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Research Article

Determination of chlorine species by capillary electrophoresis – mass spectrometry

The applicability of CZE with mass spectrometric detection for the determination of four chlorine species, namely chloride and three stable chlorine oxyanions, was studied. The main aspects of the proper selection of BGE and sheath liquid for the CE-MS determinations of anions with high mobility were demonstrated, pointing out the importance of pH and the mobility of the anion in the BGE. The possibility of using uncoated fused silica capillary and common electrolytes for the separation was shown and the advantage of using extra pressure at the inlet capillary end was also presented. The linear range was found to be 1–100 $\mu\text{g/mL}$ for ClO_3^- and ClO_4^- , 5–500 $\mu\text{g/mL}$ for ClO_2^- , and 25–500 $\mu\text{g/mL}$ for Cl^- , but the sensitivity can be greatly improved if larger sample volume is injected and electrostacking effect is utilized. The LOD for ClO_3^- in drinking water was 6 ng/mL, when very large sample volume was injected (10 000 mbar·s was applied).

Keywords:

Capillary electrophoresis / Chloride / Chlorine oxyanions / Chlorine species / Mass spectrometry
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1 Introduction

Lately, the importance of the separation and quantitative analysis of different chlorine containing species increased due to their extensive use (e.g., as disinfectants), and therefore, they are more likely to be present in the environment, in food, or in the human body. Chloride (Cl^-) is very common in nature (~2% in sea water) and in the human body (~0.1 M in blood). Chloride, chlorite (ClO_2^-), and chlorate (ClO_3^-) ions can be formed in drinking water when chlorine dioxide is used for disinfection (in normal case, ~70% of the applied chlorine dioxide converts to chlorite, thus the chlorite concentration is less than 0.2 mg/L, but in some cases can exceed 1 mg/L, (e.g., in swimming pool water [1])). The maximum acceptable concentration for chlorite and chlorate in drinking water is 1 mg/L [2]. Chlorate is also generated if common bleach, that is, sodium hypochlorite (NaOCl) is used. The chlorite and chlorate ions are also applied in the production of paper,

dyes, herbicides, or as oxidants in explosives and solid fuel rockets. The majority of perchlorates (ClO_4^-) are produced artificially to be used in fireworks or car air bags and they very rarely occur in nature, however, a space expedition revealed that the soil of Mars consists of ~0.6 w/w% perchlorate [3]. In some cases, perchlorate can be detected in drinking water in the low ppb range [4]. While chloride is a common component and an essential compound for metabolism, the other chlorine species have harmful effects on human health. Chlorate salts are used as disinfectants for food industry [5]. Since perchlorate inhibits thyroidal iodine uptake, it finally decreases the thyroid hormone production [6]. An additional chlorine oxyanion is the hypochlorite, which is unstable and it quickly degrades to chloride, oxygen, and chlorate. Due to its high reactivity, no separation method has been applied for its determination.

For the analysis of chlorine species, a separation method applicable for small ions coupled with sensitive detector should be used. According to the United States Environmental Protection Agency (EPA, USA 326.0, 2002, Revision 1.0.), chlorite and chlorate can be determined by ion chromatography (IC) with conductivity or ultraviolet/visible detectors. Besides IC [1, 7–11] or LC [12], CE [7, 11, 13–15] was reported for the analysis of chlorine species. The chlorine species were

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Abbreviations: IC, ion chromatography; iPrOH, isopropanol; SL, sheath liquid

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separated by CE using electrolyte, which contained electroosmotic flow reversal component (cationic detergent) and UV absorbing agent (e.g. chromate) for the indirect UV detection [11, 14]. The application of UV absorbing agent was not needed for C4D [15]. Perchlorate was preconcentrated with large volume electrokinetic injection to obtain sensitive detection [15]. In previous years, ICP-MS [1, 8, 9] or ESI-MS [7] was used for sensitive detection. Although ICP-MS can detect even a few ng/L for most elements, the detection of chlorine suffers from isobar interferences and poor ionization in plasma [8].

The MS detection provides several advantages over the UV or C4D detection. Because of the universal (not selective) detection mode of UV or C4D, the sure identification of the peaks based on their migration times is often not easy, especially in real samples, where peaks are very close to each other. While the indirect UV of the C4D detection is not applicable for peak purity test, the MS provides unambiguous identification and clearly indicates if a peak contains several components. CE-ESI-MS seems to be a promising combination for the analysis of chlorine species because proper separation can be achieved even in samples with complex material due to the different electrophoretic mobilities of these compounds, furthermore, sensitive detection is possible even in cases when the lack of chromophore would not allow it. However, some difficulties arise from the coupling of CE with MS and from its application for the separation of small anions with high mobility. In a typical coupling, a sheath liquid (SL) flow is added to the effluent sample, at the outlet end of the CE capillary, to ensure electrical contact for electrophoresis, and also to provide optimal conditions for electrospray ionization. In CE, EOF directed toward the cathode (negative electrode) occurs in a wide pH range. Since anions are attracted toward the anode, they only migrate toward the detector (cathode) if their migration is slower than the EOF. A further problem can emerge when EOF does not flow in the direction of the electrospray ion source (due to reversed negative polarity), which can cause a fall in the current or it may even stop the electrophoresis [16–18]. In order to decrease or reverse EOF, fused silica capillaries can be permanently coated with non-charged [16, 17] or cationic [7, 18] polymers (addition of cationic detergents to the CE electrolyte for producing dynamic coating is not advised due to their incompatibility with MS). Soga et al. studied the oxidation of the stainless steel spray needle at the anodic electrode due to electrolysis, which can lead to the plugging of the capillary owing to iron oxide precipitation [19].

Several authors who showed sensitive IC determination of inorganic anions considered the CE measurements as important complementary methods for IC [11, 14]. Although the chlorine compounds might be detected with a similar or better sensitivity with indirect UV or conductivity detection compared to ESI-MS, the MS detection provides several advantages like mass selective mode of detection, unambiguous identification, or peak purity study. The main goal of the present work is to demonstrate the simultaneous determination of four chlorine species using CE-MS and to find simple

and efficient operation conditions for the analysis. We studied the possibility of using unmodified/uncoated fused silica capillary and common MS compatible BGE electrolytes for the separation, which has not yet been mentioned in the literature. Although there is a moderate sensitivity of CE compared to chromatographic methods, we showed that the injection of large sample volume can lead to quite low LODs due to the electrostacking effects. Despite this work targeting the chlorine species, the shown approach can be applied for other high mobility anions as well.

2 Material and methods

2.1 Reagents and samples

All the chemicals were of analytical grade. Stock solutions of chloride, chlorite, chlorate, and perchlorate were freshly prepared from their sodium salts obtained from Sigma Aldrich (St. Louis, MO, USA), and diluted with de-ionized water (Milipore Synergy UV, 18.2 M Ω) prior to use. Nitric acid, formic acid, ammonium nitrate, ammonium formate, ammonium acetate, methanol, and isopropanol were purchased from Sigma. All the solutions were filtered using a membrane filter of 0.45 μ m pore size and stored at +4°C. Running buffers and standard solutions were degassed in an ultrasonic bath for at least 5 min. Prior to the first use, the fused silica capillary was rinsed with 1 M NaOH for 5 min, then with 0.1 M NaOH for 10 min, and with de-ionized water for 10 min. Commercial bleaching solution (hypo) was injected after a tenfold dilution. Swimming pool water was obtained from local swimming pool. No other sample preparation was applied before the analysis.

2.2 Instrumentation

The CE-MS measurements were performed by a capillary electrophoresis instrument (7100 CE System, Agilent, Waldbronn, Germany) coupled to an electrospray mass spectrometer (maXis II UHR ESI-QTOF MS, Bruker, Karlsruhe, Germany). Hyphenation was performed with a CE-ESI sprayer interface (G1607B, Agilent). SL was transferred with a 1260 Infinity II isocratic pump (Agilent). CE instrument was operated by OpenLAB CDS Chemstation software.

Parameters for the CZE separation: capillary: 90 cm \times 50 μ m fused silica; BGE: 100 mM ammonium formate (pH 6.5); applied voltage: –20 kV; hydrodynamic injection: 250 mbar-s; sheath liquid: 50% v/v isopropanol/water containing 0.5 mM ammonium formate; SL flow rate: 7.5 μ L/min. The electric current during the CE separation was recorded by ChemStation v. B.04.02 software (Agilent).

The following parameters were applied for the electrospray ion source (negative ionization mode): capillary voltage: 2.5 kV; end plate offset: 500 V; nebulizer pressure: 0.6 bar; dry gas temperature: 200°C, and dry gas flow rate: 4.0 L/min. The MS method was tuned according to the 30–120 m/z mass

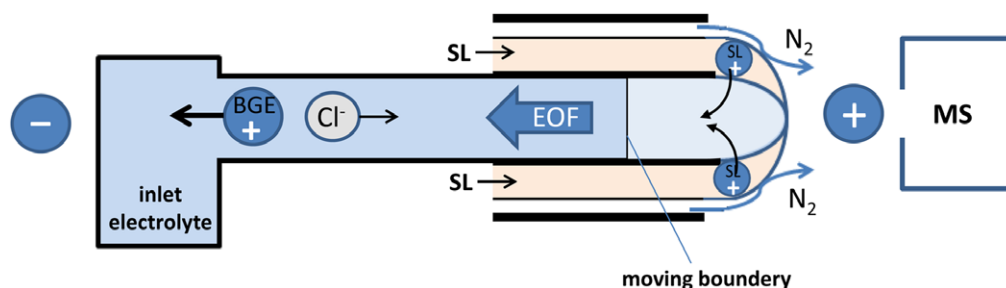


Figure 1. Schematic representation of the CE-ESI-MS interface when reversed polarity of the separation voltage is applied. The EOF is cathode directed and the analytes (chlorine compounds) migrate toward the anode. The ESI process is supported by the sheath liquid (SL) and nebulizing gas (N_2).

range. Applied spectra rate was 3 Hz. Na-formate calibrant was injected after each separation, which enabled internal calibration. Electropherograms were extracted at the masses of the examined analytes. Peaks on the extracted ion electropherograms were integrated manually. Electropherograms and mass spectra were recorded by otofControl version 4.1 (build: 3.5, Bruker) and processed by Compass DataAnalysis version 4.4 (build: 200.55.2969).

3 Results and discussion

3.1 Selection of BGE

Although there are several papers demonstrating the CE separation of chlorine species, those applied detergents which are not applicable with MS [7, 11, 13–15]. All studied chlorine compounds are negatively charged above $pH = 2$ (pK_a of chlorite is ~ 1.96 and of the others are below zero) and have small size, therefore their (negative) electrophoretic mobilities are very high. These anions migrate fast toward the anode even if oppositely directed EOF is present (Fig. 1). The negatively charged analytes and the anions of the BGE migrate toward the anode against the EOF and (in order to maintain electroneutrality) the anions leaving the capillary are substituted by anions entering at the inlet end of the capillary. The same should be valid for the cations: the number of positively charged ions (mainly BGE) leaving the capillary at the cathode is equal to the number of cations entering at the outlet capillary end. However, in CE-MS there is no BGE reservoir at the outlet capillary, only the sheath liquid can provide cations to enter the capillary. The BGE and the SL can contain the same electrolyte but not in the same concentration, because the BGE should contain an electrolyte (buffer) in a concentration large enough to keep the pH and ionic strength constant in the CE capillary, but this high concentration would cause the suppression of ionization if applied in the SL. As a consequence of the fact that different ions or same ions in different concentration enter the capillary from the SL, the pH and the ionic strength is often not homogeneous in the CE capillary. It might be noted that even if EOF directed toward the outlet end of the capillary (toward the MS) is generated, inhomogeneity in the capillary is generated due

to the formation of moving ionic boundaries as the counterions of the SL migrate and create a sharp or diffuse boundary [20, 21].

In order to study the effect of the composition of the BGE on the separation, different electrolytes with similar ionic strength (0.01 M nitric acid ($pH = 2$), 0.1 M formic acid ($pH = 2.5$), 0.01 M NH_4NO_3 ($pH = 5.1$), 0.1 M NH_4 -formate ($pH = 6.5$), and 0.1 M NH_4 -acetate ($pH = 7.0$)) were investigated (Fig. 2). At $pH = 2$ the EOF is negligible, therefore the migration of the components toward the anode is the fastest. Since the EOF is negligible, the composition (pH and ionic strength) of the electrolyte is homogeneous and the current is almost constant during the electrophoresis. Although three species are well separated, chlorite does not appear in the electropherogram (Fig. 2A), because it quickly decomposes to ClO_3^- , ClO_2 , and Cl^- [22]. When formic acid is used as BGE (Fig. 2B), chlorite appears (partially decomposed), but the peaks have the form of a triangle due to electrodispersion, since the electrophoretic mobility of the formate at $pH = 2.5$ is much smaller than that of the analyte. In this latter case, the current decreases gradually due to the weak EOF (SL flows into the CE capillary from the outlet capillary). In the case of NH_4NO_3 electrolyte (Fig. 2C) the peaks are narrow, but the chlorite peak disappears again, even though at this pH chlorite does not decompose. The current curve shows complex actions during the electrophoresis, which is hard to explain. The largely increased current indicates the replacement of NH_4^+ ions with high mobility H^+ formed at the outlet electrode. (The formed H^+ ions migrate towards the cathode (inlet electrode) and eventually replace the NH_4^+ ions of the BGE in the capillary, the latter of which leave the capillary at the cathodic (inlet) end. The strong decrease of the pH in the capillary can explain the decomposition of the chlorite and the high current, as well). This phenomenon should be further studied. The NH_4 -formate BGE enables good separation of the components with good peak shape, the migration times are increased due to the larger EOF and the current largely decreases in the beginning of the electrophoresis (Fig. 2D). In the case of NH_4 -acetate, BGE EOF is even larger, which decreases the net migration speed and force the low conductivity SL to flow in the capillary resulting in very low current, when the electrophoresis practically stops. In that case no peaks could be

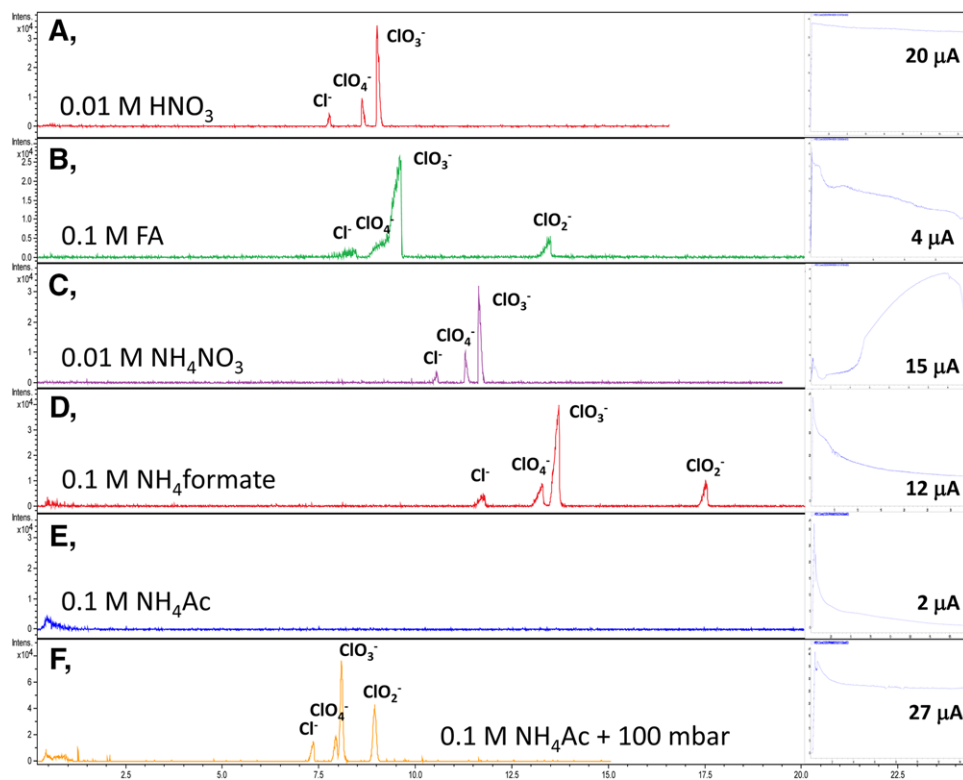


Figure 2. Separation of chlorine compounds by CE-MS using 1:1 iPrOH-water SL and different BGEs. CE: –20 kV (reversed polarity), injection: 250 mbar·s, MS: sheath flow: 0.75 mL/min; dry gas: 200°C, 4 L/min; nebulizer pressure: 0.6 bar; ESI voltage: 2.5 kV. Negative ionization mode was applied. Mass range: 30–120 m/z with a rate of 3 Hz. Electropherograms were extracted at the masses of the examined analytes (m/z : 34.989; 66.959; 82.954, and 98.949 ± 0.005 .) (f): During separation extra +100 mbar pressure is applied at the inlet end capillary. Sample: 50 $\mu\text{g/mL}$ ClO_3^- , ClO_2^- , 100 $\mu\text{g/mL}$ ClO_4^- , Cl^- . Current curves (current values (μA)) are plotted against time (min) and the current values at 20 min running time are displayed on the right side.

observed in the electropherogram (Fig. 2E). However, the application of 100 mbar pressure at the inlet end of the CE capillary led to a proper separation of the four components within 10 min (Fig. 2F) and a relatively constant current was obtained a few minutes after the electrophoresis was started. Since the best separation (without extra pressure) was gained with NH_4 -formate, the further experiments were continued with this electrolyte.

3.2 Selection of sheath flow

In order to study the effect of the composition of the SL on the separation (NH_4 -formate BGE was applied), different electrolytes with identical organic content (50% v/v isopropanol [iPrOH]) were investigated (Supporting Information Fig. 1). According to the obtained electropherograms, the SL composition has no significant effect on the separation. Surprisingly, even if pure iPrOH-water (without dissolved salts) was used as SL, the current did not decrease completely, although the neutral iPrOH-water was expected to flow into the outlet end of the CE capillary due to the cathodic EOF (Supporting Information Fig. 1a). The lack of “ion gap” in the capillary can probably be explained by the electrochemical reactions on the surface of the outlet electrode (i.e. the stainless steel ESI interface). On the outlet electrode (anode), the electrolysis (electrochemical oxidation) of water can occur and/or the material of the electrode can be oxidized. The oxidation/corrosion of the ESI interface was investigated in detail and it was found that the precipitation of iron oxides

plugged the capillary outlet, resulting in shortened capillary lifetime [18]. In our experiments this corrosion phenomenon did not cause the appearance of metal oxides at the stainless steel sprayer, as the pH values of most used SLs were not basic (which would favor metal oxide-hydroxide formation, as in Ref. 19). If iron or nickel ions get into the capillary, a small amount of metal oxide can be formed in the acidic BGE (in Ref. 19 BGE with pH = 8.5 was applied). Nevertheless, some metal oxide can be formed in the ESI interface, therefore it should be sonicated regularly. It can be assumed that mainly H^+ and some $\text{Fe}^{3+}/\text{Ni}^{2+}$ -ions - formed during electrolysis - enter the CE capillary from the anodic (outlet) end, enabling the continuous migration of cations towards the cathode (inlet end), when the SL originally does not contain ions.

The nebulizer gas develops a syphoning (Venturi) effect at the end of the ESI sprayer (arising as a consequence of gas escaping the sprayer with high speed resulting in a pressure drop). The SL (iPrOH-water) is introduced into the CE capillary at the outlet end, when the EOF (directed towards the inlet end) is greater than this flow. Therefore, the composition of the SL influences the current intensity obtained during the electrophoresis, but the low conductivity SL can under no circumstances increase the current. After a few minutes of electrophoresis, the rate of the current decrease becomes negligible.

The composition of the SL also affects the ionization efficiency of the analytes during the MS detection. In the case of the analytes studied with negative polarity MS detection, as a rule of thumb, the signal intensity should be higher when SL with minimal salt content is used.

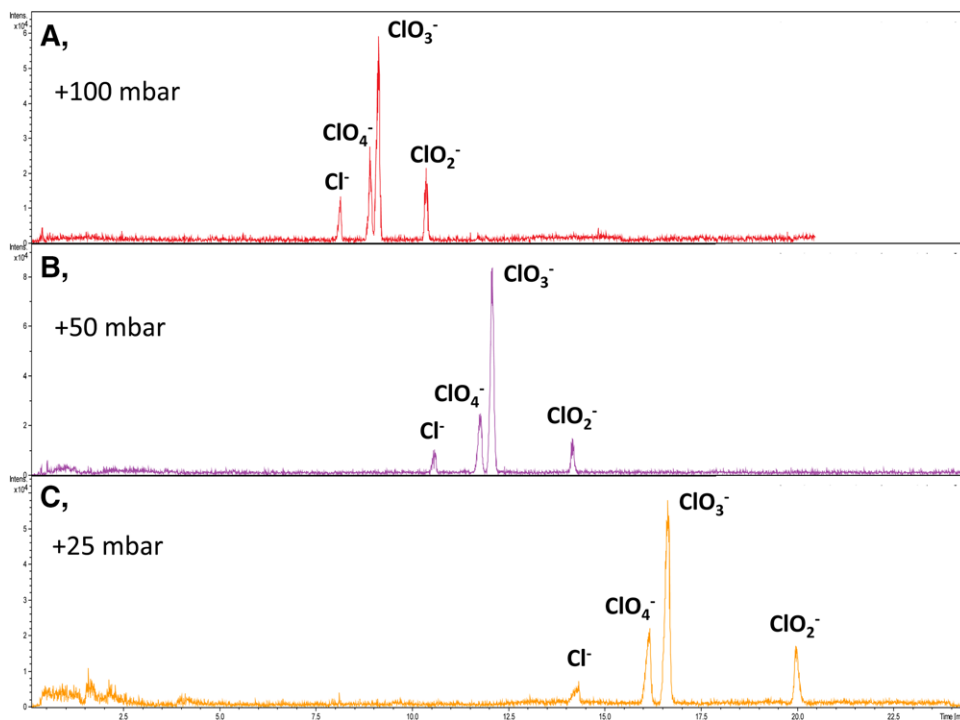


Figure 3. Separation of chlorine compounds by CE-MS using 0.1 M NH_4 -formate BGE and different SLs. The other parameters were the same as in Fig. 2. Current curves and the current values at 20 min running time are displayed on the right side.

The application of extra pressure at the inlet capillary end considerably shortens the analysis time as the analytes travel faster toward the detector. The triggered laminar flow broadens the peaks, therefore, the application of large pressure should be avoided. With the application of +100 mbar, the analysis time can be halved but the separation resolution decreases to a similar extent, as well (Fig. 3). The current intensity becomes more constant and higher as the pressure is increased.

3.3 Analytical performance

The analytical performance of the proposed CE-MS system was evaluated for the separation and detection conditions given in Section 2. For these analyses the sample was injected with 50 mbar for 10 s. The calibration diagrams showed good linearity (R^2 values were better than 0.99) in the concentration range of 1–500 $\mu\text{g/mL}$ for ClO_3^- and ClO_4^- , 5–500 $\mu\text{g/mL}$ for ClO_2^- , and 25–500 $\mu\text{g/mL}$ for Cl^- (Supporting Information Fig. 2). The LOD values (obtained with 50 mbar 50 s injection parameters) were 0.25, 0.36, and 0.45 $\mu\text{g/mL}$ for the chlorate, chlorite, and perchlorate, respectively. The LOD of chloride was 2.1 $\mu\text{g/mL}$, quite high due to its small m/z . Since the maximum acceptable concentration for chlorite and chlorate in drinking water is 1 mg/L [2], these concentrations can be measured with proper certainty if a large sample volume is injected (at least 50 mbar·200 s (Supporting Information Fig. 3) or electrostacking effects occur (at least 50 mbar·50 s [Fig. 4D and Supporting Information Fig. 6])). While there is a roughly linear relation between injection times between 2–

200 s and peak areas, the peak height is less increased due to the peak broadening (sample volume overloading). Migration times were shifted toward the larger values with increasing injection times (and thus with increased injected volumes) (Supporting Information Fig. 3).

The precision of the analysis was studied by consecutive measurements (Supporting Information Fig. 4). RSD values were 4.9–5.2 RSD% for migration times and 2.2–3.5 RSD% for peak areas ($N = 10$). The poor precision of migration times was probably caused by the weak buffer capacity of the applied BGE: presumably the pH of the BGE gradually changed during the electrophoresis, thus EOF continuously increased. The frequent change (replenishment) of the BGE vial might have improved precision. The application of 25 mbar pressure at the inlet capillary end during the electrophoresis considerably improved the RSD% values of migration times, which were 0.6–1.0 RSD%, but the precision of peak areas did not change remarkably (2.0–4.3 RSD%) for migration times (Supporting Information Fig. 5). Also, the current curves showed good similarities.

3.4 Analysis of real samples

In order to test the optimized CE-MS method, different real samples were analyzed (Fig. 4). The commercial NaClO_2 reagent (puriss. p.a., 80%, Sigma) contains three other chlorine species (and some stabilizers as sodium carbonate, sodium hydroxide, which were not detected). After dissolving the commercial solid product in water, the amount of Cl^- , ClO_4^- , and ClO_3^- were 4, 0.2, and 0.3%, respectively,

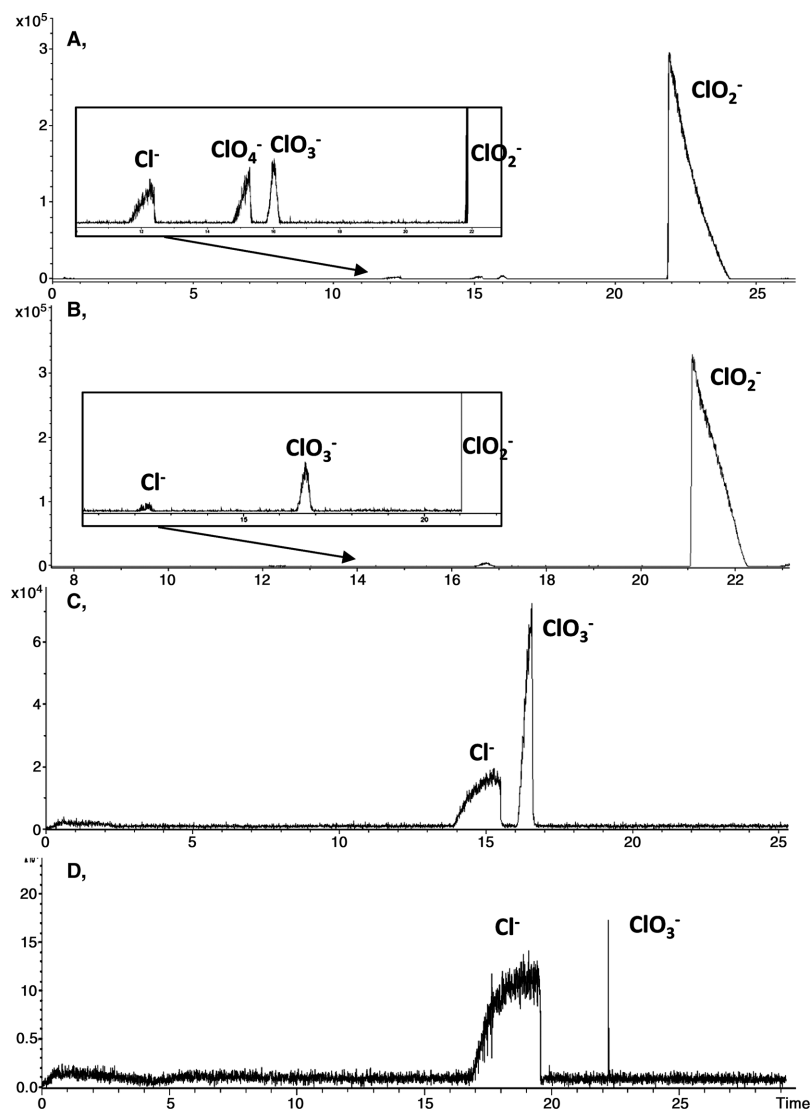


Figure 4. Separation of chlorine compounds by CE-MS using 0.05 M NH_4 -formate as BGE and 5 mM NH_4 -formate in 1:1 iPrOH-water as SL. Samples: (A) commercial NaClO_2 reagent (puriss. p.a., 80%, Sigma); (B) NaClO_2 reagent after in-lab purification; (C) commercial bleaching solution (hypo), (D) swimming pool water. During separation, extra +25 mbar pressure is applied at the inlet end capillary. Injection: 500 mbar-s for (A–C) and 10 000 mbar-s for (D). The other parameters were the same as in Fig. 2.

far below the main product of ClO_2^- (~80%) (Fig. 4A). After in-lab purification (re-crystallization, removal of carbonate with Ba^{2+}), the concentration of Cl^- and ClO_3^- were reduced to 2 and 3 $\mu\text{g/mL}$, respectively, and the ClO_4^- could not be detected, while ClO_2^- was the same (1010 $\mu\text{g/mL}$) (Fig. 4B). Commercial household bleaching solution (hypo) was analyzed after a tenfold dilution (Fig. 4C). Due to the large chloride concentration of the sample, a wide peak was obtained (*mass overloading*). The signal height of the chlorate is larger than that of the chloride, because detection sensitivity of MS is poorer at 35.4 m/z, however, the concentration of chloride was around four times larger than that of the chlorate. The hypochlorite was not detected probably due to its high reactivity with the components of the BGE or the SL during the electrophoresis (it might have decomposed in the ESI process) or due to its small electrophoretic mobility ($\text{pK}_a = 7.4$).

In the case of the analyses of swimming pool (Fig. 4D) and drinking water (Supporting Information Fig. 6a) a very large volume of sample was injected (10 000 mbar-s), therefore a wide peak was obtained for chloride (*volume overloading*). However, the chlorate appeared as an extremely sharp peak (peak width: 0.6 s) as a consequence of an electrophoretic stacking effect (the chlorate was stacked at the interface between the wide zones of the highly mobile chloride (and sulphate) and the slower formate of the BGE into a very narrow zone which contained chlorate ions in large concentrations). This over a 100-time enrichment of chlorate during the electrophoresis can be achieved only in samples having low salt content, as in drinking water or swimming pool water. When the volumes of the injected sample were increased from 1 000 to 10 000 mbar-s, the peak width of the chloride was proportionally lengthened with constant peak height, while the peak height of the chlorate was proportionally increased

by the injection time (Supporting Information Fig. 6b–d). The concentrations of chlorate were found to be 0.08 and 0.02 mg/L for swimming pool water and drinking water, respectively. These values were in similar range as reported by others using IC-MS [23, 24].

4 Concluding remarks

Although CE-MS is studied thoroughly, it is relatively rarely applied for the analysis of small anions with high electrophoretic mobility due to the difficulties arising during the electrophoresis. On the other hand, reported CE-MS methods consist of uncommon circumstances and make the analysis complicated or expensive (complex BGE [25], permanent coating of the CE capillary [7, 16–19], ESI needle tip made from platinum [19]). This work demonstrates that high mobility anions can be analyzed under simple separation conditions (bare fused silica CE capillary, simple MS compatible BGE), which is an advantageous feature of CE. The LOD values obtained for the chlorine species (0.25–2.1 µg/mL) were in a similar range as in other works with CE using indirect UV [11], conductivity [11] or ESI-MS detection [7], but considerably (even 1–2 orders of magnitude) worse compared to those who used IC with suppressed conductivity [1, 26].

This is the first CE-MS work where chloride and the three stable chlorine oxyanions have been determined simultaneously. Other chlorine oxides – like hypochlorite anion or chlorine dioxide gas – are also known, but their poor stabilities or strong reactivities make their analysis very difficult, especially when they are together with other chlorine components or matrix materials.

In this work, the main aspects of proper BGE and SL selection for the CE-MS determination of fast anions were demonstrated, pointing out the importance of the pH and the mobility of the anion in the BGE. Reversed CE polarity is rarely applied in CE-MS methods [19]. It is primarily because of the corrosion of the sprayer tip when it serves as anode. We believe that this work might shed some light onto this rarely examined field, presenting that negative CE polarity can be used in CE-MS analyses. The advantage of the use of an extra pressure at the inlet capillary end was also stated. The method enables the determination of four chlorine species at low ppm range, but sensitivity can be further improved if larger sample volume is injected or if electrostacking effect can be utilized.

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The authors have declared no conflict of interest.

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