A REVIEW OF OXYHALIDE DISINFECTION BY-PRODUCTS DETERMINATION IN WATER BY ION CHROMATOGRAPHY AND ION CHROMATOGRAPHY-MASS SPECTROMETRY

Elizabeth S. Gilchrist[a]*, David A. Healy[b], Virginia N. Morris[b] and Jeremy D. Glennon[a*]

[a] *Department of Chemistry, University College Cork, College Road, Cork, Ireland*

[b] *PepsiCo, Technical Function - R&D, Little Island, Cork, Ireland*

* Corresponding authors

Email: elizabeth.gilchrist@ucc.ie; j.glennon@ucc.ie

Tel: +353 21 490 2989; +353 21 490 2379

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Abstract

This paper is a review of ion chromatographic (IC) separations of inorganic oxyhalide disinfection by-products (DBPs) in water and beverages. The review outlines the chemical mechanisms of formation, regulation of maximum allowable levels, chromatographic column selection and speciation. In addition, this review highlights the application of IC coupled to mass spectrometry (MS) for trace and elemental composition analysis of oxyhalides, along with the analytical considerations associated to enable sensitive analysis. Furthermore, a review of literature concerning IC determination of inorganic oxyhalide DBPs in environmental matrices, including water, published since 2005 is presented, with a focus on MS detection, and a discussion on the relative performance of the methods. Finally some prospective areas for future research, including fast, selective, multi-analyte analysis, for this application are highlighted and discussed.

Contents

1. Introduction

Disinfection by-product (DBP) risk management is a major challenge for water suppliers. Disinfectants can react with naturally-occurring materials in water to form chemical by-products, which pose potential adverse health risks.

The primary requirements for water treatment are to remove organic matter, inorganic species and micropollutants as well as to preserve the purified water for human consumption. The two main options for water disinfection are chlorination and ozonation. Whilst chlorination is the more historic and widely utilised of the two, ozonation offers several advantages, such as destruction of a wider range of organisms and the removal of tastes and odours. Even using ozonation, chlorine is still required during the process for water preservation. However, elevated drinking water occurrence of chlorate (ClO_3^- ; *m/z* 83), chlorite (ClO_2^- ; *m/z* 67), perchlorate (ClO_4^- ; *m/z* 99) and also bromate (BrO_3^- ; *m/z* 128) have been identified as chlorine dioxide or ozonation DBPs formed during water treatment, generally at the µg–mg/L level [1-2]. This has resulted in significant research efforts to understand their environmental occurrence, fate and risk to humans especially *via* drinking water sources. In addition to this, it is also essential to monitor the quality of bottled beverages, such as fruit juices, to ensure the ingredient water, as well as the finished product, complies with the regulations and is safe for human consumption. The presence and levels of these DBPs will depend on the disinfection process used, as well as the chemicals already present within the source water. Several, more detailed reviews on the disinfection of water, and formation of DBPs and their potential health impacts on humans are available elsewhere and so only warrant a summary discussion here [3-4].

Alongside other techniques, the analytes of interest, bromate, chlorate and perchlorate, have been routinely and widely determined by ion chromatography (IC) for over 20 years, and a review in 2005 by Michalski discussed the analysis of inorganic oxyhalide DBPs using IC with conductivity, UV/Vis and mass spectrometry (MS) detection [4]. The ability to speciate gives IC an obvious advantage over several other analytical techniques, such as various spectroscopic methods including atomic spectroscopy. Speciation can be vital when it comes to the identification and characterisation of oxyhalides, such as in the differentiation of oxychloride species (i.e. ClO_3^-, ClO_4^-) from the free chloride ion.

The aims of this review are to (a) detail the existing (IC(-MS)) methods available from a perspective of inorganic DBPs analysis since 2005; and (b) discuss potential directions for IC-MS technologies to further advance methods in terms of analysis time, sensitivity, specificity and target analytes, for the analysis of oxyhalide DBPs.

2. Formation and regulation of bromate, chlorate and perchlorate in water

2.1. Bromate

Bromate is formed when water containing bromide is exposed to disinfection using the ozonation process. This process infuses ozone into the water in order to remove the organic and inorganic pollutants present *via* oxidation and filtration/sedimentation.

A mechanism by which bromate is formed was proposed by Legube *et al.* and is shown in Figure 1 [5]. The researchers state that reactions between ozone, bromide and hypobromite are relatively slow at low temperatures, but they are also dependent on the pH of the water and concentration of bromide (typically between trace-0.5 mg/L concentrations in fresh water [6]). Bromate can also be formed when disinfecting drinking water using concentrated sodium hypochlorite. Bromide is present in both the chlorine and sodium hydroxide used to form hypochlorite, and is quickly converted to bromate at the high pH of the solution (a 10-15 % solution of hypochlorite has a pH ~13) [7]. Once formed, bromate is very stable in water, and difficult to remove.

The International Agency for Research on Cancer (IRAC) has classified bromate in group 2B as a possible carcinogen to humans. Using the available information, the European Commission and the US Environmental Protection Agency (EPA) have set a maximum allowable level (MAL) of 10 µg/L in drinking water. The U.S. Food and Drug Administration (FDA) adopted the EPA levels for bromate and chlorite in 2001 as some food and beverage companies use ozonation or other disinfection treatments on their products [8]. This was also the case for residual disinfectants, chlorine, chlorine dioxide and chloramines. Despite these regulatory levels, in a 2005 study by Snyder *et al.,* the concentration of bromate exceeded this limit in three of the 21 tested bottled waters in the US with the highest concentration found to be 76 µg/L, almost eight times the MAL [9].

2.2. Chlorate

Chlorate, and also chlorite, are DBPs either formed by the decomposition of sodium hypochlorite, shown in the reaction below, or alternatively when chlorine, chlorine dioxide or chloramine is used to disinfect drinking water.

$$2ClO^- \rightarrow Cl^- + ClO_2^- \quad (1)$$

$$ClO^- + ClO_2^- \rightarrow Cl^- + ClO_3^- \quad (2)$$

As with bromate, these oxychlorides are more likely to occur at high pH and temperatures. It is also possible for chlorate to enter water *via* environmental contamination due to its occurrence in manufacturing and household items such as in some weedkillers. Although not classified by IRAC due to limited toxicological data, the World Health Organisation (WHO) recommends provisional guideline values for both chlorate and chlorite concentrations in drinking water at 0.7 mg/L based on a tolerable daily intake of 30 μg/kg/d (by body weight) [10]. In the study by Snyder *et al.* chlorate was detected in 71 % of samples, although below the guideline value at concentrations ≤5.8 μg/L.

2.3. Perchlorate

Another oxychloride anion, perchlorate, is particularly toxic to humans at much lower concentrations due to interference with the uptake of iodine in the thyroid and mammary glands, resulting in hypothyroid function. Due to this toxicity, the US EPA established an official reference dose of 0.7 μg/kg/d (by body weight). It again is a product of decomposition of sodium hypochlorite, however a large proportion of perchlorate contamination is environmental through the use of propellants, fireworks and explosives.

In the US, perchlorate is still under consideration for enforceable regulation by the US EPA, and is currently only regulated in drinking water at State level in the US in both Massachusetts and California at 2 and 6 μg/L respectively. In 2013, Iannece *et al.* measured concentrations between <5-75 ng/L of perchlorate in 70 % of 62 bottled waters tested from 15 of the 20 regions across Italy [11]. These found concentrations are of similar magnitude to those previously detected by Snyder *et al.* (<0.74 μg/L) and pose no immediate health concern in accordance with current recommended values [9].

3. Determination of DBPs by IC

As mentioned, oxyhalide DBPs in water have been determined by IC for over two decades, with the ability to speciate offering an advantage to oxyhalide analysis, as previously discussed in Section 1. For this reason, alongside its robust and reliable nature, and capability to achieve the required sensitivity, IC is an approved technique for the monitoring of inorganic anions and oxyhalides in environmental matrices for many agencies worldwide, such as the US EPA. Table 1 shows a list of existing IC methods, focussing on those reported since 2005 for the analysis of inorganic DBPs in environmental matrices. Relevant monitoring methods, such as those developed by the US EPA, pre-dating 2005 are also included.

As can be seen in Table 1, the two main IC column types utilised for the determination of DBPs are the Metrosep and also IonPac columns. Both of these column types consist of organic polymer particulates, allowing stability at higher pH compared to silica columns, with various capacities and selectivities. For example, the IonPac range is based on ethylvinylbenzene-divinylbenzene (EVB-DVB) with a high degree of crosslinking (<55 %) to maintain a stable structure. In general, particle size in IC is larger than reversed-phase liquid chromatography (RPLC), with a diameter <10 μm to prevent band broadening. However, in recent years there is a trend towards a reduced particle size of 4 or 5 μm, or alternatively monolithic columns, in order to increase efficiency and capacity whilst retaining the required selectivity. Functional groups are then either surface functionalised, agglomerated or grafted to the surface. Column capacity is an important factor for DBP analysis as the ions in the sample matrix can overwhelm the trace amounts of the DBP oxyhalides present. Typically for this application a moderately high capacity (~40-60 μequivalents/column for 2 mm I.D. columns) is used, as highlighted throughout this review. The selectivity of the stationary phase must also be considered, especially when used with conductivity detection, to enable the analytes of interest to be sufficiently resolved from the sample matrix.

These days the column formats are typically micro-bore (2.0 mm I.D., occasionally 1.0 mm I.D.) or standard bore (4.0 mm I.D.), with the IonPac recently expanding into capillary format (0.25 or 0.4 mm I.D.). With regards to column length, the IonPac favour a standard 250 mm, whereas the Metrosep is available in 100, 150 or 250 mm for most of their resins. The majority of columns discussed in this review are 250 x 2.0 mm I.D. unless stated otherwise.

One of the few columns demonstrated to simultaneously analyse a wide range of both oxyhalides and common anions found in water and beverages is the IonPac AS20. This micro-bore column has a comparatively high capacity of 77.5 μequivalents/column (2.0 mm I.D.), due to hyperbranched functional groups, and also displays very low hydrophobicity making it ideal for the analysis of perchlorate in environmental samples. This hyperbranched column arises as instead of coating the polymer substrate with latex particles, the first layer of stationary phase is electrostatically attached to the surface. Diepoxide monomers and primary amines added layer by layer in a polycondensation reaction which creates chains along the polymer backbone. Johns *et al.* used this column for the separation of 18 anions, potentially present in explosive resides in soil using a hydroxide gradient [12]. This was achieved in 18 min with only a minor sacrifice of resolution, as highlighted in Figure 2, showing potential for detecting trace concentrations of these analytes in water. Whilst conductivity detection was used in this case, a similar method has been utilised with MS detection [13]. However, the authors' experience has shown that the resin will display increasingly reduced capacity and require careful monitoring with regular replacement (approximately every 6 months) when used for high through-put work, such as water monitoring, or with complex sample matrices. Another hyperbranched column frequently used in the monitoring of water quality is the IonPac AS19, designed for the trace detection of bromate in drinking water [14]. Cengiz and Bilgin was reported as the first study to analyse perchlorate, nitrate and thiocyanate, as inhibitors of iodide uptake in the thyroid, with six common anions present in drinking water in a single run [15]. Using a standard 4 mm I.D. AS19 column with flow rate of 1 mL/min enabled a separation of the nine analytes in 17.5 min, a very similar separation time to that achieved on the AS20 by Johns *et al*. Retention time repeatability for all analytes was <1 %, however, long term robustness or repeatability does not seem to have been reported.

Very few IC methods utilise UV/Vis detection as a large proportion of small ions are non-absorbing species. Therefore indirect detection with a strongly absorbing eluent, such as phthalate, is often used [16]. Alternatively a post-column reaction reagent is added [17]. US EPA methods 300.1 and 317 measure oxyhalide DBPs in drinking water using IC coupled to conductivity and UV/Vis detection respectively with o-dianisidine added as the post-column reagent for bromate detection [18]. These methods employ an IonPac AS9-HC column and 9 mM carbonate eluent, with the 2.0 mm I.D. column having a capacity of 47.5 μequivalents/column [18-19]. Gandhi recently combined the two US EPA 300.1 methods (Part A for common inorganic ions, while B focuses on the analysis of DBPs) in order to reduce analysis time [20]. Instead of the AS9-HC, this approach utilised a Metrosep A Supp 7-250 (4.0 mm I.D.) with 3.6 mM sodium carbonate for the analysis of seven common anions as well as chlorite, chlorate and bromate with a separation time of 30 min. The column is designed for highly efficient separation of these analytes down to low µg/L concentrations, based upon chemical modification of a polyvinyl alcohol substrate, with a carbonate eluent preferred, which can allow the ionic strength of the eluent to be varied [21]. Using conductivity detection analytes were detected at single digit ppb levels; however direct coupling to MS would be possible with the conditions used, to lower detection limits for trace analysis. Drinking water matrices can pose problems for trace DBPs determinations due to high concentrations of interferent ions such as chloride, which can co-elute with trace oxyhalides. In order to overcome this analyte specific detection modes, such as MS, are increasingly favoured, particularly where full resolution is not achieved.

3.1. 2D-IC

Two-dimensional (2D) chromatographic configurations have also become more popular in the past decade to improve resolution, as shown in Table 2. There are several advantages to this approach including enhancement of the signal and also improved selectivity, with the possibility of resolving peaks of interest from matrix analytes due to the combination of the two different stationary phase chemistries.

A 2D-IC method for the detection of perchlorate in water using suppressed conductivity detection was developed in 2006 by Wagner and colleagues [22]. In the first dimension, a large sample volume (<4 mL) was injected onto an IonPac AS20 (4 mm I.D.), diverting the separated matrix ions to waste while the analyte(s) of interest were cut, trapped and concentrated in a concentrator column, which offers greater sensitivity over using an injector loop. These analytes were then separated on a second column, in this case an IonPac AS16 (2 mm I.D.), and detected using conductivity, shown in Figure 3. This method is included in the US EPA's publications (Method 314.2) and has since been run with a capillary column (0.4 mm I.D.) in the second dimension, marginally enhancing the lower concentration minimum reporting level (LCMRL) from 55 ng/L to 50 ng/L [23]. A similar method, which could arguably be considered multidimensional, to remove interference from high salt matrices is a cycling-column-switching mode. To enable sensitive detection of nitrate and chlorate in a high chloride matrix, Wang and colleagues trapped analytes on a concentrator column using just a single pump, analytical column (IonPac AS19) and detector, and two valves [24]. For the concentration step an IonPac AG16 was actually used. With the first part of the separation going to waste, the analytes of interest were concentrated on the concentrator column before being separated on the analytical column; these steps were repeated until the matrix was eliminated. After just two elimination steps the LOD for chlorate was 2.2 µg/L.

Zakaria *et al.* actually went a step further in terms of multidimensional separations and used a third dimension to improve the detection of bromate in seawater [25]. This extra dimension, which utilised the same phase as the second (IonPac AS24 (2 mm I.D.), allowed the interference from sulphate present in the second dimension to be removed from the third, similarly to that of chloride between the first and second, improving the LOD greatly from 1050 µg/L to 60 µg/L.

Another, arguably simpler, 2D-IC setup used two columns with different selectivities (IonPac's AS19 (2 mm I.D.) and AS20 (4 mm I.D.)) coupled in series *via* a tee-piece to allow independent control and modification of the eluent between the two columns, and only one suppressor and conductivity detector [26]. This approach separated 18 inorganic anions within 28 min including chlorite, chlorate, perchlorate and bromate. Significantly, it improved resolution (>1.3) compared to the previous single column method just utilising the AS20 [12], showing the potential of 2D-IC analysis for a larger range of inorganic anions and oxyhalides, without necessarily the need for MS detection.

4. Determination of DBPs by IC-MS and IC-ICP-MS

Michalski's 2005 review showed that the majority of IC methods were comparable, with low-µg/L levels reported for the analytes of interest regardless of detection mode. However, with MS detection it was possible to improve sensitivity by up to an order of magnitude, highlighting one of the advantages in its use [4]. Additionally, the ability to gather information about the elemental composition and structure of the analytes offers a more confident identification, particularly for complex matrices. The obvious disadvantages of MS-based detection techniques are that they add considerable complexity and significant cost to the analysis. Despite this, MS techniques have been utilised more routinely in recent years in conjunction with IC.

US EPA Method 321.8 is one of the earliest (1997) approved monitoring method using IC coupled to MS, detecting bromate in water using IC-inductively coupled plasma (ICP)-MS with a detection limit down to 0.3 µg/L, well below the MAL [27]. ICP-MS has proved to be a very useful analytical technique for the monitoring of water quality. However, there has been very little advancement in IC-ICP-MS for oxyhalide analysis since 2005, with the rapid, sensitive detection of bromate being the focus of these developments [28]. Whilst the analysis time is fast (<10 min), it does mean a sacrifice in the number of analytes analysed, with methods typically focussing on only one or two analytes, as highlighted in Table 3. An interesting paper by Schwan *et al.* looked at low mg/L concentrations for both chlorate and chlorite in blood samples, with the potential to look at other biological samples such a tissue and urine [29]. The presence of chlorate salts in animals for human consumption could be an alternative route to the ingestion of these oxyhalides and so should be regulated in much the same way as drinking water. The authors found that while chlorate is stable over several hours in whole blood, chlorite degrades very quickly (to below the LOD within 18 min). The authors also attempted to improve the detection of chlorine using a triple quadrupole mass analyser after ICP ionisation. Unfortunately chlorine contamination potentially coming from the plasma flame was an issue here. The technique can be very sensitive to isotopic interference produced by polyatomic species arising from the plasma, and therefore the development of IC-electrospray ionisation (ESI)-MS maybe considered more promising [30]. EPA method 557 (2009) is another method which will analyse bromate, along with haloacetic acids (HAAs), another group of DBPs, and dalapon, which is a herbicide, although instead of ICP-MS utilises ESI with a triple quadrupole mass analyser. Table 3 shows a comprehensive list of existing IC-MS methods for the analysis of relevant inorganic anions and oxyhalides since 2005 in a range of matrices.

As with ICP-MS, the range of chromatographic methods for trace multi-analyte IC-ESI-MS is still somewhat limited, with several methods focussing on analysis specific to perchlorate. An example of which is US EPA Method 331.0 published in 2005 [31]. This approach uses a weakly conducting eluent of 200 mM methylamine allowing it to be unsuppressed and coupled directly to a quadrupole MS due to its volatility. Wilkin *et al.* used a similar method for the analysis of perchlorate in surface water, however added acetonitrile post-column to the eluate to promote analyte volatilisation and improve the sensitivity [32]. Due to the potential for interference with a common isotope of bisulphate ($^{1}H^{34}S^{16}O_4^-$; *m/z* 99), multiple reaction monitoring (MRM) detection is recommended for perchlorate with the transition of

$[M]^-$ to $[M\text{-}O]^-$ monitored. The AS21 column has also been used for a wider range of analytes, namely perchlorate, bromate, bromide, nitrate, chlorate, chlorite and iodide in tap, ground, surface and bottled water collected in China by Wu *et al* [33]. Again this method uses methylamine in the eluent with limits of quantitation (LOQs) at 0.02, 0.17 and 0.35 µg/L for perchlorate, chlorate and bromate respectively, all below their MALs in water, using a 100 µL injection volume. This is a lower capacity version (45 µequivalents/column compared to 77.5 (2.0 mm I.D. x 250 mm)) of the AS20, and is specifically developed for MS compatibility [34].

The addition of organic solvent to the eluent can lead to changes in the column selectivity and retention behaviour, which could be considered advantageous when optimising separations for a large range of analytes. Gilchrist *et al.* showed a complete reversal in selectivity of the IonPac AS18 column with the addition of 80 % acetonitrile [35]. For the optimised separation, as well as practical coupling of IC to high resolution accurate mass (HRAM) MS, 30 mM hydroxide in 35 % acetonitrile was used to separate 11 anions of interest, including bromate, chlorate in perchlorate in <30 min. One of the two chromatographic methods specified in the US EPA Method 332.0 uses a standard-bore Metrosep A Supp 5-100 with an eluent of 30 mM hydroxide in 30 % methanol, for the specific detection of perchlorate [36]. This column has a particle size of 5 µm, smaller than most of the IonPac series, and the column used in this method (4.0 mm I.D. x 100 mm) has a capacity of 56 µequivalents/column, allowing the rapid and highly efficient separation of strongly retained anions, such as perchlorate. Although membrane suppressors can be used with <40 % organic solvent, this method uses a packed bed suppressor to guarantee compatibility with the eluent and backpressure limitations. It was possible to achieve detection limits for perchlorate in water at 0.02 µg/L using 100 µL injection volumes and a quadrupole mass analyser. However, as organic solvent in the eluent pre-separation can lead to unusual retention behaviour due to changes in the packing bed volume [35], naturally occurring perchlorate present in the samples was measured relative to an ^{18}O-enriched $^{35}Cl^{18}O_4^-$ internal standard to ensure reliable identification, as well as quantitation due to varying ionisation efficiencies. Figure 4 highlights the trace detection of perchlorate in a high matrix sample (1 µg/L in 1000 mg/L matrix) using an almost identical method (flow rate increased from 0.7 to 0.8 mL/min and MS conditions adjusted for the method), emphasising the attraction in employing MS detection over non-specific options to limit interferences and avoid false positives [37]. The alternative 332.0 method utilises the IonPac AS16 with 65 mM hydroxide, a membrane suppressor and a post-suppressor addition of acetonitrile. The detection limit for this method was again 0.02 µg/L. The AS16 is arguably the most popular column for IC analysis of perchlorate, being used by several researchers, as highlighted in Tables 1 and 3 [38-41]. Differing from the newer hyperbranched resins, the core polymer substrate is coated with functionalised 80 nm MicroBead™ latex particles, which does lower the capacity comparatively (42.5 µequivalents/column (2.0 mm I.D. x 250 mm)), however could potentially be considered more robust. As mentioned, most of these methods focus primarily on perchlorate in biological or environmental samples [42-44], using simple isocratic hydroxide eluents. However, Barron and Paull used this column to determine a range of analytes including inorganic anions, oxyhalides and HAAs in soil and water matrices shown in Figure 5 [2]. This method uses a hydroxide gradient with supplementary flow of methanol post-suppressor in order to improve the ionisation efficiency at the ESI source. Addition of organic solvent *via* a tee-piece post-column/suppressor is common as membrane suppressors have low compatibility (<40 %) with organic solvents. However, sensitivity can be affected due to dilution of the analytes. In this case, LODs were reported at 39, 9 and 10 µg/L for bromate, chlorate and perchlorate respectively with no sample pre-treatment, which falls above the MAL for bromate. An alternative approach to IC-MS is to utilise a paired-ion electrospray ionisation (PIESI) method forming ion association complexes post-column to enhance sensitivity and selectivity of these low molecular weight molecules [45-46]. This approach was recently reviewed by Breitbach *et al.* and Barron and Gilchrist and so will not be discussed extensively here [47-48]. Though, focussing on perchlorate, Martinelango and colleagues added di-cationic reagents after the IonPac AS16 resin to form ion association complexes. This not only allows detection in positive ESI mode, which generally produces a better signal, but also raises the *m/z* offset, decreasing potential for background interference. This is especially useful for improving selectivity of perchlorate against bisulphate, as bisulphate is not as amenable to forming ion-pairs as perchlorate.

As mentioned previously, the AS20 column has been utilised with both conductivity [12] and MS detection [13, 49], and frequently so. Again both IC-MS method focussed primarily on perchlorate, although one was analysing snow samples and the other infant formula. This enabled the groups to achieve fast separations (< 15 min) as resolution of a large range of other analytes was not required. Using a larger 750 µL injector loop Furdui *et al.* were able to achieve 0.3 ng/L for perchlorate in snow, rising to 1.5 ng/L for iodate. Both methods used MRM to monitor the loss of an oxygen from perchlorate.

5. Future perspectives for IC-MS analysis of DBPs

An ideal method for the analysis of DBPs would be fast to enable high through-put and cost minimisation whilst being selective for a large range of both common anions and oxyhalides. Preferably there would be limited matrix interferences without the need for sample pre-treatment. It is essential that the method be sensitive with a requirement to be down to 1 µg/L for bromate in particular.

For this particular application, higher capacity columns are generally preferred. This enables larger injection volumes (can be <5 mL) to be utilised, improving sensitivity for trace analytes in high matrix samples while maintaining a good peak elution profile. The IonPac AS27 is one of the latest columns released for the analysis of trace oxyhalides and inorganic anions in drinking water matrices [50]. It has a similar selectivity to the AS19 (also designed for this purpose); however the IonPac AS27 has a bead diameter of 6.5 µm instead of 7.5 µm, which would offer more efficient and resolved separations. The IonPac AS19 has also recently been released in a 4 µm version, increasing the capacity from 55 to 60 µequivalents/column (2.0 mm I.D. x 250 mm). Again peak efficiency and resolution would be further improved, however due to the standard dimensions of the column, when run at typical flow rates (~0.25 mL/min for micro-bore columns) the back pressure can exceed the instrumental limit, unless the instrument is specifically designed for high pressure applications [14].

As previously mentioned, due to the need for fast and efficient separations, there is an increased interest in monolithic columns, leading to a recent expansion in commercially available columns. Monoliths offer faster separations at high resolution as they consist of a single rod of solid stationary phase often with a bimodal structure of macropores (1-6 µm) and mesopores (10-20 nm) for higher through-flow and mass transfer. Due to the high pH of the hydroxide eluent, polymeric columns are preferred for their stability in alkaline conditions. Commercial polymer monoliths functionalised for anion exchange, such as the IonSwift MAX columns, have recently become available; however generally have a lower peak efficiency compared to their silica-based counterparts. The majority of these commercially available monoliths are offered in capillary-scale, again requiring specialist instrumentation.

Capillary-scale IC is another area that has garnered some attention in recent years, although a consideration for coupling to MS is analytical flow rate. To be compatible with ESI, lower flow rates are generally required, whereas band broadening increases with too low a flow rate for the separation and also source fluidics are no longer sufficiently optimised. Typically, micro-bore analytical columns (2.0 mm I.D.) are employed at flow rates between 0.1-0.7 mL/min. Capillary IC differs to other types of capillary-scale separation technologies, operating at higher flow rates (~5-10 μL/min) than typical for coupling to current nano-spray ionisation technologies (20-50 nL/min). These may also be arguably considered slightly low for ESI-MS at the micro-bore scale (~100 μL/min-1 mL/min), and therefore, coupling micro-bore IC to MS at flow rates between 0.2-0.5 mL/min is likely to still offer better performance at this time. However, it is highly likely that IC-MS will increasingly move towards capillary-scale in the future. To the best of the authors' knowledge, the IonSwift MAX-100 is the only commercially available polymer monolith at the micro-bore scale (1.0 mm I.D.). Whilst designed for the fast analysis of organic acids and inorganic anions, it's potential for the analysis of inorganic DBPs has been demonstrated with the separation of perchlorate, chlorate and several common anions in <20 min as shown in Figure 6, although this work did utilise the capillary-scale version (0.25 mm I.D.) [51].

Shorter column lengths could also be considered for faster separations. Tyrrell *et al.* separated seven anions, including chloride, chlorate, nitrate, sulphate and perchlorate in under 3 min [52] using an hydroxide ramp (Figure 7(b)) and 50 mm length column with 4 mm I.D. compared to 11 min for standard length IonPac AS20 (250 mm). Whilst the analytes of interest were not all baseline resolved, it does show the great potential shorter columns have where high throughput, fast analysis are required, such as for multidimensional chromatography.

As discussed earlier 2D-IC configurations is another area increasing in popularity. To the best of the authors' knowledge there are no existing 2D-IC-MS methods for inorganic compounds, such as oxyhalides. However, there is an example of 2D-IC-MS for small organic acids in seawater, with the first dimension used to separate the organic acids from inorganic ions, and separating these acids in the second dimension [53]. In this case the advantage of using MS was the added sensitivity it offers (LODs were ~2-5x lower than with conductivity), as well as a less ambiguous identification, offering an alternative way to achieve the selectivity and sensitivity required for the analysis of DBPs.

6. Conclusions

IC-MS technologies make a strong contribution to the analysis and monitoring of ion concentrations in drinking water and beverages. This review has highlighted the recent developments to further enhance methods for the application of oxyhalide DBPs analysis. IC-MS offers advantages over other analytical techniques in terms of its ability to speciate, which is essential in the identification of oxyhalides, as well as offering selectivity and sensitivity over traditional, non-specific detection modes such as conductivity and UV/Vis. While existing methods comply with the requirements set by regulatory agencies, predominately these will focus on a limited number of analytes. There is still opportunity to develop the use of IC-MS further not only with regards to range of analytes related to water analysis, but to improve sensitivity also with a number of exciting technological developments.

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Table 1. Comparison of ion-exchange chromatography methods for the determination of DBP related anions and oxyhalides

Analytes	Sample type	Column(s)	Eluent	Flow rate (mL/min)	Analysis time (min)	Suppressor	Detector	Post-column	LOD (µg/L)	Ref.
BrO_3^-, ClO_3^-, Cl^-, Br^-, NO_3^-, SO_4^{2-}	Water	Metrosep A Dual 1 (3x150 mm)	1 mM ortho-phthalic acid, 2 % MeCN	1	15	-	UV/Vis	-	2000-5000	[16]
F^-, ClO_2^-, BrO_3^-, Cl^-, NO_2^-, ClO_3^-, NO_3^-, SO_4^{2-}, PO_4^{3-}, ClO_4^-, CNO^-, $S_2O_3^{2-}$, SCN^-, organic acids	Soils/ residues	IonPac AS20 + AG20 (2x250 mm)	5-100 mM KOH grad.	0.375	18 + equil.	ASRS	Conductivity	-	2-27	[12]
BrO_3-, ClO_2^-, ClO_3^-, Br^-	Water	IonPac AS9-HC +AG9-HC (4x250 mm)	9 mM Na_2CO_3	1.3	25	ASRS	Conductivity/ UV/Vis	0.7 mL/min o-dianisidine	µg/L levels	[18]
ClO_2^-, ClO_3^-, BrO_3^-, Cl^-, Br^-, NO_3^-, PO_4^{3-}, SO_4^{2-}	Water	Metrosep A Supp 5 + 1 (4x250 mm)	3.2 mmol/L Na_2CO_3/ 1 mmol/L $NaHCO_3$	0.7	32	MSM	Conductivity	-	-	[54]
Part A: F^-, Cl^-, NO_2^-, Br^-, NO_3^-, PO_4^{3-}, SO_4^{2-}	Water	IonPac AS9-HC + AG9-HC (2x250 mm)	9 mM Na_2CO_3	0.4	25	ASRS	Conductivity	-	mg/L	[19]
Part B: BrO_3^-, ClO_2^-, ClO_3^-, Br^-	Water	IonPac AS9-HC + AG9-HC (2x250 mm)	9 mM Na_2CO_3	0.4	25	ASRS	Conductivity	-	1.32-2.55	[19]
F^-, Cl^-, NO_2^-, Br^-, NO_3^-, PO_4^{3-}, SO_4^{2-}, ClO_2^-, ClO_3^-, BrO_3^-	Water	Metrosep A Supp 7 (4x250 mm)	3.6 mM Na_2CO_3	0.7	-	833 MSM-II	Conductivity	-	-	[20]

Analytes	Sample type	Column(s)	Eluent	Flow rate (mL/min)	Analysis time (min)	Suppressor	Detector	Post-column	LOD (µg/L)	Ref.
Cl^-, NO_3^-, SO_4^{2-}, SCN^-, CrO_4^{2-}, ClO_3^-, ClO_4^-	Standard	IonPac AS20 (4x50 mm)	KOH grad.	1	3	ASRS	Conductivity	-	-	[52]
ClO_3^-, NO_2^-,	High salt matrices	IonPac AS19 + AG19 (4x250 mm)	10 mM KOH	1	70	electrochemical self-generation	Conductivity	AG16 (4 mm) concentrator	2.2	[24]
ClO_4^-	Atmospheric aerosol	IonPac AS16 + AG16 (2x250 mm)	120 mM NaOH	0.25	-	ASRS	Conductivity	Concentrator	0.35 ng/m^3	[55]
BrO_3^-, ClO_2^-, I^-	Water	IonPac AS9-HC (4x250 mm)	9 mM Na_2CO_3	1.1	6.5	AMMS	UV/Vis	0.4 mL/min 0.26 M KI, 43 µM $(NH_4)_6Mo_7O_{24}.4H_2O$	µg/L levels	[17]
ClO_4^-	Dust	IonPac AS16 + AG16 (4x250 mm)	25 mM NaOH	0.8	~20	Chemical mode	Conductivity	-	2	[56]
ClO_4^-	Soil leachate	IonPac AS16 + AG16 (4x250 mm)	35 mM KOH	1.25	-	ASRS	Conductivity	-	1	[57]
ClO_2^-, ClO_3^-	Soil leachate	IonPac AS18 +AG18 (4x250 mm)	23 mM KOH	1	-	ASRS	Conductivity	-	5	[57]
NO_3^-, ClO_4^-, SCN^-	Water	IonPac AS19 + AG19 (4x250 mm)	20-50 KOH grad	1	30	ASRS	Conductivity	-	3-25	[15]

Table 2. Comparison of two-dimensional ion-exchange chromatography (2D-IC) methods for the determination of DBP related anions and oxyhalides

Analytes	Sample type	Column(s)	Eluent	Flow rate (mL/min)	Analysis time (min)	Suppressor	Detector	1st-2nd dimension	LOD (µg/L)	Ref.
ClO_4^-	Water	IonPac AS20 (4x250 mm) + AG20	35-100 mM KOH grad.	1	45	ASRS	Conductivity	2 mL in concentrator column	ng/L levels	[22]
		IonPac AS16 (2x250 mm) + AG16	65 mM KOH	0.25	45	ASRS	Conductivity			
F^-, ClO_2^-, BrO_3^-, Cl^-, NO_2^-, ClO_3^-, NO_3^-, SO_4^{2-}, PO_4^{3-}, ClO_4^-, CNO^-, $S_2O_3^{2-}$, SCN^-, organic acids	Standard	IonPac AS19 (2x250 mm) +AS19	9-100 mM KOH grad.	0.25	28	-	-	tee-piece	3-80	[26]
		IonPac AS20 (4x250 mm) + AG20	69.33-99.67 mM KOH grad.	1		ASRS	Conductivity			
BrO_3^-	Water	IonPac AS19 (4x250 mm) +AG19	10-65 mM KOH	1	35	ASRS	Conductivity	~2 mL in concentrator column	0.12	[58]
		IonPac AS24 (2x250 mm) + AG24	10-65 mM KOH	0.25	35	ASRS	Conductivity			

Analytes	Sample type	Column(s)	Eluent	Flow rate (mL/min)	Analysis time (min)	Suppressor	Detector	1st-2nd dimension	LOD (µg/L)	Ref.
ClO_4^-	Water	IonPac AS20 (2x250 mm) + AG20	35-60 mM KOH grad.	0.25	45	ASRS	Conductivity	1 mL in concentrator column	0.005	[23]
		IonPac AS16 (0.4x250 mm) + AG16	65 mM KOH	0.01	45	ASRS	Conductivity			
BrO_3^-	Water	IonPac AS19 (4x250 mm) +AS19	5 mM KOH	1	40	ASRS	Conductivity	AC15 concentrator or UTAC trap column	1050	[25]
		1x or 2x IonPac AS24 (2x250 mm) + AG24	20 mM KOH	0.25		ASRS	Conductivity			
ClO_2^- , BrO_3^-, HAAs	Water	IonPac AS19 (4x250 mm) +AS19	10-45 mM KOH grad.	1	65	ASRS	Conductivity	IonSwift MAC200 trap column	0.3-0.64	[59]
		IonPac AS26 (0.4x250 mm) + AG26	6-70 mM KOH grad.	0.01		ACES	Conductivity			

HAAs – haloacetic acids

Table 3. Comparison of ion chromatography-mass spectrometry configurations for the determination of anions and oxyhalide species related to DBPs

Analytes	Sample type	Column(s)	Eluent	Flow rate (mL/min)	Analysis time (min)	Suppressor	Detector	Post-column	LOD (µg/L)	Ref.
BrO_3^-	Water	Dionex PA100	5 mM HNO_3 + 25 mM NH_4NO_3	1	7	-	ICP-MS		0.3	[27]
BrO_3^-, Br^-	Water	Selfmade polymethacrylate (4.6x150 mm)	20 mM NH_4NO_3, pH 5.8	1	7	-	ICP-MS	-	2-3	[60]
BrO_3^-, Br^-, IO_3^-, I^-, HAAs	Water	IonPac AS11-HC + AG11	30-200 mM NH_4NO_3 grad.	1	43	-	ICP-MS	-	BrO_3^-- 1.65	[61]
BrO_3^-	Water	IonPac AS19 + AG19 (4x250 mm)	40 mM KOH	1	6	-	ICP-MS	-	0.013	[28]
ClO_2^-, ClO_3^-	Blood	IonPac AS15 + AG15 (2x250 mm)	10-90 mM KOH	0.25	15	ASRS	ICP-MS/ICP-TQ-MS	-	500-1000	[29]
Cl^-, SO_4^{2-}, ClO_2^-, BrO_3^-, ClO_3^-, F^-, ClO_4^-, NO_3^-, IO_3^-	Water/ soil	IonPac AS16 + AG16 (2x250 mm)	1-20 mM NaOH grad.	0.3	71 + 16 equilb.	AEES	ESI-LIT-MS	0.12 mL/min MeOH	2-138	[2]
ClO_4^-	Infant formula	IonPac AS20 + AG20 (2x250 mm)	55 mM KOH	-	20	ASRS	ESI-TQ-MS	-	0.4	[49]
ClO_4^-, Cl^-, Br^-, BrO_3^-, ClO_3^-, ClO_2^-, IO_3^-, I^-	Snow	IonPac AS20 + AG20 (2x250 mm)	45-80 mM OH^- grad.	0.3	10.2 + equib.	-	ESI-TQ-MS	0.3 mL/min MeCN	0.0003 - 0.0015	[13]

Analytes	Sample type	Column(s)	Eluent	Flow rate (mL/min)	Analysis time (min)	Suppressor	Detector	Post-column	LOD (µg/L)	Ref.
ClO_4^-, Br^-, NO_3^-, BrO_3^-, ClO_3^-, ClO_2^-, I^-	Water	IonPac AS21 + AG21 (2x250 mm)	231 methylamine	0.3	10	None	ESI-TQ-MS	-	0.02-25*	[33]
ClO_3^-, ClO_2^-, BrO_3^-, Br^-, F^-, Cl^-, NO_2^-, NO_3^-, PO_4^{3-}, SO_4^{2-}, HAAs	Water	Metrosep A Supp 1 HS + A Supp 5 (4x250 mm)	16 mM Na_2CO_3/ 5 mM $NaHCO_3$ grad.	0.7	70	Sequential chem.	Conductivity/ ESI-trap-MS	-	µg/L levels	[62]
BrO_3^-, ClO_4^-	Water	IonPac AS21 + AG21 (2x250 mm)	200 mM methylamine	0.5	~10	None	Qtrap-MS	-	0.01-0.04	[63]
ClO_4^-	Water	IonPac AS16 + AG16 (2x250 mm)	65 mM KOH (75 mM)	0.3	~9	ASRS	ESI-SQ-MS (conductivity)	0.3 mL/min 50 % MeCN	0.02	[36]
ClO_4^-	Beverages, soil, water	IonPac AS16 + AG16/ AS20 + AG20 (2x250 mm)	45 mM OH^-	0.3	~13	ASRS-MS	ESI-TQ-MS	0.3 mL/min 50 % MeCN	0.005, 0.04 mg/kg	[64-65]
ClO_4^-	Water	Metrosep A Supp 4/5 + A Supp 5-100 (4x100 mm)	30 mM NaOH, 30 % MeOH	0.7	~9	Yes	ESI-SQ-MS	-	0.02	[36]
ClO_4^-	Water/ lettuce	Metrosep A Supp 5 (4x100 mm)	30 mM NaOH, 30 % MeOH	0.8	~14	Sequential chem..	ESI-SQ-MS	-	Sub µg/L	[37]

Analytes	Sample type	Column(s)	Eluent	Flow rate (mL/min)	Analysis time (min)	Suppressor	Detector	Post-column	LOD (µg/L)	Ref.
ClO_3^-	Soil/plant leachates	IonPac AS20 (2x250 mm)	H_2O-45 mM OH^- grad.	0.3	25.5	-	ESI-TQ-MS	0.3 mL/min 50 % MeCN	0.002	[66]
ClO_4^-	Ice	IonPac AS16 + AG16 (2x250 mm)	45 mM NaOH	0.3	-	ASRS	ESI-TQ-MS	0.3 mL/min 90 % MeCN	0.0002	[43]
ClO_4^-	Snow, ice	IonPac AS16 + AG16 (2x250 mm)	40 mM KOH	0.25	20	ASRS	ESI-TQ-MS	-	0.002	[42]
ClO_4^-	Milk, seaweed	IonPac AS21 + AG21 (2x250 mm)	15 mM KOH	0.35	-	ASRS	ESI-TQ-MS	-	0.12*	[67-68]
ClO_3^-, ClO_2^-, BrO_3^-, HAAs	Water	IonPac AS19 (2x250 mm)	5-37 mM KOH grad.	0.25	-	ASRS	ESI-SQ-MS	-	1-20	[69]
BrO_3^-, Br^-, NO_3^-, ClO_3^-, ClO_4^-, SCN^-, I^-, organic acids	GSR	IonPac AS18 (2x250 mm)	30 mM NaOH, 35 % MeCN	0.18	30	ASRS	ESI-Orbitrap	-	<10	[35]
ClO_4^-, (NO_3^-, SCN^-, I^-)	Urine	IonPac AS16 (2x250 mm)	50 mM NaOH	0.5	10	ASRS	ESI-TQ-MS	-	0.03	[38-41]
ClO_4^-	Water	IonPac AS21 + AG21 (2x250 mm)	200 mM methylamine	0.35	-	None	Qtrap-MS	0.3 mL/min MeCN	0.003-0.2	[31-32, 70]
ClO_4^-	Urine/ milk/ water	IonPac AS16 + AG16 (4x250 mm)	100 mM NaOH	1	10	ASRS	ESI-SQ-MS	dicationic reagent	0.06-3	[46, 71-73]

Analytes	Sample type	Column(s)	Eluent	Flow rate (mL/min)	Analysis time (min)	Suppressor	Detector	Post-column	LOD (µg/L)	Ref.
ClO_4^-	Dust	IonPac AS21 (2x250 mm)	20 mM methylamine	0.3	-	None	ESI-TQ-MS	-	0.02 µg/g*	[74]
ClO_4^-	Ice core	IonPac AS16 (2x250 mm)	60 mM NaOH	0.3	15	AERS	ESI-Qtrap-MS	0.3 mL/min 90 % MeCN	0.0001	[44]

* LOQ; HAAs – haloacetic acids; ICP- inductively coupled plasma; ESI – electrospray ionisation; API – atmospheric pressure ionisation ; LIT - linear ion trap; TQ – triple quadrupole; SQ – single quadrupole; GSR – gunshot residues

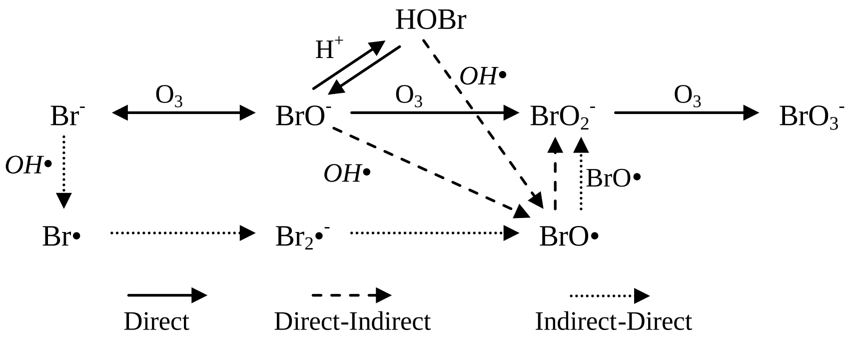

Figure 1. Bromate formation pathways during ozonation. Adapted from [5]

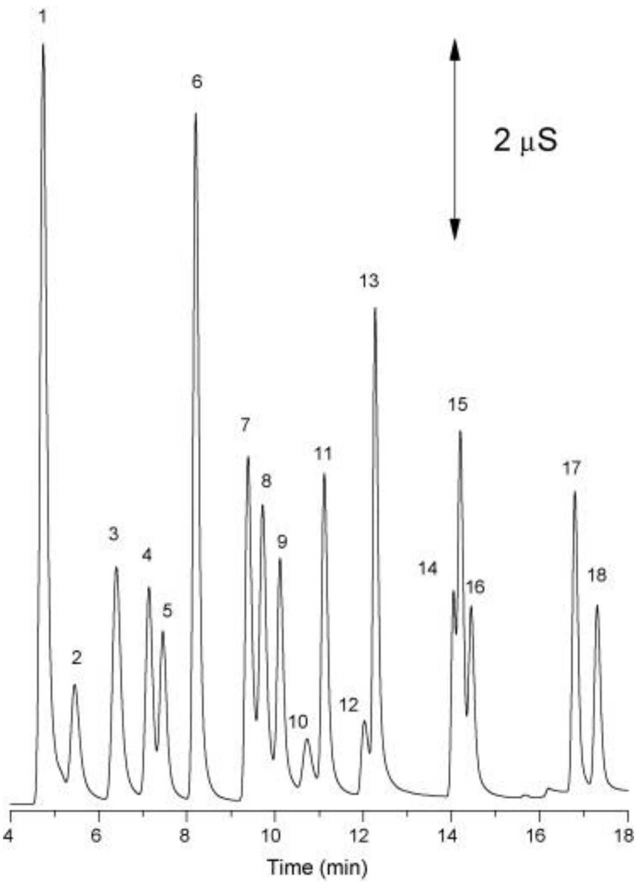

Figure 2. Separation of 5 ppm anion standards on an IonPac AS20 column with hydroxide gradient. Elution order: 1 = fluoride, 2 = acetate, 3 = formate, 4 = chlorite, 5 = bromate, 6 = chloride, 7 = nitrite, 8 = cyanate, 9 = chlorate, 10 = benzoate, 11 = nitrate, 12 = carbonate, 13 = sulphate, 14 = phosphate, 15 = chromate, 16 =

thiosulphate, 17 = thiocyanate, 18 = perchlorate. (Reprinted from [12]. Copyright 2008 with permission from Elsevier.)

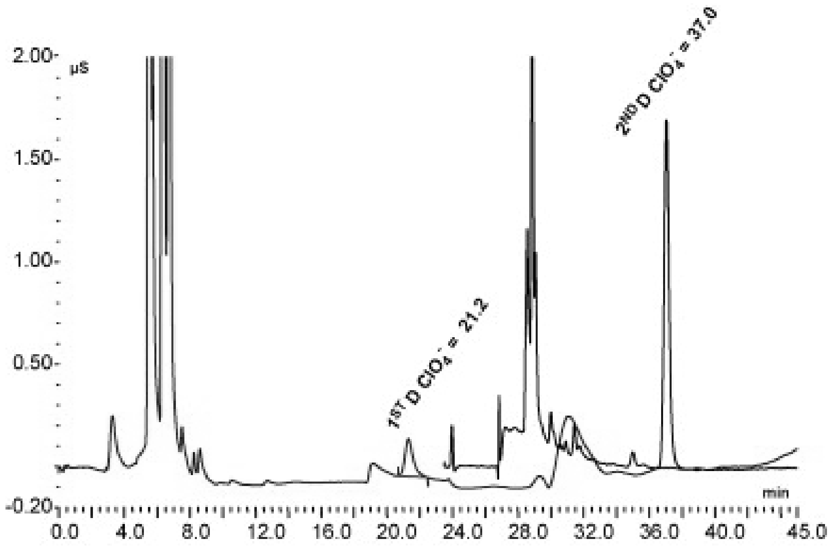

Figure 3. First- and second-dimension chromatogram using a 2.0 mL injection volume of a 25 μg/L perchlorate fortification in purified reagent water. (Reprinted from [22]. Copyright 2007 with permission from Elsevier.)

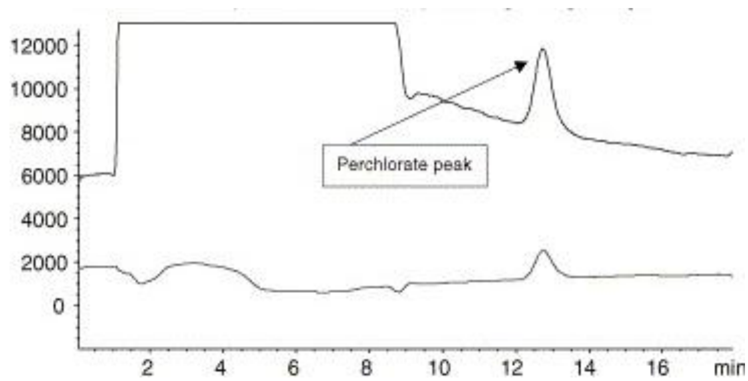

Figure 4. *m*/*z* 99 (top chromatogram) and 101 traces for 1 μg/L perchlorate in a 1000 ppm matrix of sulphate, chloride, and carbonate using a Metrosep A Supp 5 column. (Reprinted from [37]. Copyright 2005 with permission from Elsevier.)

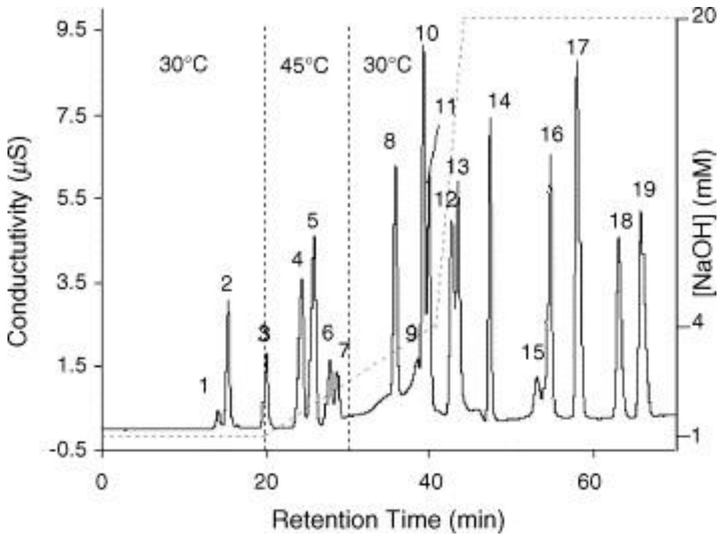

Figure 5. Optimised IC method for use with conductivity and ESI-MS detection for oxyhalides and HAAs using an IonPac AS16. Elution order: 1 = acetate, 2 = iodate, 3 = chlorite, 4 = MCA, 5 = bromate, 6 = chloride, 7 = MBA, 8 = TFA, 9 = nitrate/bromide, 10 = chlorate, 11 = DCA, 12 = CDFA, 13 = BCA, 14 = DBA, 15 = carbonate, 16 = TCA, 17 = DCBA, 18 = CDBA, 19 = perchlorate. (Reprinted from [2]. Copyright 2006 with permission from Elsevier.)

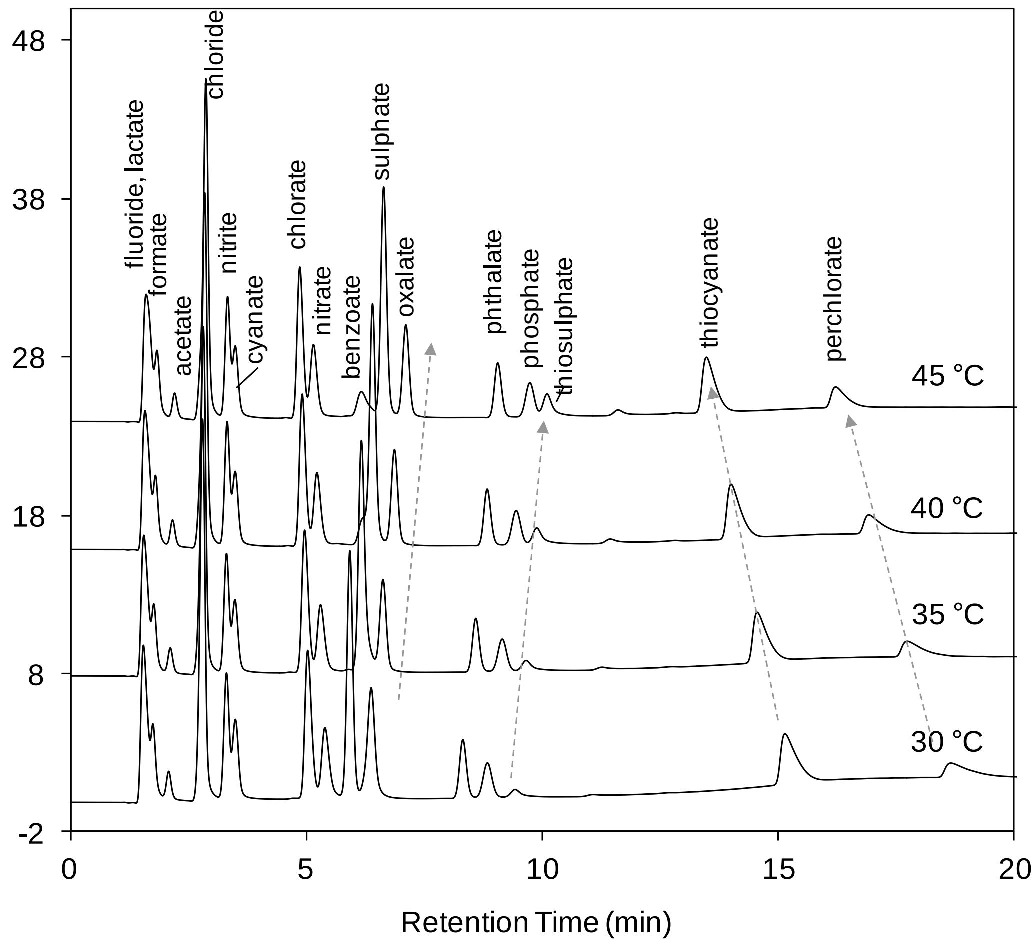

Figure 6. Fast separation of common inorganic anions, organic acids and oxyhalides on an IonSwift MAX-100 polymer monolith (0.25 x 250 mm). Reproduced from [51] with permission from the Royal Society of Chemistry.

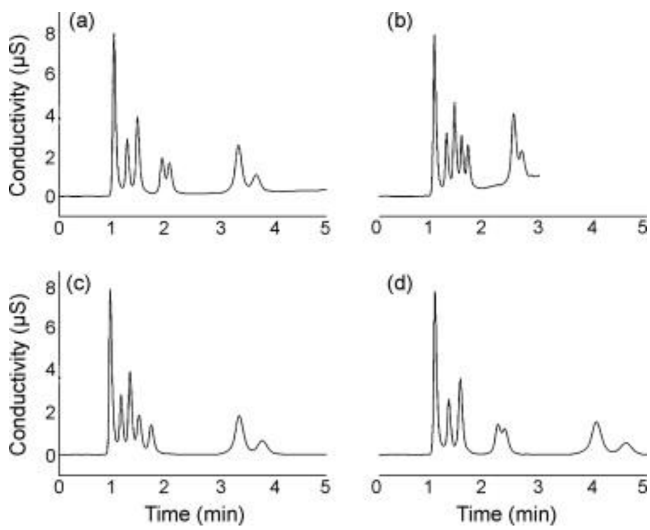

Figure 7. Optimised gradient separations of seven target anions carried out on a 4 mm × 50 mm AS20 column using (a) a ramp rate of 5 mM/t_0 (6.92 mM/min) for maximum efficiency (effective peak capacity), (b) a ramp rate of 30 mM/t_0 (41.49 mM/min) for fastest separation, (c) isocratic conditions of 31.5 mM and (d) isocratic conditions of 25 mM for approximation of most efficient gradient separation. Peak: 1 = chloride, 2 = chlorate, 3 = nitrate, 4 = chromate, 5 = sulphate, 6 = thiocyanate, 7 = perchlorate. (Reprinted from [52]. Copyright 2009 with permission from Elsevier.)