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CONFERENCE CONTRIBUTION

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A new interface for combining capillary electrophoresis with inductively coupled plasma-mass spectrometry

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Abstract This paper describes the development and design of a new, efficient, simple and robust interface for coupling capillary electrophoresis (CE) with inductively coupled plasma-mass spectrometry. The interface is based on a *modified* microconcentric nebulizer which permits a low flow rate of about 6 μL/min in the free aspiration mode. This interface construction provides an electrical connection for stable electrophoretic separations and adapts the flow rate of the electro-osmotic flow inside the CE capillary to the flow rate of the nebulizer for efficient transport of the analytes into the plasma. By optimization of the fluid mechanical properties the interface prevents the nebulizer from causing any laminar flow in the CE capillary and thus the high resolution power of CE can be preserved. Furthermore, this new device permits independent optimization of the nebulization from the CE whereby exact positioning of the CE capillary is not necessary, thus enabling fast exchange. A low dead volume spraychamber has been constructed which circumvents any band broadening of the sharp CE signals. Peak widths down to 3.5 s comparable to CE with UV detection are possible.

Introduction

During the last few years several approaches to the development of interfaces for the on-line coupling of capillary electrophoresis (CE) with ICP-MS have been described [1]. These constructions are mostly based on pneumatic [2–5], direct injection [6] or ultrasonic nebulizers [7]. There are three main requirements which an interface construction for CE / ICP-MS coupling has to satisfy:

- firstly, the interface must provide an electric connection and a stable electric current for reproducible electrophoretic separations,
- secondly, the interface must adapt the flow rate of the electroosmotic flow (EOF) inside the CE capillary to the flow rate of the nebulizer. Typical flow rates of the EOF, depending on the capillary dimensions and the voltage are between 0.1 and 0.9 μL/min; the flow rates of commercial concentric glass nebulizers (Meinhard®) are between 100 and 1000 μL/min and of microconcentric nebulizers between 10 and 100 μL/min,
- thirdly, the interface should prevent laminar flow inside the CE capillary caused by the nebulizer since this is potentially a very serious problem because it could disturb the high resolving power of the capillary electrophoresis.

Olesik et al. [2] constructed an interface based on a standard concentric glass nebulizer in which the CE capillary is coated with silver paint for electric contact. Kinzer et al. [8] from the same group described a further development of this interface, in which a conventional concentric and a high efficiency nebulizer is used and the electrical connection is provided by liquid sheath flow. Other interface constructions based on standard [9] or high efficiency [10] concentric glass nebulizers, cross-flow [9] or commercial microconcentic nebulizers [5, 11] have also been reported. In all these cases the electric contact is enabled by a liquid sheath flow, which has the additional function of adapting the flow rate of the CE to the flow rate of the nebulizer. In several approaches to solve the problem of laminar flow inside the CE capillary, pumps, which transport the liquid sheath flow, are used for creating a backpressure on the CE capillary. Lu et al. [3] and in a recent paper Taylor et al. [5] applied a negative pressure to the inlet vial of the CE to compensate the laminar flow. In all cases, sensitive equilibria between backpressure and negative pressure have to be adjusted to compensate for laminar flow in the CE capillary. In [3] the influence of sheath flow rate on nebulizer suction, CE resolution, time and peak shape was studied.

Liu et al. [6] described an efficient interface built with a direct injection nebulizer (DIN), which causes no laminar flow or back pressure during CE separation and shows

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good peak shapes and sensitivities for arsenic and selenium species.

Another approach has been pursued by Michalke and Schramel [4]. They did not monitor the separated species on-line in real time, but divided the analysis into two steps: in a first step the analytes were separated in the capillary by electrophoresis and in a second step they were flushed into the nebulizer interface (a modified concentric glass nebulizer) by pressure. They reported that the capillary position is critical and that under optimized interface conditions and with a long CE capillary of about 150 cm, laminar flow inside the CE capillary was not observed.

An interface based on an ultrasonic nebulizer has been described by Lu and Barnes [12] as well as by Caruso et al. [7]. The advantage of this construction is that the nebulizer does not cause suction, but a higher background noise level than with pneumatic nebulizers was observed [12].

The aim of this work was to develop an efficient, simple and robust CE/ICP-MS interface which fulfils the above mentioned requirements. The design of the interface is of prime importance and in particular, prevention of laminar flow inside the CE capillary is the key for successful hyphenation of CE with ICP-MS. This new interface should overcome the major drawbacks of laminar flow caused by nebulizer suction and should enable effective analyte transport into the plasma. The new ideas are:

(i) An optimization of the fluid mechanical properties of the construction by a modification of the nebulizer capillary to avoid any negative pressure at the end of the CE capillary. Therefore this interface should not need any pumps or negative pressure to counterbalance the flows and pressures in the CE capillary.
(ii) A minimization of the make-up flow rate also by changing the nebulizer capillary to minimize the dilution of the analytes. The low make-up flow rate should also enable the construction of a low dead volume spraychamber to minimize any bandbroadening.
(iii) An independent optimization of the nebulization from the CE by dividing the interface construction into two parts: the nebulizer capillary and the CE capillary. The CE capillary is not inserted into the nebulizer capillary.

In this paper the set-up and the properties of the new interface are descibed. Furthermore, the optimization of the flow rate of the nebulizer for efficient analyte transport and the prevention of laminar flow inside the CE capillary is discussed. First results for the separation of a standard solution containing arsenic and lead species and a comparison with a CE/UV electropherogram are presented.

Experimental

CE/ICP-MS system. The instrumental set-up of the CE/ICP-MS system consists of an HP 3D capillary electrophoresis with fused silica capillaries, with lengths between 30 and 60 cm, an inner diameter (i.d.) of 75 μm and an outer diameter (o.d.) of 150 μm (purchased from Thermo Separation Products, Egelsbach, Germany), a recently developed interface and the Finnigan ICP – sector field – MS Element. The experimental conditions of the CE/ICP-MS set-up are shown in Table 1.

Table 1 Experimental conditions of the CE / ICP-MS set-up

Capillary electrophoresis	
Buffer solutions	25 mmol/L CAPS, pH 10; 4 μg Cs/L 4 mmol/L borate; pH 9.3; 4 μg Cs/L
Voltage	30 kV
Injection	hydrodynamical, 200 mbar•s
Make-up liquid	1.5% (m/v) nitric acid; 1 μg In/L
ICP-MS	
Cool gas	14 L/min
Auxiliary gas	0.95 L/min
Nebulizer gas	0.6–1.2 L/min
Power	1075 W

The interface. The newly developed interface (Fig. 1) is based on a modified microconcentric nebulizer (MCN 100, Fa. CETAC, Omaha, USA). The difference between the nebulizer constructed and the commercial one is that the nebulizer capillary has been changed to a narrower i.d., so that flow rates in the self aspiration mode between 2 and 12 μL/min are possible and nebulizer suction is minimized. Detailed construction of the interface is descibed in [13]. The nebulizer is connected with a cross-piece which is made of poly-ether-etherketone (PEEK) and has two horizontal fittings, one for the platinum electrode and a second one for the make-up liquid (liquid sheath flow) and a vertical fitting for the CE capillary. The make-up liquid is transported by self-aspiration of the nebulizer, grounded by the platinum electrode and is mixed with the CE buffer at the end of the CE capillary. In this way, the make-up liquid provides the electrical connection for the electrophoresis and additionally the make-up liquid adapts the flow rate of the electro-osmotic flow to the flow rate of the nebulizer.

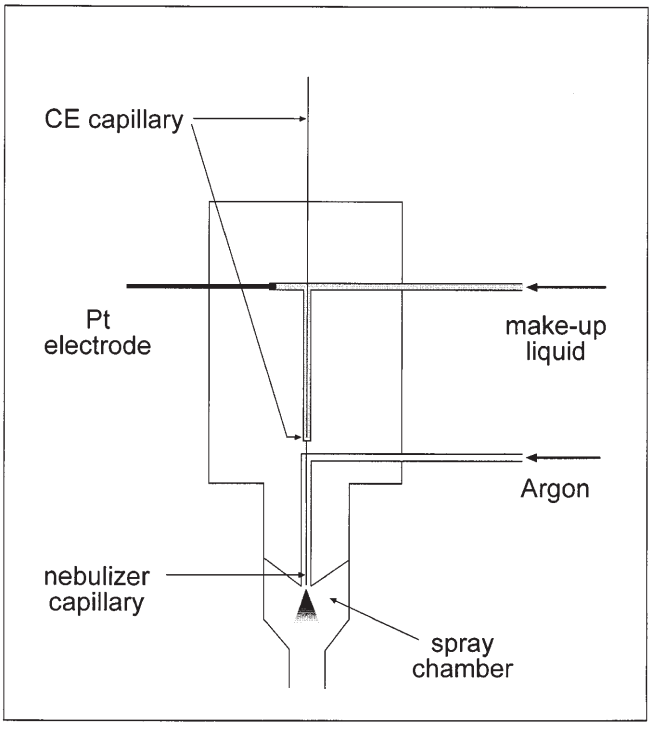

Fig. 1 Schematic view of the interface

The position of the nebulizer capillary can be optimized for an optimal nebulization independently of the position of the CE capillary which guarantees a simple exchange of the CE capillary.

The novelty in the design is that the dimensions of the nebulizer capillary are calculated and optimized for a minimized negative pressure at the end of the CE capillary, to avoid any laminar flow inside the CE capillary. This is achieved by adapting the flow resistance of the nebulizer capillary in order to minimize the negative pressure which occurs at the orifice of the nebulizer, along the nebulizer capillary. As laminar flow inside the CE capillary is avoided by the changed dimensions of the nebulizer capillary, no pumps or negative pressure at the inlet vial for compensating laminar flow are necessary. As a further consequence, the make-up liquid can be transported by self-aspiration of the nebulizer. Additionally, this device enables the use of short capillaries down to 30 cm with wider i.d. than 50 μm.

The nebulizer is plugged into a low dead volume spray chamber of about 5 mL for minimizing band broadening of the CE signals. The spray chamber is connected by a teflon tube with an i.d. of 4 mm and a length of 60 cm to the ICP-MS torch. A schematic view of the interface is shown in Fig. 1.

Sample injection. The sample injection is carried out hydrodynamically with 200 mbar•s, which is equal to a sample volume of 28 nL (capillary 75 μm i.d. and 55 cm length). During sample injection, the nebulizer gas has not to be swiched off which permits stable running of the ICP-MS.

Chemicals. Deionized water was obtained from a Millipore-system. Arsenite standard solution (1000 mg As / L) was prepared by dissolution of diarsenic trioxide (As_2O_3, Merck, p.a.) in 30% (m/v) NaOH (Merck, suprapur) and was acidified with 6 mol HCl/L (Merck, suprapur). Standard solutions of monomethylarsonic acid (MMA), dimethylarsinic acid (DMA), arsenocholine and arsenobetaine (all solutions 1000 mg As/L) were prepared by dissolving MMA (disodium salt, hexahydrate), arsenocholine and arsenobetaine (all purchased from Argus Chemicals, Vernio, Italy) and DMA (sodium salt, trihydrate, Merck) in water. Standard solutions of trimethyl lead (33.7 mg Pb/L) and triethyl lead (200 mg Pb/L) were prepared by dissolving trimethyl lead chloride and triethyl lead chloride (provided by GALAB, Geesthacht, Germany) in methanol.

Arsenate, cesium, indium and rubidium standard solutions (1000 mg As, Cs, In, or Rb in 0.5 mol HNO_3/L) were purchased from Merck.

All standards containing the arsenic and lead species were stored at 10 °C in the dark, other standards were stored at room temperature. Standard solutions of lower concentrations were prepared by appropriate dilution with water. The resulting solutions were filtered (0.45 μm) before use.

Nitric acid (Merck, suprapur) was cleaned by subboiling in a quartz apparatus and diluted with water. Borate buffer solution (pH 9.3; 50 mmol/L) was purchased from Hewlett-Packard, CAPS (3-(cyclohexylamino)-propane-1-sulfonic acid) buffer solution (pH 10; 25 mmol/L) from Microsolve.

Results and discussion

Optimization of the flow rate of the nebulizer (make-up flow rate)

The flow rate of the nebulizer must be as low as possible in order to avoid too much dilution of the analytes and to avoid condensation in the spray chamber. The nebulization must be as stable as possible, so that the signals show good precision. These limitations were tested by varying the make-up flow rate of the nebulizer in the self-aspiration mode by varying the i.d. of the tube of the make-up liquid. The make-up liquid contained 1 μg In/L so that the intensity (in counts/s) and the standard deviation of the indium signal indicate the nebulizer performance. Figure 2 shows the results of this experiment: below a flow rate of 2 μL/min the nebulization is irregular; above a flow rate of 11 μL/min condensation in the spray chamber takes place. The intensity of the indium signal increases linearly with the flow rate, but the precision of the signals is best between 4 and 6 μL/min, so that for further experiments a flow rate about 6 μL/min was deemed to be optimal.

The flow rate of the electroosmotic flow was between 0.1 and 0.9 μL/min depending on the dimensions of the CE capillary and the voltage, so that the dilution factor of the analytes is approximately between 5 and 20.

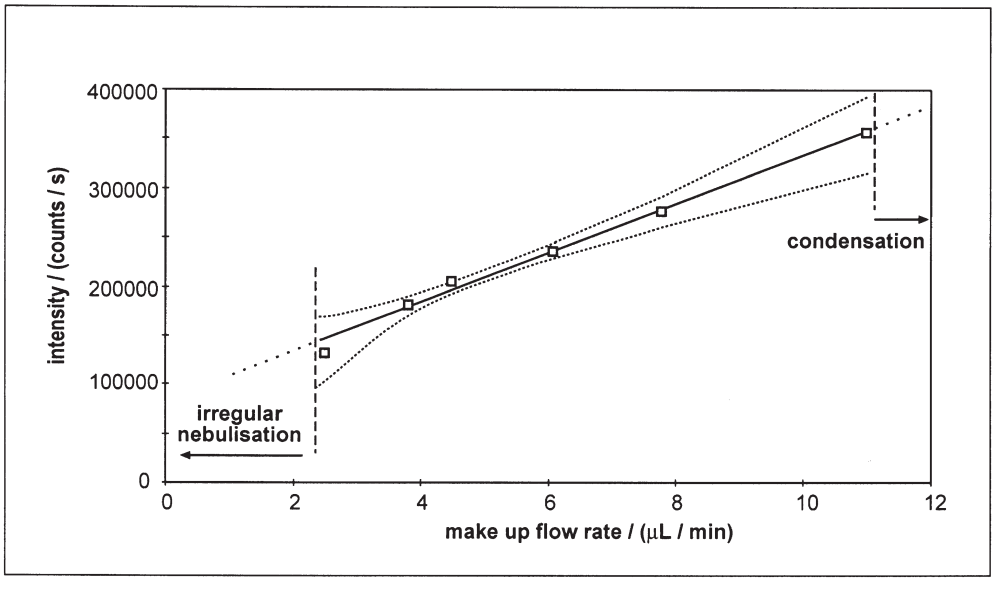

Fig. 2 Optimization of the make-up flow rate by measuring the intensity and precision of the ^{115}In signal of a 1 μg In/L standard solution

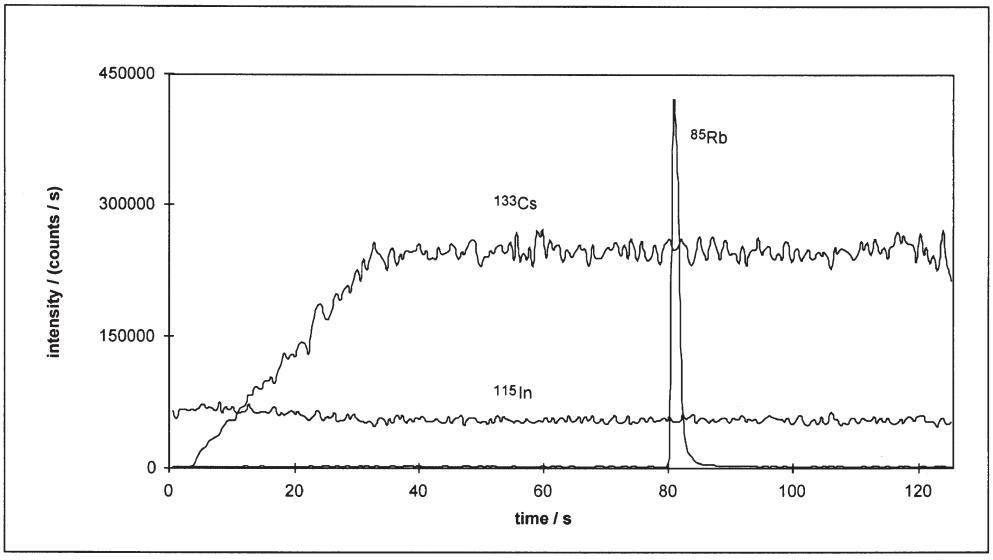

Fig. 3 Monitoring of EOF (^{133}Cs) and make-up flow (^{115}In) during an electrophoresis of a test solution of 20 µg Rb/L; voltage 30 kV, CAPS buffer (25 mmol/L, pH 10)

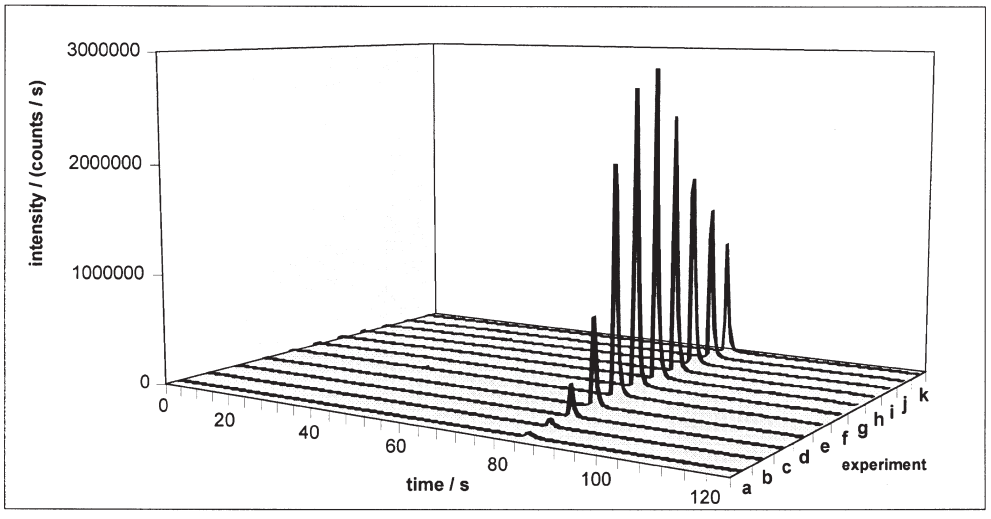

Fig. 4 Migration time of a test sample containing 100 µg Rb/L independent of the argon flow rate; experiments with different argon flow rates (in L/min): (*a*) 0.6; (*b*) 0.7; (*c*) 0.8; (*d*) 0.9; (*e*) 0.925; (*f*) 0.95; (*g*) 0.975; (*h*) 1.0; (*i*) 1.05, (*j*) 1.1; (*k*) 1.2; CAPS buffer (25 mmol/L, pH 10); hydrodynamic injection, 200 mbar•s; 30 kV

Electrophoretic conditions

A stable and continuous electric contact at the end of the CE capillary is required for reproducible electrophoretic separations. Figure 3 shows that the CE/ICP-MS set-up works under stable conditions. Under a default voltage (e.g. 30 kV) a stable electroosmotic flow can be observed. The EOF was monitored by the ^{133}Cs signal, which also indicates stable analyte transport from the CE capillary into the ICP-MS. A test solution of 20 µg Rb/L was injected and a peak was detected after a migration time of 81 s. This very sharp rubidium signal with peak width about 4 s also indicates that any band broadening caused by the dead volume of the interface and the spraychamber is negligible. Additionally, it can be observed, that the nebulization monitored by ^{115}In is also stable and independent of the electrophoresis. Therefore, the nebulization can be optimized simply by varying the position of the nebulizer capillary; the position of the CE capillary has no influence on the nebulization. The current was measured by the CE instrument. The CE buffer contained 4 µg Cs/L, the make-up liquid 1 µg In/L as marker for observing the electroosmotic flow and the make-up flow.

Laminar flow

Laminar flow inside the CE capillary could be avoided, thus preserving the high separation efficiency of the capillary electrophoresis. With the interface developed, laminar flow is negligible; this was verified with the experiment shown in Fig. 4: a test solution of 100 µg Rb/L was injected and the electrophoresis was started at different argon flow rates of the nebulizer. The Rb signal was always observed at a migration time of 81 s, independent of the argon flow rate. This indicates that the argon flow rate has no influence on the migration time and this means that the nebulizer causes no laminar flow inside the CE capillary. Otherwise the migration time would decrease with increasing argon flow rate. The large influence of the argon

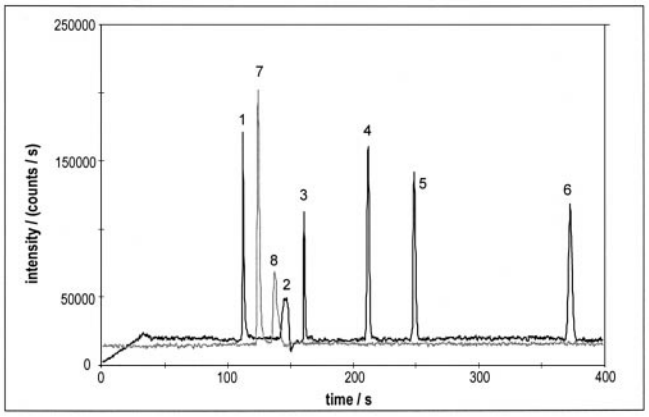

Fig. 5 Separation of (*1*) arsenocholine, (*2*) arsenobetaine, (*3*) arsenite, (*4*) dimethylarsinic acid, (*5*) monomethylarsonic acid, (*6*) arsenate, (*7*) triethyl lead, (*8*) trimethyl lead; 100 µg As/L resp. 20 µg Pb/L of each species; borate buffer (4 mmol/L, pH 9.3); 30 kV; capillary 55 cm length and 75 µm i.d.

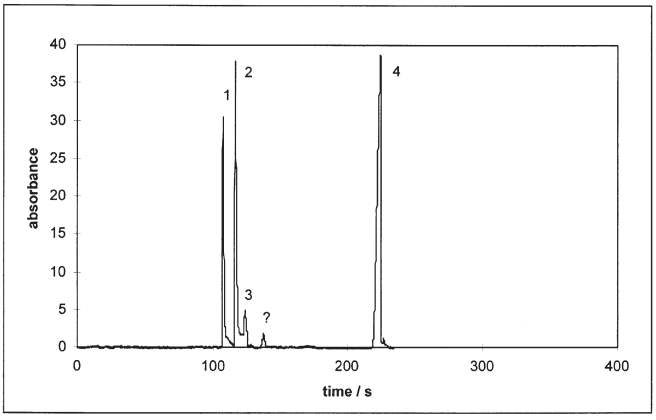

Fig. 6 CE/UV electropherogram of (*1*) triethyl lead (20 mg Pb/L), (*2*) trimethyl lead (33.7 mg Pb/L), (*3*) arsenite (100 mg As/L) and (*4*) dimethylarsinic acid (135 mg As/L); borate buffer (20 mmol/L, pH 9.3); 30 kV; detection at 191 nm; capillary 40 cm to the detector, 48.8 cm total length and 50 µm i.d.

flow rate on nebulizer suction and migration time, found when using interfaces based on commercial nebulizers, has been described and demonstrated in [9].

Additionally, the optimal argon flow rate can be observed which is in the range between 0.9 and 1.0 mL/min. The exact value must be adjusted by tuning the ICP-MS instrument.

Two further experiments according to [4] were carried out to verify that there is no detectable laminar flow:

(i) The electric current of 15 µA at 30 kV voltage was measured again after keeping the capillary inlet in air for 1 h while the nebulizer was working. This indicates that no air bubble, which would disconnect the electric circuit, is sucked into the CE capillary by nebulizer suction.

(ii) After flushing the CE capillary with water, the capillary was put into the inlet vial which contains buffer solution with 4 µg Cs/L. After 1 h no intrusion of cesium into the CE capillary by nebulizer suction could be ascertained.

Separations

The CE/ICP-MS coupling was evaluated by analyzing a test sample containing six arsenic and two lead species (100 µg As resp. 20 µg Pb/L). The electropherogram is shown in Fig. 5 with peak widths from 3.5 s to 6 s. For comparison, a CE separation of two arsenic and two lead species with UV detection was carried out (Fig. 6). Here, peak widths are between 2.4 s for triethyl lead and 5.4 s for dimethylarsinic acid. This comparison demonstrates that the high resolving power of the capillary electrophoresis in combination with ICP-MS detection can be preserved and any band broadening which may be caused by the interface and spray chamber is negligible. The CE/ICP-MS electropherogram shows excellent peak shapes in a short analysis time.

Conclusions

In conclusion it can be stated that a successful hyphenation of CE with ICP-MS has been achieved, in which the key to this coupling are the fluid mechanical properties of a newly developed interface. It was succesfully demonstrated that this newly constructed device prevents any laminar flow in the CE capillary while the make-up liquid is transported by self-aspiration of the nebulizer. Therefore no pumps or negative pressure are necessary to counterbalance laminar flow.

The prevention of laminar flow results in (i) preservation of the high resolving power of capillary electrophoresis and (ii) excellent peak shapes in short analysis times. These demonstrate the capabilities of this CE/ICP-MS coupling as a powerful analytical technique for element speciation.

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