionalized graphene oxide/neutral alumina nanocomposite based solid-phase extraction coupled with ion chromatography-mass spectrometry for the determination of trace haloacetic acids in drinking water, Analytical Methods, 9 (2017) 2425-2432.

[13] S.D. Richardson, F. Fasano, J.J. Ellington, F.G. Crumley, K.M. Buettner, J.J. Evans, B.C. Blount, L.K. Silva, T.J. Waite, G.W. Luther, A.B. McKague, R.J. Miltner, E.D. Wagner, M.J. Plewa, Occurrence and Mammalian Cell Toxicity of Iodinated Disinfection Byproducts in Drinking Water, Environmental Science & Technology, 42 (2008) 8330-8338.

[14] Y. Li, J.S. Whitaker, C.L. McCarty, Analysis of iodinated haloacetic acids in drinking water by reversed-phase liquid chromatography/electrospray ionization/tandem mass spectrometry with large volume direct aqueous injection, Journal of Chromatography A, 1245 (2012) 75-82.

[15] U.S. Environmental Protection Agency, Method 300.1: Determination of Inorganic Anions in Drinking Water by Ion Chromatography, Revision 1.0. Cincinnati, OH, (1997).

[16] U.S. Environmental Protection Agency, Method 314.0 Determination of Perchlorate in Drinking Water Using Ion Chromatography. Revision 1.0. Cincinnati, OH, (1999).

[17] H.P. Wagner, B.V. Pepich, D.P. Hautman, D.J. Munch, US Environmental Protection Agency Method 326.0, a new method for monitoring inorganic oxyhalides and optimization of the postcolumn derivatization for the selective determination of trace levels of bromate, Journal of Chromatography A, 956 (2002) 93-101.

[18] S.A. Snyder, B.J. Vanderford, D.J. Rexing, Trace analysis of bromate, chlorate, iodate, and perchlorate in natural and bottled waters, Environ Sci Technol, 39 (2005) 4586-4593.

[19] Y. Hsieh, Potential of HILIC-MS in quantitative bioanalysis of drugs and drug metabolites, Journal of Separation Science, 31 (2008) 1481-1491.

[20] R. Slingsby, C. Saini, C. Pohl, The determination of haloacetic acids in real world samples using IC-ESI-MS-MS, Journal of chromatographic science, 47 (2009) 523-528.
[21] C. Yang, S. Henday, Application Note 454. Analysis of haloacetic acids in drinking water by IC-MS/MS, AN62963_E 01/09S, Thermo Fisher Scientific, Sunnyvale, CA, USA., (2009).
[22] R. Loos, D. Barceló, Determination of haloacetic acids in aqueous environments by solid-phase extraction followed by ion-pair liquid chromatography–electrospray ionization mass spectrometric detection, Journal of Chromatography A, 938 (2001) 45-55.
[23] S. Wu, T. Anumol, J. Gandhi, S.A. Snyder, Analysis of haloacetic acids, bromate, and dalapon in natural waters by ion chromatography–tandem mass spectrometry, Journal of Chromatography A, 1487 (2017) 100-107.
[24] Q. Luo, D. Wang, Z. Wei, Z. Wang, Optimized chromatographic conditions for separation of halogenated acetic acids by ultra-performance liquid chromatography–electrospray ionization-mass spectrometry, Journal of Chromatography A, 1277 (2013) 26-34.
[25] Thermo Scientific, Product Manual for Dionex IonPac AS23-4µm, Document n. 065711-01, June 2016, (2016).
[26] B. De Borba, J. Rohrer, Application Note 184, Determination of Trace Concentrations of Chlorite, Bromate, and Chlorate in Bottled Natural Mineral Waters, AN70407-EN 08/16S, Thermo Fisher Scientific, Sunnyvale, CA, USA, (2008).
[27] M.C. Bruzzoniti, E. Mentasti, C.A. Pohl, J.M. Riviello, C. Sarzanini, Effect of ion-exchange site and eluent modifiers on the anion-exchange of carboxylic acids, Journal of Chromatography A, 925 (2001) 99-108.
[28] J.J. Conboy, J. Henion, M.W. Martin, J.A. Zweigenbaum, Ion Chromatography/Mass Spectrometry for the Determination of Organic Ammonium and Sulfate Compounds, Analytical Chemistry, 62 (1990) 800-807.
[29] A. Shrivastava, V. Gupta, Methods for the determination of limit of detection and limit of quantitation of the analytical methods, Chronicles of Young Scientists, 2 (2011) 21-25.
[30] H. Shi, C. Adams, Rapid IC–ICP/MS method for simultaneous analysis of iodoacetic acids, bromoacetic acids, bromate, and other related halogenated compounds in water, Talanta, 79 (2009) 523-527.
[31] L.L. Lifongo, D.J. Bowden, P. Brimblecombe, Photodegradation of haloacetic acids in water, Chemosphere, 55 (2004) 467-476.

Table 1. Optimised MS transitions for each compound of this study.

Analyte	Assigned internal standard	Precursor ion (*m/z*)	Product ion (*m/z*)	RF lens (V)	CE (V)
MCAA	MBAA-^{13}C	93.113	35.444	55.18	10.253
Chlorite	MBAA-^{13}C	67.262	51.286	65.49	13.64
MBAA-^{13}C	-	137.848	79.058	50.629	10.253
MBAA	MBAA-^{13}C	136.991	79.04	53.663	10.253
MIAA-D3		186.862	126.946	53.36	13.89
MIAA	MIAA-D3	184.878	126.889	51.236	10.253
Bromate	MBAA-^{13}C	126.9	110.929	131.933	22.792
DCAA-^{13}C	-	128	84.04	66.101	10.253
DCAA	DCAA-^{13}C	127.052	83.04	73.382	10.253
BCAA	DCAA-^{13}C	172.87	128.889	61.551	10.253
CIAA	MIAA-D3	218.862	126.911	64.28	21.78
DBAA	DCAA-^{13}C	216.83	172.778	64.888	10.253
Chlorate	DCAA-^{13}C	83.162	67.125	95.83	20.01
DIAA	MIAA-D3	310.725	266.679	70.65	10.25
TCAA	TCAA-^{13}C	160.839	116.946	43.652	10.253
TCAA-^{13}C	-	161.909	117.946	40.92	10.25
DCBAA	TCAA-^{13}C	162.839	81.071	57	10.253
DBCAA	TCAA-^{13}C	207.052	79.04	70.652	11.77
TBAA	TCAA-^{13}C	252.726	81.071	83.393	19.809

Table 2. Eluent gradient optimization for the separation and detection of DBPs in drinking water matrix.

	MCAA	ClO_2^-	MBAA	MIAA	BrO_3^-	Cl^-	DCAA	BCAA	CIAA	DBAA	CO_3^{2-}	ClO_3^-	SO_4^{2-}	DIAA	NO_3^-	TCAA	DCBAA	DBCAA	TBAA
Eluent										**t_r (min)**									
#1 [a]	12.9	13.1	14.7	15.4	15.7	20.3	24.9	26.6	28.6	28.9	32.7	33.0	35.3	35.9	37.1	39.5	41.6	44.6	48.8
#2 [b]	12.7	13.0	14.3	15.0	15.1	20.2	24.0	25.5	27.3	27.5	28.5	29.1	28.5	29.8	31.9	32.8	37.8	40.7	43.5

[a] Eluent #1: 7 mM KOH: t=0-15 min; 7-18 mM KOH: t=15.1-30.8 min; 60 mM KOH: t=31 min, keep until 46 min; 70 mM KOH; t=47-58 min. Diversion valve to the waste: 19-24 min, 35.1-35.6 min, 37.4-38.2 min.

[b] Eluent #2: 7 mM KOH: t=0-15 min; 7-15 mM KOH: t=15.1-23.8 min; 60 mM KOH: t=23.9 min, keep until 46 min; 7 mM KOH; t=47-58 min. Diversion valve to the waste: 18-23 min, 28.3-28.8 min, 30.5-32.3 min

478 **Table 3.** Limits of detection (LOD) and quantitation (LOQ) for the fifteen DBPs.

Analyte	**Regression equation**	**R^2**	**LOD (µg/L)**	**LOQ (µg/L)**
Chlorite	0.0646x+0.0073	0.9999	0.036	0.110
MCAA	0.0461x+0.011	0.9999	0.134	0.405
MBAA	0.3863x+0.0038	0.9999	0.026	0.078
MIAA	0.5391x+0.0059	0.9999	0.045	0.136
Bromate	0.3860x+0.0628	0.9998	0.042	0.127
DCAA	0.3451x+0.0109	0.9999	0.059	0.177
BCAA	0.2764x+0.0008	0.9999	0.037	0.111
DBAA	0.5612x+0.0005	0.9999	0.055	0.166
CIAA	0.0745x+0.0047	0.9999	0.085	0.256
Chlorate	0.0334x+0.0095	0.9999	0.188	0.569
DIAA	1.1879x+0.0861	0.9999	0.036	0.109
TCAA	0.3032x+0.1699	0.9999	0.113	0.342
DCBAA	0.0136x+0.0052	0.9999	0.099	0.301
DBCAA	0.0108x+0.0048	0.9998	0.108	0.326
TBAA	0.0167x+0.0051	0.9995	0.037	0.111

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Table 4. Mean percentage recovery and relative standard deviation (n=24) at different concentration levels for the fifteen DBPs. Inter-day (4 days, 57 replicates) and intra-day precision (15 replicates in one day) for 4 µg/L internal standards is also shown.

Analyte	Recovery % (RSD%, n=24)					Inter-day precision	Intra-day precision
	0.25	0.5	1	10	20		
			µg/L				
Chlorite	71.3±8.0 (11)	74.5±8.4 (11)	105±4.3 (4.1)	103±2.4 (2.4)	94.5±1.4 (1.5)		
MCAA	88.1±10.6 (12)	99.7±4.6 (4.6)	107±3.2 (3.0)	106±1.7 (1.6)	95.0±2.0 (2.0)		
MBAA-^{13}C						4.2	2.0-3.7
MBAA	88.7±5.6 (6.3)	96.8±3.6 (3.7)	104±3 (2.9)	101±1.2 (1.2)	95.5±1.4 (1.5)		
MIAA-D3						4.1	1.6-6.1
MIAA	105±1.4 (1.3)	99.7±1.7 (1.7)	101±1.2 (1.2)	104±0.7 (0.7)	104±1.0 (1.0)		
Bromate	85.6±5.2 (6.1)	95.6±3.6 (3.7)	102±2.1 (2.1)	99.1±1.4 (1.4)	92.3±1.3 (1.4)		
DCAA-^{13}C						1.9	0.9-2.1
DCAA	105±2.0 (1.9)	97.7±4.7 (4.8)	96.1±1.2 (1.3)	99.2±1.1 (1.1)	98.8±1.1 (1.1)		
BCAA	102±4.7 (4.6)	96.3±2.2 (2.3)	96.1±1.4 (1.4)	99.3±1.1 (1.1)	99.8±1.2 (1.2)		
DBAA	109±2.9 (2.7)	99.4±1.5 (1.5)	95.9±1.2 (1.2)	99.6±0.9 (1.1)	99.5±1.2 (1.2)		
CIAA	134±4.5 (3.4)	112±34 (30)	103±1.5 (1.5)	102±1.4 (1.4)	103±1.3 (1.2)		
Chlorate	88.41±5 (5.7)	85.4±3.0 (3.5)	104±3.0 (2.9)	99.6±2.6 (2.6)	94.6±2.3 (2.4)		
DIAA	105±1.7 (1.6)	111±5.0 (4.6)	97.6±1.0 (1.0)	100±2.2 (2.2)	99.0±1.6 (1.6)		
DCAA-^{13}C						2.2	1.4-29
TCAA	120±6.7 (5.6)	106±6.2 (5.9)	108±14 (13)	103±1.9 (1.9)	100±2.1 (2.1)		
DCBAA	105±37 (36)	102±8.2 (8.0)	99.0±8.1 (8.1)	108±2.7 (2.5)	102±3.4 (3.3)		
DBCAA	106±25 (24)	90.7±17 (19)	111±13 (12)	106±9.1 (8.6)	99.9±4.9 (4.9)		
TBAA	106±10 (9.4)	103±8.8 (8.5)	105±8.2 (7.8)	99.6±19 (19)	96.8±3.2 (3.3)		

Table 5. Recovery of 5 µg/L HAAs (including emergent compounds) and 5 µg/L bromate spiked on five water samples withdrawn from intermediate and final purification stages of three potabilization plants.

	Intermediate treatments			Finished waters		
	DSB1	**DSB2**	**CB3**	**E1**	**E2**	**E3**
MCAA	69±5.9 (8.5)	69.1±5.9 (8.5)	113±3.6 (2.3)	62.2±5.7 (9.2)	79.6±4.7 (6.0)	94.8±6.1 (6.5)
MBAA	101±2.1 (2.1)	100±3.7 (3.7)	104±2.9 (2.8)	103±2.6 (2.5)	103±2.6 (2.5)	100±1.3 (1.3)
MIAA	100±1.0 (1.0)	99.7±1.1 (1.2)	98.9±0.9 (1.0)	100±0.9 (0.9)	99.3±1.2 (1.2)	99.2±1.3 (1.3)
Bromate	111±3.7 (3.3)	113±3.4 (3.0)	115±2.9 (2.5)	116±2.4 (2.1)	116±5.1 (4.4)	115±3.8 (3.3)
DCAA	96.2±8.1 (8.4)	99.5±5.0 (5.0)	101±2.4 (2.4)	102±1.0 (1.0)	101±1.9 (1.9)	102±1.0 (1.0)
BCAA	96.0±6.0 (6.2)	98.6±6.4 (6.5)	100±2.5 (2.5)	100±3.8 (3.8)	101±2.6 (2.6)	101±1.2 (1.1)
DBAA	97.7±3.9 (3.9)	97.7±2.6 (2.7)	99.3±2.7 (2.7)	97.8±1.6 (1.6)	98.9±2.0 (2.1)	99.7±1.0 (1.0)
CIAA	98.7±1.9 (2.0)	99.5±2.9 (3.0)	99.6±0.9 (0.9)	98.9±2.2 (2.2)	98.0±2.2 (2.3)	98.4±2.7 (2.7)
DIAA	97.9±1.6 (1.6)	97.4±3.7 (3.8)	97.1±1.0 (1.1)	97.9±2.4 (2.5)	96.4±2.6 (2.7)	95.5±2.4 (2.5)
TCAA	91.4±9.1 (9.9)	93.2±9.5 (10.2)	94.2±1.5 (1.6)	91.8±2.2 (2.4)	93.5±3.5 (3.7)	95.9±1.3 (1.3)
DCBAA	107±12 (11)	92.4±12 (13)	103±6.9 (6.7)	105±1.3 (1.3)	104±4.1 (3.9)	105±4.7 (4.4)
DBCAA	93.5±8.9 (9.6)	91.5±17 (18)	89.2±25 (29)	108±23 (21)	111±21(19)	110±25 (23)
TBAA	81.6±18 (22)	85.2±15 (17)	95.9±9.5 (9.9)	87.2±9.8 (11)	93.7±14 (15)	104±4.3 (4.1)

Mean chlorite concentration, mg/L (n=5): DSB1: 395; DSB2: 340; E1: 350; E2: 230, E3: 85.

Mean chlorate concentration, mg/L (n=5): DSB1: 420; DSB2: 440; CB3: 80; E1: 470; E2: 450, E3: 165.

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504 **Table 6.** Concentrations (expressed in µg/L) of the fifteen DBPs along the treatment train of three
505 potabilization plants evaluated by the method developed.
506

Day	Treatment stage	Analyte (µg/l)															
		ClO_2^-	MCAA	MBAA	MIAA	BrO_3^-	DCAA	BCAA	CIAA	ClO_3^-	DBAA	DIAA	TCAA	DCBAA	DBCAA	TBAA	Sum[a)]
	Raw river water	0.49	nd	nd	<LOQ	nd	nd	<LOQ	nd	<LOQ	nd	<LOQ	<LOQ	nd	nd	nd	-
1	DSB1	550	nd	0.24	<LOQ	0.91	2.56	1.79	nd	350	0.87	nd	1.53	0.86	nd	2.25	10.1
1	E1	297	nd	nd	<LOQ	0.52	0.26	0.33	nd	580	<LOQ	nd	0.72	0.41	nd	0.88	1.3
1	CB3	-	nd	<LOQ	<LOQ	1.04	0.97	0.78	nd	89	0.37	nd	0.38	nd	2.69	0.89	6.1
1	E3	100	nd	nd	<LOQ	0.45	<LOQ	0.11	nd	211	<LOQ	nd	Nd	nd	nd	nd	0.1
2	DSB1	408	nd	0.16	<LOQ	0.55	1.64	1.20	nd	380	0.55	nd	0.85	0.44	nd	1.42	6.3
2	E1	313	nd	nd	<LOQ	0.49	0.34	0.33	nd	446	<LOQ	nd	0.56	nd	nd	1.28	2.5
3	DSB1	330	nd	<LOQ	<LOQ	0.41	1.47	1.16	nd	451	0.62	nd	0.41	0.19	nd	1.69	5.5
3	E1	418	nd	nd	<LOQ	0.49	0.23	0.29	nd	431	<LOQ	nd	0.89	nd	nd	1.12	2.5
3	DSB2	340	nd	<LOQ	<LOQ	0.65	1.84	1.34	nd	395	0.47	nd	1.29	0.83	nd	2.08	7.8
3	E2	267	nd	nd	<LOQ	0.59	0.42	0.35	nd	367	<LOQ	nd	0.66	nd	nd	1.48	2.9
3	CB3	-	<LOQ	<LOQ	<LOQ	0.84	0.94	0.67	nd	57	0.40	nd	0.5	nd	nd	nd	2.5
3	E3	113	nd	nd	<LOQ	0.43	<LOQ	0.12	nd	136	Nd	nd	Nd	nd	1.07	nd	1.2
4	DSB1	248	nd	<LOQ	<LOQ	0.19	1.73	1.25	nd	459	0.53	nd	0.75	0.38	nd	1.88	6.5
4	E1	369	nd	nd	<LOQ	0.52	0.30	0.30	nd	762	<LOQ	nd	0.62	0.64	nd	1.53	6.1
4	DSB2	279	nd	<LOQ	<LOQ	0.59	1.78	1.30	nd	508	0.56	nd	0.84	0.75	nd	2.29	7.5
4	E2	231	nd	<LOQ	<LOQ	0.63	0.50	0.11	nd	645	<LOQ	nd	0.42	<LOQ	nd	1.15	2.2
4	CB3	-	<LOQ	<LOQ	<LOQ	1.27	1.02	0.81	nd	133	0.44	nd	0.35	nd	nd	0.53	3.1
4	E3	90	nd	nd	<LOQ	0.51	<LOQ	nd	nd	147	Nd	nd	Nd	nd	nd	0.26	0.3
4	DSB1	344	nd	<LOQ	<LOQ	0.16	1.59	1.11	nd	488	0.52	nd	0.58	0.39	nd	0.96	5.2
4	E1	336	nd	nd	<LOQ	0.14	0.36	<LOQ	nd	560	<LOQ	nd	0.52	0.29	nd	<LOQ	1.2
4	DSB2	328	nd	<LOQ	<LOQ	0.14	1.62	1.17	nd	408	0.52	nd	0.68	<LOQ	nd	1.36	5.3
4	E2	215	nd	<LOQ	<LOQ	0.17	0.53	0.40	nd	408	<LOQ	nd	0.33	<LOQ	nd	0.94	2.2
4	CB3	-	<LOQ	<LOQ	<LOQ	1.03	0.81	0.78	nd	88	0.40	nd	<LOQ	nd	nd	nd	2.0
4	E3	30	nd	nd	<LOQ	0.46	<LOQ	nd	nd	132	<LOQ	nd	Nd	nd	nd	nd	-

[a)] Sum of the nine HAAs as foreseen by the proposal for the revision of the Drinking Water Directive

nd: not detected

Table 7. Analysis of drinking waters of different origins by the method developed. A,B: houses (Turin, Italy) ; C: house (Monte Carlo, Principality of Monaco); D: drinking fountain (Imperia, Italy). Concentrations are expressed in μg/L.

Analyte	**A**	**B**	**C**	**D**
Chlorite	nd	nd	nd	173
MCAA	nd	nd	nd	nd
MBAA	<LOQ	<LOQ	<LOQ	nd
MIAA	nd	nd	<LOQ	<LOQ
Bromate	nd	nd	<LOQ	nd
DCAA	nd	<LOQ	nd	nd
BCAA	<LOQ	0.29	0.28	nd
CIAA	nd	nd	nd	nd
DBAA	<LOQ	<LOQ	0.72	nd
Chlorate	13.0	15.3	nd	7.00
DIAA	nd	nd	nd	nd
TCAA	<LOQ	<LOQ	nd	<LOQ
DCBAA	nd	nd	<LOQ	nd
DBCAA	nd	nd	nd	nd
TBAA	nd	nd	nd	nd

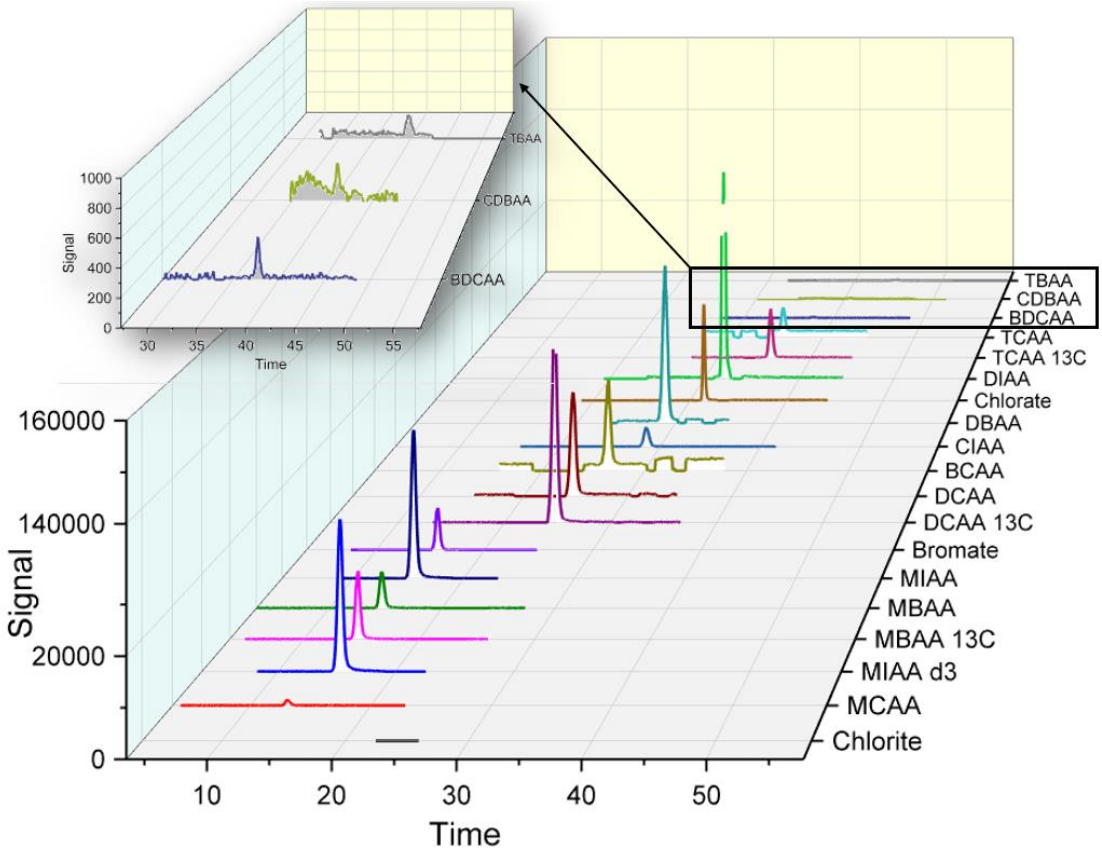

Figure 1. IC-MS/MS separation of fifteen DBPs and isotopically enriched internal standards (2 µg/L each).

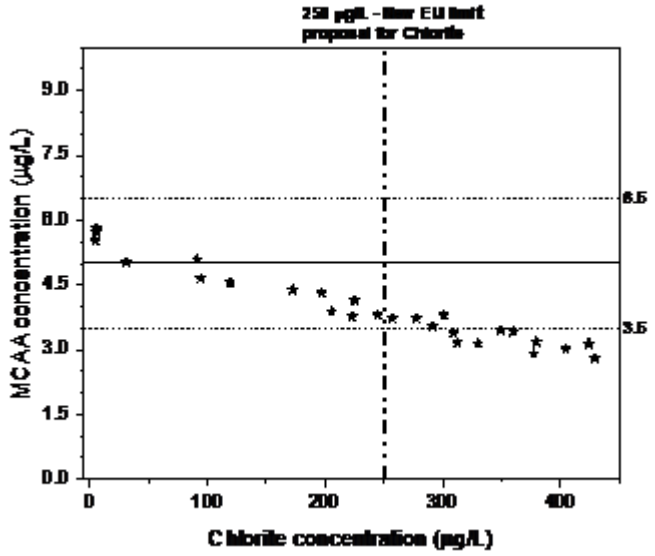

Figure 2. Effect of chlorite concentration on the suppression of MCAA signal. Continuous line: spiked MCAA concentration (5 µg/L); dotted lines: ±30% requisite (3.5 and 6.5 µg/L).

	MCAA	ClO_2^-	MBAA	MIAA	BrO_3^-	Cl^-	DCAA	BCAA	CIAA	DBAA	CO_3^{2-}	ClO_3^-	SO_4^{2-}	DIAA	NO_3^-	TCAA	DCBAA	DBCAA	TBAA
Eluent										**t_r (min)**									
#1 [a]	12.9	13.1	14.7	15.4	15.7	20.3	24.9	26.6	28.6	28.9	32.7	33.0	35.3	35.9	37.1	39.5	41.6	44.6	48.8
#2 [b]	12.7	13.0	14.3	15.0	15.1	20.2	24.0	25.5	27.3	27.5	28.5	29.1	28.5	29.8	31.9	32.8	37.8	40.7	43.5

Analyte	**Eluent**	
	#1 [a]	**#2** [b]
	tr (min)	
MCAA	**12.9**	**12.7**
ClO_2^-	**13.1**	**13.0**
MBAA	**14.7**	**14.3**
MIAA	**15.4**	**15.0**
BrO_3^-	**15.7**	**15.1**
Cl^-	**20.3**	**20.2**
DCAA	**24.9**	**24**
BCAA	**26.6**	**25.5**
CIAA	**28.6**	**27.3**
DBAA	**28.9**	**27.5**
CO_3^{2-}	**32.7**	**28.5**
ClO_3^-	**33.0**	**29.1**
SO_4^{2-}	**35.3**	**28.5**
DIAA	**35.9**	**29.8**
NO_3^-	**37.1**	**31.9**
TCAA	**39.5**	**32.8**
DCBAA	**41.6**	**37.8**
DBCAA	**44.6**	**40.7**
TBAA	**48.8**	**43.5**