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A soft on-column metal coating procedure for robust sheathless electrospray emitters used in capillary electrophoresis-mass spectrometry

An on-column metal coating procedure was developed for sheathless electrospray emitters, based on Justus von Liebig's electroless silver mirror reaction followed by electrochemical deposition of gold onto the silver layer. The coating procedure is straightforward, mild, inexpensive, and can be performed with standard laboratory equipment. A long-term (600 h) stability investigation of the conductive coating was carried out by continuous electrospray in the positive electrospray mode, and no degradation in performance was found. The simplicity of the coating procedure and the robustness of the spray tips makes the spray tips highly suitable to couple delicate wall-coated or monolithic capillary columns to mass spectrometry. Peptide mixtures were separated by capillary electrophoresis and injected into either a Hadamard-transform time-of-flight mass analyzer or a commercial quadrupole mass analyzer using the described sheathless electrospray emitters. The performance was judged to be excellent.

Keywords: Capillary electrophoresis / Electroless/electrochemical coating / Mass spectrometry / Sheathless electrospray emitter / Silver-gold coating DOI 10.1002/elps.200410152

1 Introduction

Electrospray emitters are commonly used to transfer analytes emerging from capillary or chip format separation techniques into charged species for mass analysis [1–10]. Thus, electrospray emitters have found use in capillary electrophoresis (CE), capillary electrochromatography (CEC), open capillary electrochromatography (o-CEC), and nanoscale liquid chromatography (nano-LC). Sheathless electrospray and nanospray meet the demands for high sensitivities, low flow rates, and reduced peak-broadening effects on separations, whereas the widely used and very robust sheath-flow interfaces dilute the eluting analytes with additional liquid and therefore cause a decrease in sensitivity at very low flow rates [11–21]. Electrospray is achieved by applying a high potential (between 2 and 5 kV) to the spray tip, relative to the orifice of the mass spectrometer which represents the counter electrode [22–25]. In sheathless electrospray emitters the electrical potential is applied to a conductive coating on the outside of the spray tip, which is ideally part of the separation capillary so that it does not introduce dead-volumes or flow distortions. The high electric field strength leads to sputtering of the coating, as well as electrochemical reactions at the interface, mainly electrolysis of water in the positive spray mode. The use of sheathless electrospray emitters is therefore limited by short lifetimes that are typically up to 100 h for standard electrospray and 6 h for nanospray [26, 27]. In addition, gas formation caused by solvent oxidation and corrosion of the conductive metal surface can result in mechanical and oxidative stress on the coating. The use of aqueous buffer systems guarantees that no electrochemical reaction at a more positive potential than the oxidation of water will occur ($H_2O \rightarrow 4H^+ + O_2 + 4e^-$; +1.23 V *vs.* normal hydrogen electrode (NHE)).

Several coating procedures have been described in the literature ranging from vapor deposition of noble metals, the application of conductive polymers [28], to gluing gold particles ("Fairy Dust") [15, 17, 18, 20], or graphite [29] ("Black Dust" [19] and "Black Jack" [20]) onto fused-silica capillaries. The latter methods produce very stable sheathless ESI emitters with exceptional lifetimes of over 300 h of continuous use [27]. Thin, smooth metal films facilitate the electrospray process by creating a high surface tension at the very small contact area of the eluent with the electrode. Vapor deposition of metals and their combinations, *e.g.*, silver [12], gold [15, 17, 18, 20], titanium [21], and chromium [18], onto the spray tip is usually achieved in vacuum [30]. This procedure, however, can-

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Abbreviations: HT, Hadamard transform; **o-CEC**, open capillary electrochromatography; **SEM**, scanning electron microscope not be applied to very delicate capillary columns modified with monolithic materials or wall coatings as stationary phases, which require storage under a buffer solution or solvent to prevent desiccation. Here we present a straightforward, mild, and inexpensive wet two-step coating procedure that does not require heating, gluing, or the use of vacuum. Moreover, this procedure can be performed with standard laboratory equipment.

2 Materials and methods

2.1 Reagents and materials

Concentrated ammonia, ethanol, methanol, potassium cyanide, potassium hydroxide, silver nitrate, sodium hydrogenphosphate, and sodium sulfite were purchased from Mallinckrodt (Phillipsburg, NJ, USA), acetic acid, ammonium acetate, angiotensin II, bradykinin (for quadrupole experiments), caffeine, formic acid, D-glucose, gold(III)-chloride, gramicidin S, poly(vinyl alcohol), methionine-enkephelin, reserpine, and tetrabutylammonium acetate were from Sigma-Aldrich (Milwaukee, WI, USA), polypropylene glycol standard (PPG 450, narrow molecular weight distribution) was from Scientific Polymer Products (Ontario, NY, USA), angiotensin I human, angiotensin II human, angiotensin II (fragment 3–8), angiotensin III human, substance P, substance P (fragment 1–4), and substance P (fragment 7–11) were obtained from American Peptide Company (Sunnyvale, CA, USA). High-purity water (18.2 MΩ) obtained from a Millipore-Q System (Millipore, Marlborough, MA, USA), was used to prepare the buffer and metal coating solutions. Fused-silica capillaries (ID 50 μm and 75 μm, OD 360 μm) were purchased from Polymicro Technologies (Phoenix, AZ).

2.2 Tapering of electrospray emitters

Fused-silica capillaries were tapered according to a procedure developed by Barnidge *et al.* [16, 17]. The capillary protected with a short piece of Teflon tubing is loaded into a chuck of a hand-held drill. The hand-held drill is rotated while pressure is applied to the capillary tip, which is pushed against a rotating piece of sand paper (800 grit). The tapering of the capillary is controlled with a microscope to achieve a symmetrical cone. The capillary is rinsed with water and methanol to remove dust and particles.

2.3 Silver coating procedure

For the silver coating, two stock solutions are prepared having the following composition: solution I is 3 g silver nitrate dissolved in 90 mL deionized water; solution II is 2 g potassium hydroxide dissolved in 90 mL deionized water. 75 mL of solution I are mixed with concentrated ammonia solution, until the formed precipitate has dissolved. Then solution II is slowly added, during which a brown precipitate is formed. This mixture is carefully titrated with concentrated ammonia solution until everything has been dissolved. It is important to avoid excess of free ammonia. Finally, the remaining 15 mL of solution I are added and the resulting solution is filtrated to remove colloidal silver hydroxide. This solution can be stored in a dark bottle in a freezer (−18°C) for several months without formation of any precipitate. Prior to the silver coating the tapered end of the fused-silica capillary is carefully cleaned from grease and dust by rinsing the outer wall with an ammonia/ethanol solution (25 mL concentrated ammonia are mixed with 75 mL ethanol) and water to remove ammonia. Then the capillary is dipped into a 15 mL glass vial containing 10 mL of the silver coating solution. To this, 5 mL glucose solution (12.5 g dissolved in 200 mL deionized water) are added and carefully mixed. The mixture turns dark immediately, and after approximately 4 min a shiny silver coating is visible at the wall of the glass vial, while the color of the solution changes to yellow. The capillary tip is removed and carefully rinsed with deionized water. Subjecting the silver coating to an annealing process at room temperature for 48 h yields a very stable film.

2.4 Gold coating procedure

A stainless steel wire coil is used to make electrical contact to the silver-coated capillary tip. Then the silver-coated capillary tip is dipped into one side of a U-tube containing a solution of gold(III)-chloride (200 mg), potassium cyanide (200 mg), sodium hydrogenphosphate (6 g), and sodium sulfite (1 g), all of which is dissolved in 100 mL deionized water. On the other side of the U-tube a stainless steel anode is placed. For the deposition of gold −1.5 V to −2.2 V are applied to the silver-coated capillary with a direct current (DC) power supply. The current should not exceed 0.9 mA, and formation of hydrogen bubbles should be avoided. After 5 min, the white-silver color changes to yellow-gold because of the deposited gold layer. The capillary is removed from the U-tube and rinsed with water to remove traces of cyanide.

2.5 Long-term fatigue tests of metal-plated electrospray emitters

To test the long-term stability of the silver-gold-coated electrospray emitters, capillaries (length 1 m, ID 50 μm, OD 360 μm) were prepared according to the procedures described above and placed into the insulated chuck of a *x,y,z* micropositioning stage (*cf.* Fig. 1b). A voltage of +2.5 kV was applied to the capillary tip, and a solution of 100 mM tetrabutylammonium acetate dissolved in 65 mL deionized water, 5 mL acetic acid, and 30 mL methanol was infused at a rate of 400 nL/min. A heated counterelectrode (120°C) was placed at a distance of 8 mm. The spray current was recorded in 0.5–30 s intervals with a picoamperometer (Keithley Instruments, Cleveland, OH, USA; Model 6485) connected to the counterelectrode and the data was collected on a personal computer.

2.6 Capillary electrophoresis-Hadamard transform-time of flight-mass spectrometry (CE-HT-TOF-MS)

Electrophoretic separations were performed with a Beckman P/ACE 2000 (Beckman Instruments, Fullerton, CA, USA) equipped with the Beckman MS kit. The CE instrument was modified to allow application of external pressure to the buffer vial to perform pressure-assisted separations at 0.4 psi. About 20 cm of the 1-m separation capillary (poly(vinyl alcohol)-coated fused-silica capillary [31] OD 360 μm, ID 50 μm) was maintained at 20°C in the cartridge and the 80 cm section leading to the *x,y,z* micropositioning stage of the ESI source was maintained at room temperature. Injections were done at a pressure of 0.5 psi and the injection times varied from 2 to 5 s. A peptide mixture was prepared by mixing 100 μL of 200 μM stock solutions of each of angiotensin I human, angiotensin II human, angiotensin II (fragment 3–8), angiotensin III human, bradykinin, gramicidin S, substance P, substance P (fragment 1–4), and substance P (fragment 7–11). The final concentration of the peptides in the stock solution is 22 μM. All analyses were carried out in a 1:1 mixture of 50 mM formic acid/ammonium acetate buffer solution (pH 2.8) and methanol. A separation voltage of +28 kV was applied to the inlet buffer vial and the spray tip was held at +3.6 kV with an external power supply connected to a resistor network. A 470 Ω resistor was placed between the spray tip and the power supply and a 20 MΩ resistor was connected with the high-voltage power supply output and ground to stabilize the electrospray voltage. A detailed description of the HT-TOF mass spectrometer [32, 36] is given in [37]. In the following the ion source conditions used in the experiments are briefly described. The spray tip is held at a distance of 5–8 mm to the sampling orifice of the mass spectrometer. The spray source temperature is 220°C and the orifice and end cap of the heated transfer capillary were set to +57 V. Ions were extracted from the silent zone of the mach disk emerging from the metal spray nozzle with a skimmer (1 mm orifice ID, +23 V). The focusing entrance lens in the second stage was set to +21.2 V, the amplitude of the hexapole ion guide (length 21.9 cm, frequency 2.9 MHz) was set to 1600 V and the focusing exit lens was at −21.0 V. The ions were accelerated to kinetic energies of 1500 eV by an asymmetric immersion lens and then collimated by an Einzel lens (−465 V). The modulation frequency of the ion beam was set to 5 MHz and a 10-bit pseudo-random encoding sequence was applied. The effective flight path in the reflectron configuration corresponds to approximately 2.2 m. Real-time deconvolution and data processing is performed with a program written in Delphi. Mass calibration was achieved by quadratic regression analysis between the flight times and the known molecular weights of caffeine, polypropylene glycol (PPG 450), bradykinin, and reserpine.

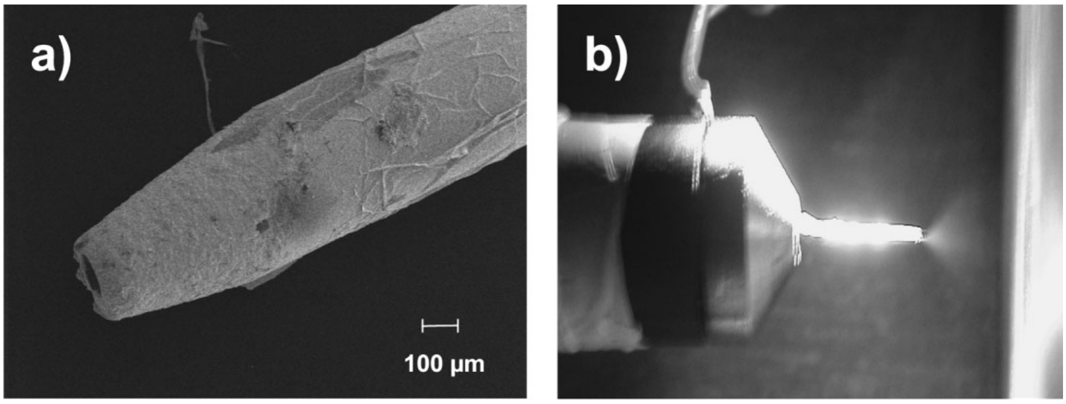

Figure 1. (a) SEM picture of the silver-gold-coated tip of a tapered fused-silica capillary (ID 75 μm, OD 360 μm). (b) Close-up of a silver-gold-coated sheathless electrospray emitter (ID 75 μm, OD 360 μm, flow rate 400 nL/min, spray voltage 2.4 kV). The formation of a symmetrical Taylor cone emerging from the spray tip is visible.

2.7 Capillary electrophoresis-quadrupole mass spectrometry (CE-Q-MS)

The capillary electrophoretic separations that were coupled to a quadrupole mass spectrometer were performed using a home-built CE setup. This setup used a Glassman high-voltage power supply for the separation voltage and a separate power supply for the electrospray voltage. The 35 cm capillary (polyimide-coated fused silica, 360 μm OD, 50 μm ID) leads from the inlet buffer vial to the *x,y,z* micropositioner of the ESI source. The metal-coated tip of the capillary is centered on the inlet orifice of the mass spectrometer, and located at a distance of 5–8 mm from the orifice. Samples were injected by a pressure of 1 psi for 1 s. These samples consisted of a mixture of three peptides (angiotensin II, bradykinin, and methionine-enkephalin) at a concentration of 0.1 mg/mL, in a solution of 5 mM ammonium acetate (pH 4.3) in water. The running buffer for these experiments was 5 mM ammonium acetate (pH 4.3) in water. A separation voltage of 20 kV was applied to the buffer at the inlet buffer vial. When used in conjunction with an electrospray voltage of 2.6 kV, these conditions led to a stable current in the capillary of about 15 μA. Mass spectra for these experiments were recorded on a Finnigan SSQ 7000 single quadrupole mass spectrometer, equipped with an API interface. The heated capillary inlet of the API source was maintained at 200°C for all measurements. Spectra were acquired at the rate of 2 per second over the mass range from 10 to 700 *m/z.*

3 Results and discussion

It is known since 1835 when Justus von Liebig described the analytical identification of aldehydes by reduction of the silver amine complex (Tollen's reagent; silver mirror reaction) that silver forms a stable, metallic, conductive coating on glass surfaces [38]. In contrast to this behavior, the deposition of gold on glass is more difficult and results in less stable films. For electrospray emitters the use of an inert noble metal is advantageous because of its stability against oxidative stress, which is a major cause of rapid destruction of the metal coating. Commonly used techniques for the application of noble metals to fused-silica capillaries involve vacuum deposition or glue. Both techniques have significant drawbacks, such as the destruction of sensitive coating or filling materials used as stationary phases by vacuum or the incompatibility of the glue coating with organic solvents in the mobile phase.

As a consequence, we have developed a wet coating strategy based on a silver primer. We use the silver mirror reaction followed by electrochemical deposition of gold to produce very stable electrospray emitters. Prior to the coating procedure, the fused-silica capillaries were tapered at one end according to the procedure of Barnidge *et al.* [16, 17] and cleaned from grease and small particles. The silver mirror reaction was optimized with regard to the deposition speed on fused silica by adjusting the ratio between the reducing agent (glucose solution) and the basic silver amine complex solution. If the reaction rate is too fast, a very thin and unstable film is formed. In addition, it was found that annealing the silver coating for at least 48 h at room temperature improves the stability of the film. Silver-coated fused-silica electrospray emitters were tested and yielded stable electrospray currents for approximately 80 h. By additional electrochemical deposition of gold from gold(III)-cyanide complex solution the stability of the coating could be markedly increased. The deposition of gold onto the silver layer requires the application of a controlled electrolytic potential to prevent displacement of silver atoms by gold leading to weakening of the silver primer. Weakening is facilitated by the fact that three equivalents of silver atoms are displaced by one equivalent of gold atom and that free cyanide ions lower the potential for the oxidation of silver by oxygen. The weakening can be observed by treating a silver-coated capillary with the gold solution without application of an electrolytic potential. The silver-coating is completely dissolved and only aggregated gold flakes remain, which do not dissolve in 65% nitric acid. The application of an electrolytic potential between -1.5 V and -2.2 V yielded the best results. The electrolytic current allows the control of the thickness of the gold film (0.6804 mg/C). Under the experimental conditions described here approximately 180 μg of gold are deposited on the silver primer, which corresponds to a layer of at least 10 Å for a 5 mm spray tip. After the deposition of a gold layer rinsing the spray tip with 65% nitric acid does not affect the silver-gold coating whereas uncovered silver is immediately removed by this solution. Figure 1a shows the scanning electron microscopy (SEM) picture of the silver-gold-coated tip of a tapered fused-silica capillary. The metal surface is relatively smooth and increases the surface tension of the eluent which improves the formation of a stable Taylor cone (*cf.* Fig. 1b) for the electrospray. With the gold solution and procedure described here it is also possible to refresh the gold coating of used spray tips.

To evaluate the long-term stability of the shaped fused-silica electrospray emitters with silver-gold coating, several capillaries (length 1 m, ID 50 μm, OD 360 μm) were prepared according to the procedures described above and placed into a bench-top electrospray device described in the experimental section. A spray voltage of +2.5 kV was applied to the coated capillary tip and a solution of 100 mM tetrabutylammonium acetate dissolved in 65 mL deionized water, 5 mL acetic acid, and 30 mL methanol was infused at a rate of 400 nL/min. The spray current was recorded in 0.5 s to 30 s intervals with a picoamperometer at the heated counterelectrode. Heating was necessary to avoid formation of droplets on the counterelectrode causing change of the electrical field strength. From time to time the spray tip was rinsed with some droplets of buffer to remove dust particles attracted by the high potential. Addition of methylene blue to the buffer solution revealed the formation of a perfect circle (d = 4.5 mm) of the sprayed aerosol on the counterelectrode centered to the axis of the electrospray emitter. In Fig. 1b the Taylor cone emerging from a very short jet is visible. The spray current was stable at 121.6 ± 2.5 nA for at least 600 h. The slope determined by a linear regression of 12 h time intervals is in the range of ±0.09 nA/h. A trend could not be observed. During this time the coating of the spray tip was observed with a microscope and no changes were visible. Figure 2 demonstrates the spray stability over a 12 h period (slope = 0.08 nA/h).

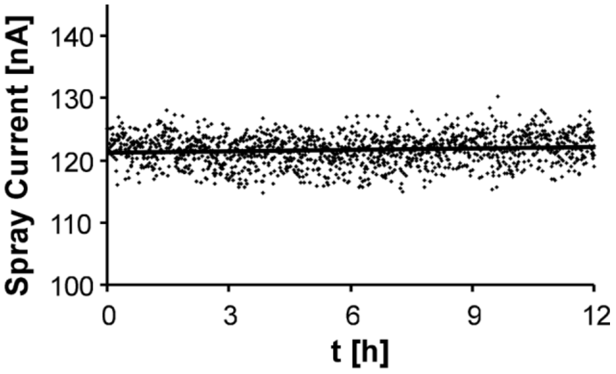

Figure 2. Stability of spray current of a silver-gold-coated sheathless electrospray emitter (ID 50 μm, OD 360 μm, flow rate 400 nL/min, spray voltage 2.5 kV) recorded over 12 h from 336 h to 348 h of continuous operation.

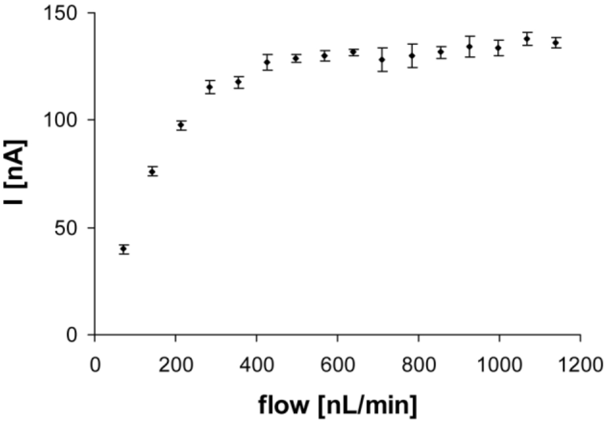

Figure 3. Spray current dependence on the flow rate (ID 50 μm, OD 360 μm, 2.5 kV spray voltage).

Depending on the flow rate of the infused buffer, stable electrospray conditions were obtained by varying the spray voltage between +2.0 kV and +3.6 kV and the distance of the spray needle to the counterelectrode between 4.0 mm to 12.0 mm. Figure 3 shows the dependence of the spray current on the flow rate. Even at very low flow rates less than 100 nL/min a stable spray current is obtained. With increasing flow rates the spray current converges to the asymptotic limit of approximately 125 nA.

CE in combination with MS is a well-established technique. It is characterized by the production of fast and efficient separations and the identification of the constituents found in complex sample mixtures. To apply this combination to analyze small volumes of sample requires an MS interface with minimized dead volumes and interruption-free electrical contact to provide a continuous separation and electrospray process. To investigate the performance of the on-column sheathless electrospray emitters described here, the CE separation was coupled to a HT-TOF mass spectrometer (HT-TOF-MS). For a single-channel configuration a duty cycle of 50% can be achieved, *i.e.*, 50% of all ions reaching the mass analyzer are detected whereas in conventional TOF-MS up to 95% of all ions are lost. For the separation and coupling with the MS a poly(vinyl alcohol)-coated fused-silica capillary (1 m, ID 50 μm, OD 360 μm) was tapered and coated with silver and gold as described above. A mixture of nine peptides, consisting of angiotensin I human, angiotensin II human, angiotensin II (fragment 3–8), angiotensin III human, bradykinin, gramicidin S, substance P, substance P (fragment 1–4), and substance P (fragment 7–11), was pressure-injected (2 s at 0.5 psi, corresponding to 1.3 nL) and a potential of +28 kV was applied to the buffer vial (1:1 mixture of 50 mM formic acid/ammonium acetate buffer, pH 2.8, and methanol). The concentration of each peptide was 22.2 μM, which corresponds to 28 fmol in the injected sample volume. The effective potential across the separation capillary was 24.4 kV because the spray tip was held at +3.6 kV. For the data acquisition with the HT-TOF-MS a 10-bit binary pseudo-random sequence with 200 ns time bins (5 MHz) and summation of 10 000 passes was selected.

The three-dimensional plot in Fig. 4 represents the result of the pressure-supported CE-HT-TOF-MS experiment. Depending on the duration of the sample injection and the applied pressure during the separation, an efficiency of between 100 000 and 220 000 theoretical plates N ($N = 5.545 \cdot (t_R / w_h)^2$; with the migration time t_R and the peak width at half height w_h) was achieved (calculated for gramicidin; t_R = 4.75 min, w_h between 1.4 and 2.1 s). All nine peptides could be separated and identified by their mass

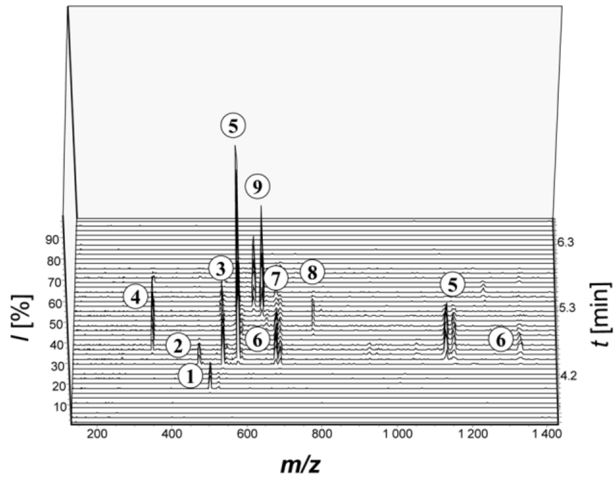

Figure 4. Pressure-assisted CE separation of a mixture of nine peptides and detection by sheathless ESI-HT-TOF-MS (1 m poly(vinyl alcohol)-coated fused-silica capillary, ID 50 μm, OD 360 μm; 1:1 mixture of 50 mM formic acid/ammonium acetate buffer, pH 2.8, and methanol; +28 kV separation voltage; +3.6 kV spray voltage; 0.4 psi back pressure at inlet vial). (1) Substance P (fragment 1–4; RPKP), (2) angiotensin III human (RVYIHPF), (3) bradykinin (RPPGFSPFR), (4) angiotensin II human (DRVYIHPF), (5) gramicidin S (cyclo-(VOLFP)$_2$), (6) substance P (RPKPQQFFGLM-NH$_2$), (7) angiotensin I human (DRVYIHPFHL), (8) angiotensin II (fragment 3–8; VYIHPF), (9) substance P (fragment 7–11; FFGLM-NH$_2$).

spectra and comparison with neat peptides. It is important to note that direct infusion of the mixture of the nine peptides leads to decreased peak intensities and signal-to-noise ratios and the mass spectrum is dominated by gramicidin S, which can be attributed to competitive ionization.

In Fig. 5 selected mass spectra of substance P (fragment 1–4; RPKP), gramicidin S (cyclo-(VOLFP)$_2$), and substance P (fragment 7–11; FFGLM-NH$_2$) from the CE-HT-TOF-MS experiment are depicted. For substance P (fragment 1–4) and substance P (fragment 7–11) the sodium adducts are present. It is evident from these mass spectra that a very good signal-to-noise ratio ($SNR_{max} \approx 48$) and sensitivity even for low sample quantities (28 fmol) is achieved with the silver-gold-coated on-column sheathless electrospray emitters.

The coupling of these sheathless electrospray emitters to a commercial quadrupole mass spectrometer demonstrates the widespread potential application of such devices. When coupled to the quadrupole-MS (Q-MS) to perform a CE separation, the electrospray emitters demonstrated a high signal-to-noise ratio (SNR) in both the electropherogram (*cf.* Fig. 6) and the individual spectra taken during each peak (*cf.* Fig. 7). Most importantly, these emitters were able to maintain the stable electrical connection necessary for electroosmotic flow (EOF), over the course of a large number of separations. No break in current inside the column was observed.

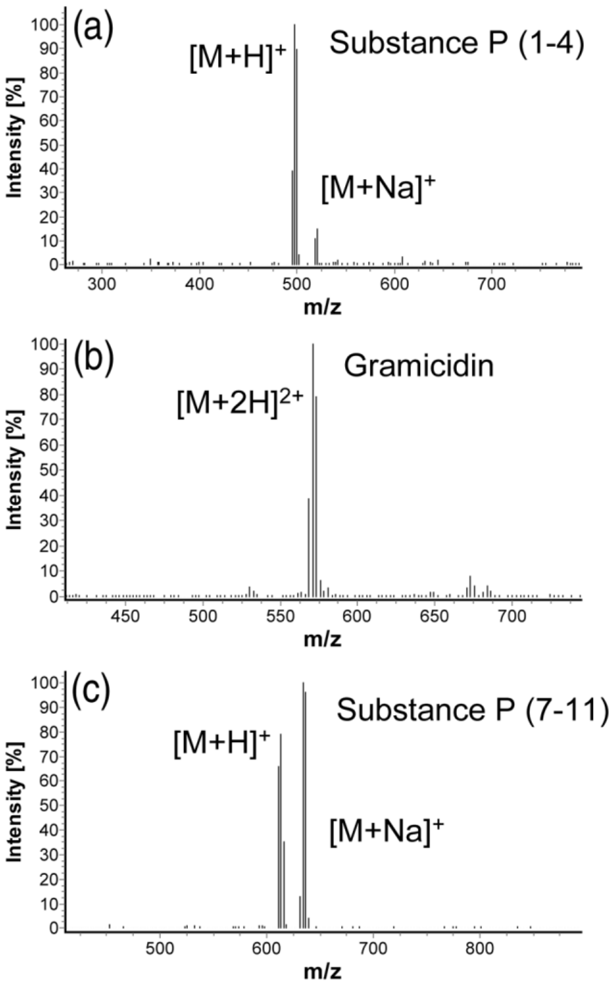

Figure 5. Selected HT-TOF mass spectra of the mixture of nine peptides separated by CE (1 m poly(vinyl alcohol)-coated fused-silica capillary, OD 360 μm, ID 50 μm; 50 mM formic acid/ammonium acetate buffer, pH 3.0, 50% methanol; +28 kV separation voltage; 3.6 kV spray voltage). (a) Substance P (fragment 1–4; RPKP), (b) gramicidin S (cyclo-(VOLFP)$_2$), (c) substance P (fragment 7–11; FFGLM-NH$_2$).

4 Concluding remarks

We successfully demonstrated a straightforward silver-gold coating procedure for tapered fused-silica capillaries, allowing them to be used as stable and robust electrospray emitters. Silver deposited in a electroless wet process according to the silver mirror reaction gives an excellent primer for the electrochemical deposition of

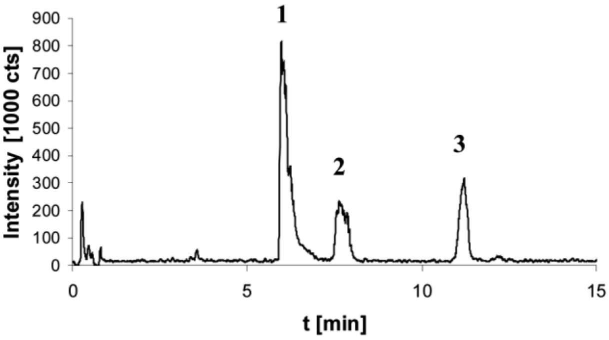

Figure 6. CE separation of a mixture of three peptides and detection by sheathless ESI-Q-MS (35 cm polyimide-coated fused-silica capillary, ID 50 μm, OD 360 μm; 5 mM ammonium acetate, pH 4.3; +20 kV separation voltage, +2.6 kV electrospray voltage). (1) Bradykinin, (2) angiotensin II, (3) methionine-enkephalin.

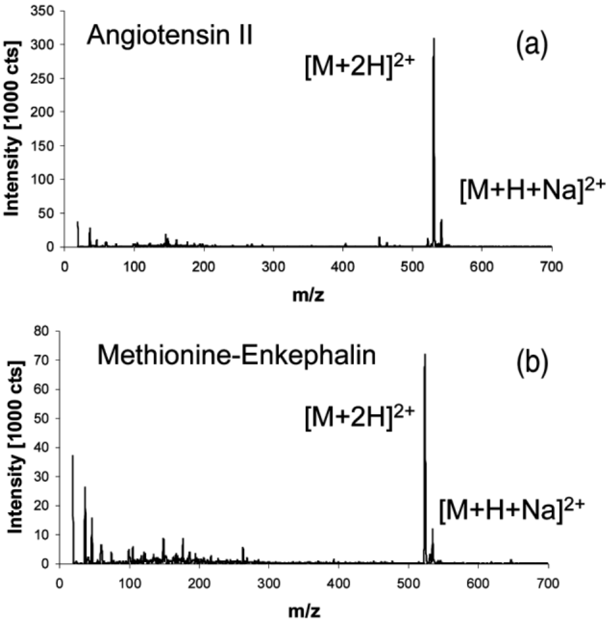

Figure 7. Selected quadrupole mass spectra of the mixture of three peptides separated by CE (35 cm polyimide-coated fused-silica capillary, ID 50 μm, OD 360 μm; 5 mM ammonium acetate, pH 4.3, +20 kV separation voltage, +2.6 kV electrospray voltage). (a) Bradykinin avg. of spectra from retention time interval 5.94–6.10 min, (b) angiotensin II avg. of spectra from retention time interval 7.49–7.93 min.

gold. The whole coating process is soft and compatible with delicate capillary column fillings. It does not require harsh conditions like vacuum or heat. As only neat and noble metals are deposited on the surface of the spray tip, contamination of the sample can be excluded. Long-term stability experiments suggest a lifetime of at least 600 h without any mechanical or electrochemical change. In addition, the gold coating can be easily refreshed, if necessary. Characterization experiments at flow rates less than 100 nL/min show that the electrospray emitters can be employed in low-flow separation techniques, such as CE, CEC, o-CEC, and nano-LC. Coupling of CE with HT-TOF-MS and Q-MS interfaced by these on-column sheathless electrospray emitters provided spectra with high signal-to-noise ratios and sensitivity. The long lifetime of these sheathless electrospray emitters makes them ideal for unsupervised and automated high-throughput CE-MS applications.

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