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Use of coupled open-tubular capillaries for in-line ion-exchange preconcentration of anions by capillary electrochromatography with elution by a transient isotachophoretic gradient

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Abstract

Open-tubular capillaries have been joined together for use in on-column ion-exchange preconcentration of anions by capillary electrochromatography (CEC) with elution by a transient isotachophoretic gradient. This involved the coupling of a preconcentration capillary and a separation capillary using a PTFE sleeve. Such coupling allowed precise lengths of differently coated capillaries to be joined in-line to form a single multi-mode column. The different segments could be tailored to optimize a separation by either altering the length of each segment to precisely manipulate the amount of stationary phase present or by changing the internal diameter of each segment to alter the phase ratio in the chromatographic column without affecting the path length for UV detection. In this work, a segmented in-line capillary was used in conjunction with a fluoride–octanesulfonate discontinuous electrolyte system to increase the number of anions that could be preconcentrated and separated. Quaternary ammonium functionalised latex particles were used for creating the preconcentration segment and the separation segment was coated with poly(diallyldimethylammonium chloride). This allowed the detection of trace anions in drinking water and in situ sampling of river water for the analysis of trace inorganic anions. The repeatability of producing the quaternary ammonium functionalized latex-coated segments was assessed and the effect of segmentation on peak efficiency was investigated.
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1. Introduction

Coupled capillary systems have been used in capillary electrophoresis (CE) since the early 1990s. Nashabeh and El Rassi were the first to use a polytetrafluoroethylene (PTFE) sleeve to couple capillaries in CE [1] where they used a polyether-coated capillary joined to an uncoated fused silica capillary in order to give a tunable electroosmotic flow (EOF) dependent upon segment length. In this case the segments were coupled after the point of detection to increase the separation velocity and separation efficiency of proteins. Other research using this technique from the same authors has involved joining the separation capillary to different post-column capillaries to obtain a stepwise increase of the

EOF [2]. A post-column multiple capillary device [3] was then constructed containing several capillaries of differing zeta potentials and this provided stepwise control of the EOF during analysis and was also used for the fraction collection of proteins. Yang and El Rassi used coupled capillaries in capillary electrochromatography (CEC) where one segment was packed with silica to be used as an EOF accelerator and this was attached to the separation segment by means of a frit [4]. More recently, Tegeler and El Rassi [5] have performed on-column trace enrichment of insecticides using a coupled capillary approach in CEC. Rathore and Horváth [6] have reviewed the use of partially packed columns in CEC and the axial nonuniformities relating to conductance, joule heating and the EOF.

The controllable range of the EOF in the studies performed by Nashabeh and El Rassi [2] was narrow due to the use of uncoated fused silica capillary. Control of the EOF over the wider pH range of 2–13 using capillaries

joined with PTFE was performed by Katayama et al. [7] by creating successive coated multiple ionic-polymer layers (SMIL) and joining these together. Rapp and Bayer [8] used a PTFE/fluorinated ethylene propylene (FEP) shrink tube connector to create a fritless capillary column by attaching a packed column which was tapered at the end to an unpacked capillary which had the UV detection window. This had the benefit that if the fragile UV window broke, this segment could be replaced. Waterval et al. set up an on-line analyte preconcentration system for the preconcentration of peptides interfaced to a mass spectrometer using PTFE [9–11].

Preconcentration is one way to improve the relatively poor detection sensitivity of CE [12]. There are several preconcentration methods which have been used, including velocity difference induced focussing (V-DIF) [13–16], field amplified sample stacking [17–21], large volume sample stacking, pH mediated focusing [22,23] isotachophoretic stacking [24–27] and solid-phase extraction (SPE) [28–33]. Sample stacking methods can be used only with sample volumes which are less than one capillary volume. In contrast, SPE preconcentration permits the use of multiple capillary volumes of the sample, with the analytes being retained and then subsequently eluted from the SPE stationary phase. On-line ion-exchange SPE has been demonstrated by Arce and co-workers [34–36] who used a flow injection analysis (FIA) system containing an ion-exchange preconcentration column prior to CE analysis. Novic and Gucek [37] used carbonate and hydroxide eluents to remove adsorbed anions from an off-line ion-exchange SPE column, followed by protonation of weak acid anions to form acids using an ion chromatography suppressor. The protonated effluent was collected and injected into a CE machine. The disadvantages of both these approaches are that they require instrumental modification and not all of the preconcentrated analyte was injected into the capillary.

On-column ion-exchange preconcentration of inorganic anions in open-tubular CEC with elution by a transient isotachophoretic gradient is an alternative in-line SPE technique [38–40]. It can be performed using a conventional CE instrument without modification. This method utilizes a single capillary in which a short section (approx. 10 cm) has been wall-coated with nanometer-sized latex particles functionalized with quaternary ammonium groups, forming an open-tubular anion-exchange column. The remainder of the capillary can be coated with various dynamic or permanent coatings to achieve a desirable EOF. Therefore in the one capillary, a preconcentration zone and a separation zone are formed. The preconcentration zone acts as an open-tubular ion-exchange SPE column, which is used for the adsorption of analyte ions. The analyte is loaded after the stationary phase in the capillary has been conditioned with a background electrolyte (BGE) having a weak ion-exchange selectivity coefficient (termed the weak electrolyte, WE) in order to achieve the greatest possible binding of analytes to the stationary phase. A BGE having a high ion-exchange selectivity coefficient (termed the strong electrolyte, SE) is then placed in the electrolyte vials prior to voltage being applied. This discontinuous electrolyte system forms a transient isotachophoretic gradient which moves through the capillary, eluting the analytes from the stationary phase and compressing the analytes into a sharp band. When the analytes are eluted fully from the preconcentration segment they are then separated in the remainder of the capillary according to their electrophoretic mobilities.

In the present study, segmented capillary systems joined with PTFE are investigated as a practical means of coupling capillaries coated with different substances for in-line preconcentration/separation systems. In our previous studies the internal diameter (i.d.) of the capillary was the same in the preconcentration and separation zones. By joining capillaries with a PTFE sleeve, different diameter capillaries can be coupled together allowing the path length of the separation section to be optimized whilst retaining an optimal phase ratio in the preconcentration section. A novel transient isotachophoretic gradient has been formulated and used in a segmented column to increase the range of anions that can be preconcentrated and detected.

2. Experimental

2.1. Apparatus

The CE instrument used was a Hewlett-Packard ^{3D}CE (Hewlett-Packard, Waldbronn Germany). Separations were carried out using Polymicro (Phoenix, AZ, USA) fused silica capillary of various lengths and internal diameters of 75, 50 and 25 μm. UV detection at 195 nm was used.

2.2. Reagents

Dionex AS5A quaternary ammonium fully functionalised latex particles with an approximate diameter of 75 nm were supplied as an 11% (w/v) suspension from Dionex (Sunnyvale, CA, USA). Analytical grade tris(hydroxymethyl)aminomethane (Tris) was obtained from Sigma–Aldrich (Milwaukee, WI, USA). Acetone and thiourea were used as neutral markers to measure the EOF. Standards of 10 mM Br^-, I^-, NO_3^-, Cl^-, ClO_3^-, BrO_3^-, IO_3^- and benzenesufonate were prepared from sodium or potassium salts of analytical or reagent grade and were diluted as required. The perchlorate strong electrolyte was prepared by titration of Tris with perchloric acid to a pH of 8.05. The octanesulfonate strong electrolyte was prepared from the sodium salt of octane sulfonic acid. The fluoride weak electrolyte solution was prepared from the sodium salt. Electrolyte solutions were degassed prior to use by vacuum sonication for 2 min and filtered through a 0.45 μm membrane filter.

2.3. Capillary coating procedure

The latex particles were cleaned as reported previously [41]. The preconcentration capillary was prepared by pumping several capillary volumes of a dilute suspension of latex particles at 50 mbar for 15 min through a 32 cm long section (this was the minimum length required to fit into the HP [3D]CE cassette and was later cut to size). The latex suspension was then flushed out of the capillary with water at low pressure. This process was repeated three times. A separate length of capillary was flushed with a 0.1% solution of poly(diallyldimethylammonium chloride) (PDDAC) for 15 min to ensure that the EOF was in the same direction throughout the two capillary segments. The segments were then joined using a PTFE sleeve, which had an internal diameter matching the outside diameter of the capillary (approx. 370 μm). Prior to joining, the capillary ends were cut with a HP diamond-edge capillary cutter to obtain a square end and were butted together inside the 1 cm PTFE sleeve to ensure there was minimal dead volume in the PTFE sleeve.

3. Results and discussion

3.1. Advantages of coupled capillaries

In previous studies, coating a capillary with two different materials to create preconcentration and separation zones required the removal of the polyimide coating at the end of the desired preconcentration section to form a detection window which could be used to observe the passage of the latex coating solution and hence to control the length of the preconcentration section of the capillary. The secondary coating with PDDAC was performed by simply flushing the entire capillary, including the latex-coated section. This method introduced some uncertainty into the precise final length of the latex-coated section. This practical difficulty was a strong motivation for the use of segmented capillaries, wherein the preconcentration section could be pre-formed using a capillary of suitable diameter and a precise length and then coupled to the PDDAC-coated separation capillary. Fig. 1 shows a schematic representation of a 25 μm
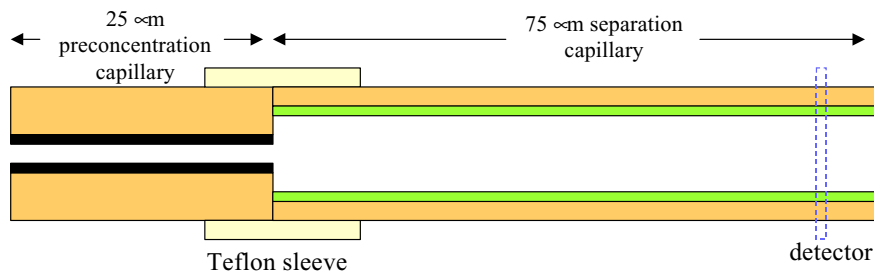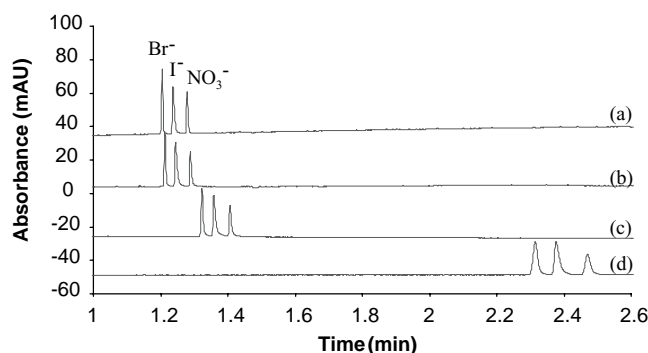

Fig. 2. Comparison of separations performed on: (a) an unsegmented PDDAC open-tubular capillary, (b) the same capillary after cutting at 10 cm from the inlet and coupling the two segments, (c) a 50 μm capillary coupled with a 75 μm capillary, (d) a 25 μm capillary coupled with a 75 μm capillary. Conditions: capillaries: (a) and (b) 57 cm total length of 75 μm capillary with window 8.5 cm from end; (c) 10 cm × 50 μm capillary coupled with 47 cm × 75 μm capillary; (d) 10 cm × 25 μm capillary coupled with 47 cm × 75 μm capillary. All capillaries were wall-coated with PDDAC to reverse the EOF; BGE: 10 mM Tris–Cl; injection: 0.2 mM sample injected for 10 s 10 mbar (3.0×10^{-12} mol); run voltage: -30 kV; temperature: 25 °C.

preconcentration capillary coupled with a 75 μm separation capillary. The characteristics of the two capillaries can be manipulated precisely according to literature coating procedures [42,43] and this approach avoids breakage problems at the point where the polyimide coating is removed when a single capillary houses both coatings.

3.2. Effect of segmentation on peak shape

The effect of the joint on the performance of the coupled capillaries was evaluated. No leakage of electrolyte occurred at applied pressures up to 12 bar (the maximum pressure accessible on the Agilent CE used) and when voltage was applied the current was stable throughout the separation.

To determine whether there was a loss of separation efficiency due to the joint, a 75 μm length of capillary was coated with PDDAC and a separation at -30 kV was performed between bromide, iodide and nitrate. The capillary was then cut 10 cm from the inlet and rejoined with a PTFE sleeve. Fig. 2 and Table 1 show that there was a

Fig. 1. Schematic representation of a 25 μm preconcentration segment coupled to a 75 μm separation segment via the use of a PTFE sleeve which matches the outside diameter of the capillary segments.

Table 1
Peak efficiency and mobility of the EOF for the separations in Fig. 2

	75 μm	75/75 μm	50/75 μm	25/75 μm
Number of plates				
Bromide	408 800	279 000	248 700	122 200
Iodide	184 000	152 500	129 100	112 300
Nitrate	548 100	253 200	200 500	110 600
Mobility of the EOF ($\times 10^9\,\mathrm{m^2\,V^{-1}\,s^{-1}}$)				
EOF	−41.18	−39.85	−34.72	−15.48

Table 2
Total capacity of various preconcentration capillaries coated with AS5A latex using 0.01 mM solutions of weak (Br^-), medium (I^-) and strong (SCN^-) ion-exchange anions, loaded at a velocity of 5.4 cm/s

	75 μm	75 μm	75 μm	50 μm	25 μm
Anion used	Br^-	I^-	SCN^-	Br^-	Br^-
Capacity ($\times 10^{-12}$ eq./cm)	6.8	5.5	5.8	12.5	3.7
Theoretical capacity ($\times 10^{-12}$ eq./cm)	2.1	2.1	2.1	1.4	0.7

The theoretical capacity has been calculated using data supplied from Dionex.

significant loss of efficiency in the segmented capillary but the peak broadening was not such that the analytes could not be separated. Table 1 also shows that the EOF in the segmented capillary was slightly less than that in the intact capillary. Coupling of capillaries of differing internal diameters was also studied and Table 1 shows that both the decrease in efficiency and the reduction in EOF were greatest when the 25 μm capillary was coupled to a 75 μm capillary.

When two or more capillary columns for which the magnitude of the zeta potentials are different are coupled in series, a constant EOF should be established according to the weighted average of the EOF of the two segments [1]. However, while the linear velocity of the EOF can be expected to be similar in the two segments, the volumetric flow through the smaller diameter will be lower and will therefore reduce the overall EOF mobility. Consequently, the deterioration in plate numbers is a result of the slowing EOF in the differing diameter systems. It has also been shown that increased band broadening in wall-coated systems will result when the analyte has a strong ion-exchange interaction will the wall [44]. Breadmore et al. [40] have demonstrated that the BGE used for the separation must therefore contain sufficient ion-exchange competing ions to suppress these wall interactions.

The effect of the internal diameter of the preconcentration segment was examined for capillaries having diameters of 75, 50 and 25 μm, coupled to a 75 μm separation segment. In all cases, equimolar amounts of bromide, iodide and nitrate were preconcentrated and the electrolyte system was 10 mM NaF–10 mM Tris–perchlorate. It was observed that a similar slowing of the EOF caused the analytes to be eluted later in the 50/75 μm system and even later in the 25/75 μm system. This resulted in some deterioration of peak efficiencies, but the efficiencies were better in the 25/75 μm system than the 50/75 μm system. This may possibly be attributed to a more efficient elution from the smaller diameter preconcentration zone.

3.3. Characteristics of AS5A-coated segments

The uniformity of the AS5A latex coating produced within a single length of capillary was evaluated by coating the minimum length that will fit in the HP ^{3D}CE cartridge (approx. 30 cm) and then cutting this into 10 cm lengths.

The EOF of a coupled capillary formed by joining each of these short segments separately to the same 25.3 cm length of PDDAC-coated 75 μm capillary (the latex-coated segments were too short for direct measurement of EOF). The EOF values in all three cases were very similar (approx. $-30 \times 10^{-9}\,\mathrm{m^2\,V^{-1}\,s^{-1}}$), which indicated that the coating procedure produced an even coating of latex over the entire capillary.

The binding capacities of the three latex-coated segments produced above were determined by performing a breakthrough study using 0.1 mM Br^- solution as the loading solution. The UV absorbance of the effluent leaving the capillary was monitored at 210 nm in order to detect any Br^-. The results for the three segments, expressed as the number of capillary volumes of solution before breakthrough were 2.01, 2.05 and 1.65 for segments 1, 2 and 3, respectively. These results suggest that the third segment had a slightly lower coverage of latex than the other two segments. However, this trend was not evident in the EOF results suggesting that there may other factors involved.

Further breakthrough studies were performed to determine total effective ion-exchange capacity of AS5A preconcentration segments of equal length but of 75, 50 and 25 μm internal diameter. Values are provided in Table 2, together with theoretical capacities calculated from the diameter and ion-exchange capacity of the latex particles and assuming a monolayer coverage. Table 2 shows that the experimental capacities were not dependent on the ion-exchange selectivity coefficient of the analyte ($K_{SCN} \gg K_{Br}$ [39]), suggesting that quantitative binding had occurred in each case. The calculated capacities were considerably lower than the experimental values, indicating that the latex coating was probably more than a monolayer. Finally, it can be noted that the 50 μm capillary showed the highest capacity, perhaps because this diameter offered a good compromise between ease of coating and favorable mass-transfer characteristics for sample binding.

The effect of the velocity of flow during sample loading on the sample loading capacity was evaluated by using loading velocities of 0.14, 0.28 and 5.4 cm/s for an AS5A-coated 75 μm capillary, with bromide as the analyte. The loading capacities were 6.0, 6.1 and 6.8×10^{-12} eq./cm, respectively, demonstrating that over the range studied, the loading velocity exerted only a marginal effect on loading capacity.

3.4. Optimization of the transient isotachophoretic gradient

Previous studies on transient isotachophoretic (tITP) gradients have utilized perchlorate and 1,5-naphthalenedisulfonate [38–40] as the strong electrolytes. These electrolytes were found to be unsuitable for the desired analysis. Perchlorate has a high electrophoretic mobility which allows only a small range of anions to be preconcentrated and to travel in front of the gradient for detection. On the other hand, naphthalenedisulfonate has a suitable electrophoretic mobility but possesses a high ion-exchange selectivity coefficient, making it difficult to regenerate the preconcentration capillary into the weak electrolyte form. The ideal strong electrolyte should have a low electrophoretic mobility so a large range of anions can be preconcentrated and travel in front of the isotachophoretic gradient and should also possess an ion-exchange selectivity coefficient which is large enough to elute most anions. Octanesulfonate satisfies these two criteria ($\mu = -13.82 \times 10^{-9}\,\mathrm{m^2\,V^{-1}\,s^{-1}}$ and has an ion-exchange selectivity coefficient relative to fluoride of 118 [39]). Moreover, the combination of fluoride/octanesulfonate as weak and strong electrolytes, respectively, produces a stepwise tITP gradient front and allows efficient elution of analytes as sharp preconcentrated bands from the preconcentration capillary.

Such an tITP gradient is suitable for preconcentration and separation of anions ranging in electrophoretic mobility from $-33.12 \times 10^{-9}\,\mathrm{m^2\,V^{-1}\,s^{-1}}$ (benzenesulfonate) to $-77.42 \times 10^{-9}\,\mathrm{m^2\,V^{-1}\,s^{-1}}$ (bromide) and ion-exchange selectivity coefficients relative to fluoride of 2.6 (iodate) to 711 (iodide). This gradient was used in the sample analyses discussed in the following section.

3.5. Applications of preconcentration using coupled capillaries

One of the potential advantages of the use of coupled capillaries is that the sample loading step can be performed in a different location and at a different time than the separation step. One application is the analysis of river water, where sampling and preconcentration are performed in situ, followed by laboratory analysis of the loaded sample after coupling to a separation capillary. Sample loading involves drawing a known volume of the water sample through the preconcentration capillary using a microlitre syringe attached to the capillary using a PTFE sleeve. Direct binding of the sample anions to the stationary phase eliminates the possibility of contamination due to transport of the sample. Further, sample clean-up steps can also be performed on the loaded preconcentration capillary if required before it is coupled to the separation capillary. Contamination of the separation capillary by the sample matrix ions is also avoided.

To illustrate this process, a river water sample was injected through the preconcentration segment in situ from the Hobart Rivulet in South Hobart, Tasmania, Australia.
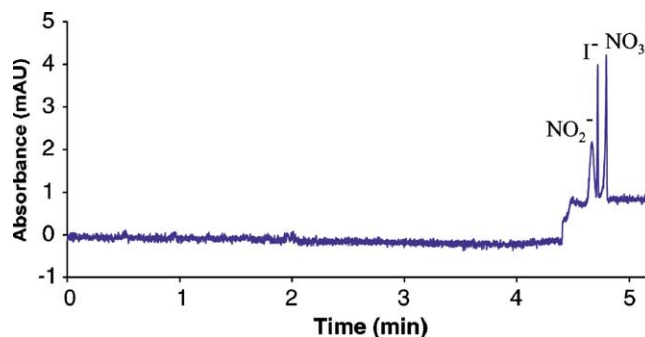

Fig. 3. River water sample taken from Hobart Rivulet and loaded directly onto a preconcentration segment. Conditions: capillaries: $10\,\mathrm{cm} \times 25\,\mu\mathrm{m}$ i.d. AS5A-coated preconcentration segment attached to a $42\,\mathrm{cm} \times 75\,\mu\mathrm{m}$ PDDAC-coated separation capillary; weak electrolyte:10 mM NaF; strong electrolyte: 10 mM octanesulfonate; injection: $0.5\,\mu\mathrm{l}$ of river water loaded onto preconcentration segment only; voltage: $-30\,\mathrm{kV}$; temperature: $25\,^\circ\mathrm{C}$.

The loaded preconcentration capillary was then rinsed with deionized water to remove matrix material, prior to coupling the preconcentration and separation capillaries. The analyte ions were then eluted and separated using the fluoride–octanesulfonate tITP gradient. Fig. 3 shows that nitrite, nitrate and iodide were detected in the sample. Other ions might also have been present but these were either eliminated by the water flushing step or they were not detected as a result of the use of direct UV detection at 195 nm. It can be seen from Fig. 3 that the efficiency for nitrite was not as high as the other ions, which was attributed to its weaker retention on the stationary phase resulting in less efficient peak compression by the gradient front. Using an external calibration method, the concentration of these analytes were estimated to be 0.60, 0.18, 0.58 μM of nitrite, iodide and nitrate, respectively. The separation was not optimized since the objective was only to show that the preconcentration capillary could be decoupled for in situ sampling in the field.
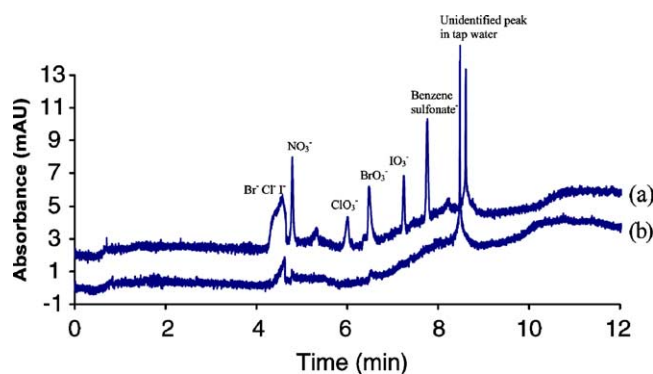

Fig. 4. Preconcentration and separation of anions in: (a) tap water spiked with $2\,\mu$M Br$^-$, I$^-$, NO$_3^-$, IO$_3^-$, $4\,\mu$M ClO$_3^-$, BrO$_3^-$, 0.5 mM benzenesulfonate and (b) tap water. Conditions: capillaries:10 cm $\times$ 50 μm AS5A segment coupled to a 50 cm $\times$ 75 μm PDDAC segment; injection: 10 min at 950 mbar (approx. 20 capillary volumes); weak electrolyte: 10 mM NaF; strong electrolyte: 10 mM octanesulfonate; run voltage: -30 kV; temperature: $25\,^\circ$C.

A tapwater sample spiked with μM levels of some anions was also analyzed, as shown in Fig. 4. In this case, a 50 μm preconcentration capillary was used to aid in the retention of weaker analytes on the stationary phase, while a 75 μm diameter PDDAC-coated capillary was used as the separation capillary. Use of a longer section of the separation capillary would allow for better separation of chloride, bromide and iodide.

4. Conclusions

Coupled capillaries have been used for detachment of the preconcentration capillary from the separation capillary for in-line capillary ion-exchange preconcentration in open-tubular CEC with elution by a transient isotachophoretic gradient. This allowed optimization of the coating procedure of each capillary and flexibility in the design of the preconcentration and separation systems with respect to preconcentration efficiency and detection sensitivity. The fluoride/octanesulfonate electrolyte system used was suitable for the preconcentration and separation of a range of anions having higher electrophoretic mobilities than octanesulfonate and useful for off-line analysis of water systems reducing decomposition and contamination. The coupled capillary approach also permitted the sample loading and preconcentration step to be performed remotely from the laboratory.

Coupled capillaries can be applied not only to open tubular preconcentration but also to preconcentration using packed capillaries and monolithic preconcentration capillaries. The method could also be extended to the detection of a wider range of analytes if a more universal detection method (e.g. using indirect spectrophotometric detection) was used.

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