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Review

Monitoring environmental pollutants by microchip capillary electrophoresis with electrochemical detection

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Abstract

During the past decade, significant progress in the development of miniaturized microfluidic systems has occurred due to the numerous advantages of microchip analysis. This review focuses on recent advances and the key strategies in microchip capillary electrophoresis (CE) with electrochemical detection (ECD) for separating and detecting a variety of environmental pollutants. The subjects covered include the fabrication of microfluidic chips, ECD, typical applications of microchip CE with ECD in environmental analysis, and future prospects. It is expected that microchip CE–ECD will become a powerful tool in the environmental field and will lead to the creation of truly portable devices.

Keywords: Microchip; Capillary electrophoresis; Environmental pollutants; Amperometry; Conductivity; Electrochemistry; Detectors

Contents

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1. Introduction

Microfluidic analytical systems fabricated on silica, glass, and polymer microchips have undergone an explosive growth during the past decade. Capillary electrophoresis (CE) microchips have received much attention because of their high degree of integration, portability, minimal solvent/reagent consumption, high performance, and speed. They hold considerable promise for applications such as environmental monitoring, biomedical and pharmaceutical analysis, clinical diagnostics, and forensic investigations [1–4]. Many microfluidic systems were produced on glass substrates using standard photolithographic techniques [5,6], while some polymer chips were fabricated based on techniques such as in situ polymerization [7], laser ablation [8], imprinting [9], and injection-molding [10]. Microchip CE has been investigated for several years to analyze various pollutants. Microchip CE in its various modes of operation offers advantages from the viewpoint of cost, analysis times, and environmental impact in addition to high resolving power, high separation efficiency, and unique selectivity. Optical, electrochemical, and mass spectrometric detection modes have become routine for microfluidic chips. Electrochemistry (EC) offers great promise for such microsystems, with features that include remarkable sensitivity, inherent miniaturization of both the detector and control instrumentation, independence of sample turbidity or optical path length, low cost, minimal power demands, and high compatibility [11–13]. Many of these separation and detection systems offer effective alternatives to analytical methodologies currently in use for characterizing many environmental pollutants.

This review focuses on recent advances in the application of the microchip CE with electrochemical detection (ECD) for analyzing environmental pollutants. This field of study has grown considerably in the past decade. Reports ranging from basic research to devices intended for onsite use have been published. The following sections will cover the design of the chips, ECD, and recent application of microchip CE–ECD to the analysis of a variety of environmental pollutants.

2. Fabrication of the microfluidic chips

Most CE microchips have been made from glass or quartz using photolithography, wet-etching, and thermal bonding [5,6,14,15]. However, their application was limited because of high cost, harmful and complicated fabrication procedures, and the limitation on the geometric modification of the chip channel. Therefore, polymers are becoming the most promising materials for microsystem technology because they can be produced with mass-replication technologies, such as injection-molding and hot embossing [16,17]. A wide variety of polymer materials have been evaluated for fabricating microchips instead of glass, in which poly(dimethylsiloxane) (PDMS) and poly(methyl methacrylate) (PMMA) are the two most commonly used polymers because they are inexpensive, easy to fabricate, and have excellent optic transparency. PDMS microchips were mainly fabricated by soft lithography [18]. Wu et al. [19] employed a microfabrication technique for the first time to simultaneously integrate a three-electrode electrochemical detector and decoupler with an O_2-plasma-treated PDMS layer containing a CE channel to complete a CE–ECD microchip. The novel setup of this CE–ECD microchip was believed to be more convenient and represented the latest design of a replaceable microelectrode. Wang's group [20,21] used PMMA microchip CE to separate and identify inorganic and organic ions. Since polymer materials are often used to fabricate the microchip, surface pretreatment of the channel wall was usually employed to enhance the CE separation performances [22].

Usually, sampling interfaces, separation channel, and detection systems need to be integrated on a microchip platform to fabricate a microchip CE system. It is a challenge to find a suitable microfabrication technology for constructing a microdevice in the recent microchip CE study. Baldwin et al. [23] integrated both CE high-voltage electrodes and ECD electrodes directly into a glass microchip to construct a microchip CE system. The microfabrication techniques used were photolithographic patterning, wet chemical etching, direct current sputtering, and thermal wafer bonding. Berthold et al. [24] integrated insulated microelectrodes for contactless conductivity detection (CD) inside a microchannel in a glass microchip. Low-temperature glass-to-glass anodic bonding, channel etching, fabrication of buried metal interconnects, and deposition of thin plasma-enhanced chemical vapor deposition silicon carbide layers have been employed in this work [24].

Recently, Chen et al. designed a novel CE microchip with a simple and efficient sample-introduction interface for analyzing nitroaromatic pollutants [25]. This idea came from the designs of the miniaturized CE systems [26]. Both sides of the conventional single-cross glass chip were cut to leave a separation channel. The outlet side near the four-way cross facilitates the end-column ECD. The inlet side was sharpened with a diamond saw. The sample introduction is carried out directly on the separation channel through a sharp inlet tip placed in the sample vial. Alternate placement of the inlet tip in vials containing the sample and buffer solutions permits a volume-defined electrokinetic sample introduction. Such fast and simple sample introduction leads to highly reproducible signals with no observable carry over between different analyte concentrations. The performance of the system was demonstrated in CE measurements of three nitroaromatic pollutants, 1,3,5-trinitrobenzene (TNB), 2,4,6-trinitrotoluene (TNT), and 2,4-dinitrotoluene (2,4-DNT). The fast and reproducible sample introduction was coupled to a well-defined concentration dependence. Employing an 8 cm long separation channel and a separation voltage of 4000 V offers high-throughput flow-injection assays of 100 samples/h with a relative standard deviation of 3.7% for TNT ($n = 100$). Such ability to continuously introduce discrete samples into

micrometer channels indicates great promise for high-speed microchip analysis.

In addition, we have developed a novel dual-injection electrophoretic PMMA microchip [27]. It consists of two crosses on both sides of the chip and one separation channel. Anions and cations can be injected from both crosses to the separation channel and then separated and detected simultaneously. A movable contactless conductivity detector was put along the separation channel between the two crosses for detecting the ions [28]. The feasibility, utility, and advantage of this new system has been demonstrated by injecting, separating, and detecting ammonium, methyl ammonium, sodium, chloride, nitrate, and perchlorate, six anions of environmental concern. The simultaneous detection of anionic and cationic explosives and nerve agent degradation products by the newly designed chip has also been demonstrated.

3. Electrochemical detection

As with other analysis systems for pollutants, sensitive and selective detection techniques are also required for microchip CE. Most reports on microchip CE relied on laser-induced fluorescence (LIF) for detection [12,13]. Mass spectrum (MS) also received much attention to meet the requirements of proteomic analysis. However, both LIF and MS need sophisticated and expensive instrumentation. LIF typically requires pre- or postcapillary derivatization of the sample with a fluorophore and are limited to fluorescent analytes and analyte derivatives [29]. Commercially available MS systems are not inherently portable and are more costly and less sensitive than LIF. Recently, ECD has attracted considerable interest for an electrophoretic microchip system [12,13,29]. It offers great promise for microchip CE systems, with features that include high sensitivity, inherent miniaturization of both the detection and control instrumentation, low cost and power demands, and high compatibility with microfabrication technology [12,13]. In principle, ECD can be classified into three general modes, conductimetry, potentiometry, and amperometry. However, only conductimetry and amperometry have been commonly used for the detection of microchip CE. Both detection modes have also been applied for monitoring environmental pollutants.

3.1. Amperometric detection

Amperometry is the most widely reported EC detection method for chip-based separations [29–35]. It is accomplished by applying a constant potential to the working electrode and measuring the resulting current that is proportional to the concentration of analytes oxidized or reduced at the electrode surface.

Mathies and co-workers reported a CE chip with an integrated amperometric detector for the first time [30]. A band platinum detection electrode was fabricated just outside the exit of separation channel using a photolithographlic process. In this flow-by design, the surface of the band platinum electrode was parallel to the flow direction. Wang's group described a planar screen-printed carbon line electrode for the microchip CE system. The detection electrode was mounted perpendicular to the flow direction, ca. 50 μm away from the capillary outlet. A flow-onto thick-film amperometric detector has been non-permanently mounted perpendicular to the channel outlet, allowing easy and fast replacement [36]. The amperometric detection system was successfully employed to detect nitroaromatic explosives, phenols, nerve agents, etc. [12]. The major limitation that has held back the routine application of amperometric detection for CE is the precise alignment between the separation channel and the working electrode [37]. Another attractive route is to place the detector directly around the exit of the channel, based on electroless deposition and sputtering techniques. The microfluid can flow through the ring detection electrode. Hilmi and Luong [38] described the use of electroless deposition for preparing on-chip gold electrodes. The electroless protocol allows deposition of the gold film directly onto the capillary outlet. This simple low-cost electroless preparation route obviates the need for photolithographic electrode fabrication or careful channel/electrode alignment. The detector performance had been characterized using a mixture of nitroarometric explosive compounds.

3.2. Conductivity detection

For the analysis of small inorganic and organic ions, CD is particularly promising, with potential applications in environmental analysis. Conductimetry measures the conductance of a solution in the microchannels, and the response is proportional to the concentration of the analyte ions [29]. CD can be classified into contact and contactless modes. Contact CD was carried out by galvanic contact between the measurement electrodes and the solution while contactless CD was carried out through the use of external electrodes that are coupled capacitatively to the electrolyte. Comparatively, contact CD is more sensitive. However, the galvanic contact with the solution is a potential source of problems for microchip CE. The bubble generation caused by electrolysis and electrode fouling may disturb the CE analyses [39]. Furthermore, special protection of the detector circuit and electronics was required to prevent damage from the high electric field. Contactless CD for microchip CE avoids the problems associated with direct solution contact by insulating the measurement electrodes electrically from the electrolyte.

Recently, contact CD was used for several microchip-based analyses, such as CE separation of several inorganic ions [40] and various bimoleculars [41]. Because of its special attributes, contactless CD has attracted much attention. Laugere et al. [42] developed a chip-based system with thin-layer platinum electrodes directly fabricated in the channel with the electrode electronically insulated with silicon carbide. Wang et al. [43] reported a miniaturized analytical system for separating and detecting inorganic explosive residues,

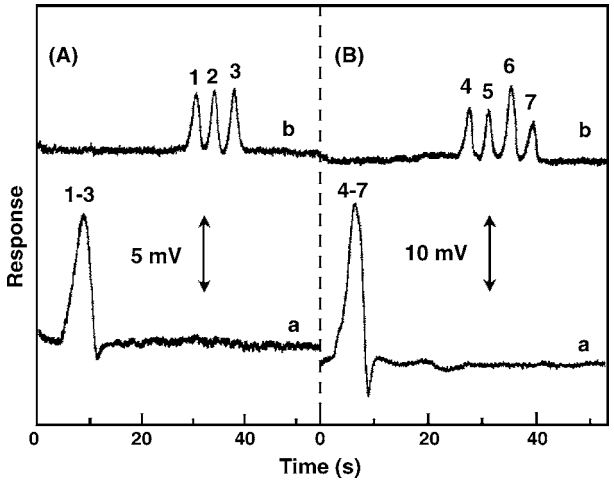

Fig. 1. Electropherograms showing the separation of (A) explosive related anions and (B) cations, using the mobile conductivity detector located at the beginning (a, 0.8 cm to the injection cross) and the end (b, 4.8 cm to the injection cross) of the separation channel. (A) Mixture containing 1 mM chloride ions (1), nitrate ions (2), and perchlorate ions (3); (B) Mixture containing 0.7 mM ammonium (4), methylammonium (5), potassium (6), and sodium (7). Conditions: separation voltage, −1500 V; injection voltage, −500 V; running buffer, MES/His (20 mM, pH 6.1) (A); separation voltage, 1000 V; injection voltage, 500 V; running buffer, MES/His (20 mM, pH 6.1) sinus waveform with frequency of 200 kHz; and a peak-to-peak voltage of 5 V (B) (reprinted with permission [28]).

based on the coupling of a micromachined CE chip with a contactless conductivity detector for the rapid measurement of seven explosive-related cations and anions. The detector performance was also illustrated by separating potassium, sodium, barium, and lithium cations and chloride, sulfate, fluoride, acetate, and phosphate anions [21]. The response was linear (over the 20 μM–7 mM range) with detection limits of 2.8 μM and 6.4 μM for potassium and chloride, respectively.

Wang et al. have developed a new movable contactless-CD system for microchip CE [28]. Such a versatile system relies on positioning the detector at different points along the separation channel by sliding the electrode holder. The movable microchip detection system offers distinct improvements compared to common fixed-location conductivity detectors. For example, placing the detector at different locations along the microchannel offers useful insights into the separation process. As shown in Fig. 1, the system enables rapid switching between "total" (unresolved) and "individual" (resolved/fingerprint) signals on the basis of placing the detector at the beginning and end of the separation channel, respectively. These and other improvements in the analytical performance and insights into the separation process are illustrated in connection with the detection of low-energy ionic explosives and nerve agent degradation products.

4. Applications

Some recent developments in the major applications of microchip CE–ECD for analyzing environmental pollutants (including phenols, aromatic amines, hydrazines, nerve agents, nitroaromatic compounds, nerve agents and chemical warfare agents, residues, and inorganic and organic ions) are reviewed in the following sections. Because some environmental pollutants are not electroactive or the over-potentials of the redox for these species are very high, derivatization are needed [44].

4.1. Phenols

Phenol is an important class of toxic pollutant. Wang et al. [45] have developed a microchip CE system with an amperometric detector for separating and detecting toxic phenolic compounds. The integrated microsystem offers a rapid simultaneous measurement of seven priority chlorophenolic pollutants: phenol, 2-chlorophenol, 2,4-dichlorophenol, 2,3-dichlorophenol, 2,4,5-trichlorophenol, 2,4,6-trichlorophenol, and 2,6-dichlorophenol within 4 min (Fig. 2). Using a gold-coated screen-printed carbon electrode, these compounds could be detected down to the 1 μM level with linearity up to the 200 μM level examined. The applicability of this method was demonstrated by detecting phenols in river water samples. Recently, a diamond electrode and a carbon nanotube-modified carbon electrode have been employed to detect phenols after separation by microchip CE with satisfactory results [3,46].

4.2. Aromatic amines

It has been demonstrated that aromatic amines are tumor-inducing agents. They mainly come from dye plants. Shin et al. [47] developed a method based on microchip CE with a boron-doped diamond electrochemical detector to analyze aromatic amines. The diamond electrode was used as an end-column amperometric detector to detect the dye-related amino-substituted aromatic compounds, 4-

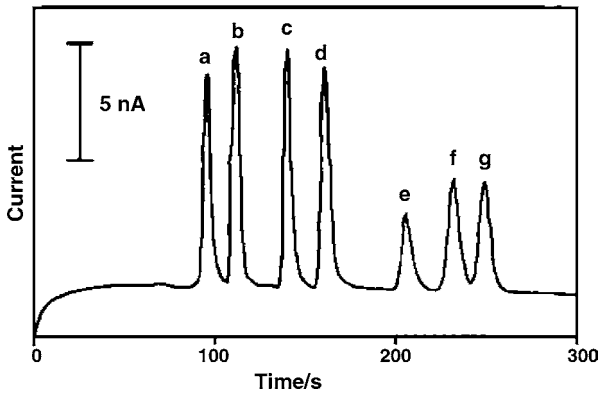

Fig. 2. Separation and detection of phenol and six chlorophenols: (a) 100 μM phenol; (b) 100 μM 2-chlorophenol; (c) 200 μM 2,4-dichlorophenol; (d) 200 μM 2,3-dichlorophenol; (e) 200 μM 2,4,5-trichlorophenol; (f) 200 μM 2,4,6-trichlorophenol; (g) 200 μM 2,6-dichlorophenol. Separation buffer, 10 mM borate and 10 mM phosphate (pH 8.0); separation and injection voltage, +1500 V; injection time, 2 s; detection potential, +1.0 V (vs. Ag/AgCl wire) (reprinted with permission [45]).

aminophenol, 1,2-phenylenediamine, 2-aminonaphthalene, 2-chloroaniline, and *o*-aminobenzoic acid. The diamond-based ECD system displayed a favorable analytical performance, including lower noise levels, higher peak resolution with enhanced sensitivity, and improved resistance against electrode passivation. The diamond detector displayed detection limits of 2.0 μM and 1.3 μM for 4-AP and 2-AN, respectively, and a wide linear response for these compounds over the 2–50 μM range.

Recently, Wang and Chen [48] developed a method based on microchip CE with amperometric detection for the rapid separation and direct detection of oxidizable aromatic amino acids. The working electrode was a thick-film carbon strip electrode positioned opposite the outlet of the separation channel. The five aromatic amino acids: tyrosine, 5-hydroxytryptophan, tryptophan, *p*-aminobenzoic acid, and *m*-aminobenzoic acid, can be well separated within 5 min using a separation voltage of 2000 V and a 25 mM phosphate buffer (pH 7.0) containing 50 mM sodium dodecylsulfate as a running buffer. Linear calibration plots were observed for micromolar concentrations of the oxidizable amino acids. The new protocol offers good stability and reproducibility for both migration times and peak currents.

4.3. Hydrazines

Only few studies have addressed the use of microchip CE and related techniques for determination of hydrazines of environmental concern. Wang et al. [49] introduced a method based on microchip CE for rapid separation of four hydrazines: hydrazine, methylhydrazine, dimethylhydrazine, and phenylhydrazine within 2 min at a separation voltage of +1000 V. The detection electrode employed was a palladium-modified screen-printed carbon electrode at a potential of +0.5 V (versus Ag/AgCl). The running buffer used was 10 mM phosphate buffer at pH of 7.3. Such compounds could be detected down to 1.5 μM with linearity over the 20–200 μM range examined. Recently, a carbon nanotube modified electrode was coupled to a microchip CE system as an amperometric detector to detect hydrazines, offering much higher sensitivity than the bare carbon electrode [46].

4.4. Nitroaromatic compounds

As neutral compounds, nitroaromatic compounds were usually separated by micellar electrokinetic capillary chromatography (MECC) and detected in reduction mode for amperometric detection. Hilmi and Luong developed micromachined electrophoresis chips with electrochemical detectors to analyze explosive compounds in soil and groundwater [50]. As part of the ECD system, the working gold electrode was inserted into a specially designed detection cell with its sensing area positioned just outside the separation channel outlet. The separation buffer was 15 mM borate (pH 8.7) containing 25 mM sodium dodecylsulfate (SDS). TNT and four other nitroaromatic explosives were well separated with detection limits of 100–200 μg/L. In addition, they have developed a microchip CE system with an integrated electrochemical detector that was fabricated based on electroless gold deposition onto the capillary outlet [38]. The system was employed to separate and detect TNT, 2,4-dinitrotoluene, 2,6-dinitrotoluene (2,6-DNT), and 2,3-dinitrotoluene (2,3-DNT). The detection limit of the four explosives was estimated to be 24 μg/L for TNT, 33 μg/L for 2,4-DNT, 35 μg/L for 2,3-DNT, and 36 μg/L for 2,6-DNT. Wang et al. also did a significant amount of work for separating and detecting nitroaromatic explosives [51,52]. They [51] developed a single-channel chip-based analytical microsystem that allows rapid flow injection measurements of the total content of organic explosive as well as detailed micellar chromatographic identification of the individual ones. The protocol involves repetitive rapid flow injection assays and MECC separation. Switching between the "flow injection" and "separation" modes is accomplished by rapidly exchanging the SDS-free and SDS-containing buffers in the separation channel. Recently, a diamond electrode was employed as an ampermetric detector for the microchip CE system to detect nitroarometric explosives [3]. The favorable signal-to-background characteristics of the diamond-based CE detector are coupled with a greatly improved resistance to surface fouling and greater isolation from high separation voltages. A highly linear response is obtained for the explosives 1,3-dinitrobenzene (1,3-DNB) and 2,4-DNT over the 200–1400 ppb range with detection limits of 70 ppb and 110 ppb, respectively.

4.5. Nerve agents and chemical warfare agent residues

Wang et al. [53] have developed a miniaturized analytical system for separating and detecting toxic organophosphate nerve agent compounds, based on the coupling of a micromachined CE chip with a thick-film amperometric detector. Using a 72 mm long separation channel and a separation voltage of +2000 V, baseline resolution was observed for four nerve agents, paraoxon, methyl parathion, fenitrothion, and ethyl parathion in 140 s. Applicability to spiked river water samples is demonstrated, and the implications for onsite environmental monitoring and rapid security screening/warning are discussed. They [54] also reported a microfluidic device for the screening of organophosphonate nerve agent degradation products. The miniaturized system relies on an efficient chip-based separation of alkyl methylphosphonic acids (degradation products of Sarin, Soman, and VX nerve agents) followed by their sensitive contactless CD. Applicability to river water samples has been demonstrated.

Wang et al. [55] have reported an on-chip enzymatic assay for screening organophosphate (OP) nerve agents, based on a pre-column reaction of organophosphorus hydrolase (OPH), electrophoretic separation of the phosphonic acid products, and their contactless CD. The complete bioassay requires 1 min of the OPH reaction, along with 1–2 min for separating

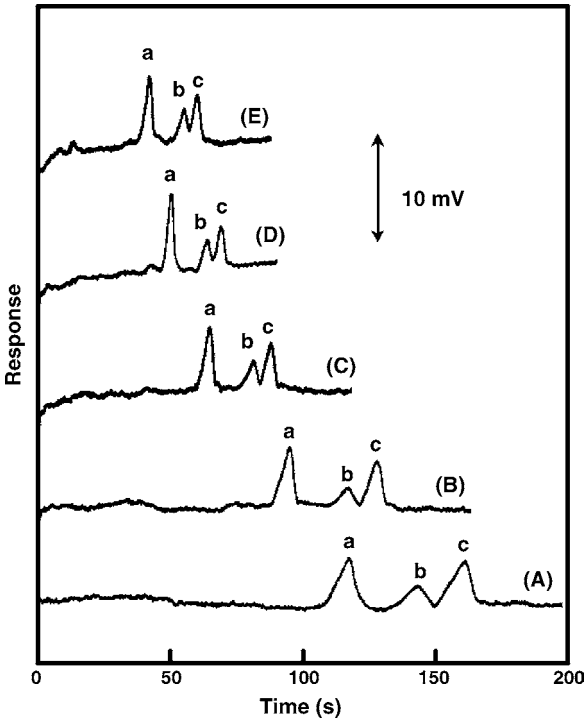

Fig. 3. Effect of the separation voltage upon the enzymatic assay of selected nerve agents, 50 ppm each of (a) methyl parathion, (b) parathion, and (c) paraoxon. Separation voltages: (A) −700 V, (B) −1000 V, (C) −1500 V, (D) −2000 V, and (E) −2500 V (reprinted with permission [55]).

and detecting the reaction products. The response is linear, with detection limits of 5 mg/L and 3 mg/L for paraoxon and methyl parathion, respectively. The attractive behavior of the new OPH-based biochip indicates great promise for field screening of OP pesticides and nerve agents. Fig. 3 shows the effect of the separation voltage upon the assay of selected nerve agents.

In addtion, Wang et al. have developed a microchip protocol for the CE separation and ECD of thiol-containing degradation products of V-type nerve agents [56]. The microchip assay relies on both off-chip and on-chip precolumn derivatization reactions of 2-(dimethylamino) ethanethiol (DMAET), 2-(diethylamino) ethanethiol (DEAET), and 2-mercaptoethanol (ME) with *o*-phthaldialdehyde in the presence of valine along with amperometric monitoring of the isoindole derivatives. The microchip CE system offers a rapid simultaneous detection of micromolar concentrations of DMAET, DEAET, and ME within 4 min with the detection limits of 5 μmol/L and 8 μmol/L for DMAET and DEAET, respectively. The feasibility for assays of environmental matrixes was demonstrated for the determination of DMAET and DEAET in untreated tap and river water samples.

4.6. Inorganic and small organic ions

Ions are usually detected by CD after separation by microchip CE. Deng and Collins [57] reported an application example of microchip CE to separate and detect six toxic metal ions (Cd^{2+}, Pb^{2+}, Cu^{2+}, Co^{2+}, Ni^{2+}, and Hg^{2+}) of environmental concern. Colorimetric metal complexation agent was added for transverse absorbance detection. By combining metal chelation with SPE on a C18 silica gel microcolumn, the detection limits have been improved several hundred fold for the CE microchip measurements of toxic metal ions in water, ranging from 0.4 mg/L to 1.2 mg/L. Collins and Lu [58] developed a CE microchip with a red LED light source and a DAD detector for the sensitive and selective detection of uranium(VI). The Arsenazo III was introduced to the microchip to selectively react with lanthanide metal ions. Carbowax 20,000 was incorporated into the BGE to eliminate the EOF and prevent dye adsorption on the microchannel walls. The separation of uranium from four lanthanide metal ions was achieved within 2 min. A direct load was also investigated to inject a precomplexed metal ion mixture onto the microchannel with a detection limit of 23 mg/L for uranium(VI) in the presence of seven lanthanide impurities (1.5 mg/L each). In addition, the analysis of inorganic arsenic species [59] and selenium species [60] using isotachaphoresis (ITP) chips with integrated conductivity electrodes have been reported. The first study [59] reported the rapid analysis of inorganic arsenic species within 600 s. Detection limits of 1.8 mg/L and 4.8 mg/L have been achieved for arsenic(V) and arsenic(III), respectively. The simultaneous separation of arsenic(III), arsenic(V), antimony(III), molybdenum(VI), and tellurium(IV) with the miniaturized device was also demonstrated. In the second study [60], Se(IV) and Se(VI) were separated within 210 s with detection limits of 0.52 mg/L and 0.65 mg/L, respectively.

5. Conclusions and outlook

Microchip CE is characterized by a high degree of integration, portability, minimal solvent/reagent consumption, high performance, and speed. The coupled ECD offers such microsystems remarkably sensitive detection, inherent miniaturization of both the detector and control instrumentation, and high compatibility. Microchip CE has been employed to separate and detect a variety of pollutants. Only a few reports have used it for real sample analyses. A major obstacle to the realization of real-life applications of such microdevices is that only electroactive or ionic pollutants can be detected directly. Other pollutants need derivatization before detection. The ongoing maturation of microchip CE and further developments in ECD and preconcentration methods will provide separation, quantitation, and characterization of complex mixtures of various pollutants, such as those described in this review. Undoubtedly, microchip CE will become a more firmly established methodology for the analysis of pollutants, as further investigations will be devoted to evaluate the role of microchip CE in environmental studies effectively.

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References

[1] D.R. Reyes, D. Iossifidis, P.A. Auroux, A. Manz, Anal. Chem. 74 (2002) 2623.
[2] P.A. Auroux, D. Iossifidis, D.R. Reyes, A. Manz, Anal. Chem. 74 (2002) 2637.
[3] J. Wang, G. Chen, M.P. Chatrathi, A. Fujishima, D.A. Tryk, D. Shin, Anal. Chem. 75 (2003) 935.
[4] M. Pumera, Talanta 66 (2005) 1048.
[5] J.D. Harrison, A. Manz, Z.H. Fan, H. Ludi, H.M. Widmer, Anal. Chem. 64 (1992) 1926.
[6] S.C. Jacobson, R. Hergenroder, L.B. Koutny, J.M. Ramsey, Anal. Chem. 66 (1994) 1114.
[7] Z.F. Chen, Y.H. Gao, R.G. Su, C.W. Li, J.M. Lin, Electrophoresis 24 (2003) 3246.
[8] M.A. Roberts, J.S. Rossier, P. Bercier, H. Girault, Anal. Chem. 69 (1997) 2035.
[9] L. Martynova, L.E. Locascio, M. Gaitan, G.W. Kramer, R.G. Christensen, W.A. MacCrehan, Anal. Chem. 69 (1997) 4783.
[10] R.M. McCormick, R.J. Nelson, M.G. AlonsoAmigo, J. Benvegnu, H.H. Hooper, Anal. Chem. 69 (1997) 2626.
[11] W.R. Vandaveer, S.A. Pasas, R.S. Martin, S.M. Lunte, Electrophoresis 23 (2002) 3667.
[12] J. Wang, Talanta 56 (2002) 223.
[13] N.A. Lacher, K.E. Garrison, R.S. Martin, S.M. Lunte, Electrophoresis 22 (2001) 2526.
[14] R.G. Su, J.M. Lin, K. Uchiyama, M. Yamada, Talanta 64 (2004) 1024.
[15] C.T. Culbertson, S.C. Jacobson, J.M. Ramsey, Talanta 56 (2002) 365.
[16] E. Verpoorte, Electrophoresis 23 (2002) 677.
[17] H. Becker, L.E. Locascio, Talanta 56 (2002) 267.
[18] J.C. McDonald, J.R. Anderson, D.T. Chiu, H. Wu, O.J.A. Schueller, G.M. Whitesides, Electrophoresis 21 (2000) 27.
[19] C. Wu, R. Wu, J. Huang, Y. Lin, H. Chang, Anal. Chem. 75 (2003) 947.
[20] J. Wang, M. Pumera, G.E. Collins, A. Mulchandani, Anal. Chem. 74 (2002) 6121.
[21] M. Pumera, J. Wang, F. Opekar, I. Jelinek, J. Feldman, H. Lowe, S. Hardt, Anal. Chem. 74 (2002) 1968.
[22] V. Dolník, Electrophoresis 25 (2004) 3589.
[23] R.P. Baldwin, T.J. Roussel Jr., M.M. Crain, V. Bathlagunda, D.J. Jackson, J. Gullapalli, J.A. Conklin, R. Pai, J.F. Naber, K.M. Walsh, R.S. Keynton, Anal. Chem. 74 (2002) 3690.
[24] A. Berthold, F. Laugere, H. Schellevis, C.R. de Boer, M. Laros, R.M. Guijt, P.M. Sarro, M.J. Vellekoop, Electrophoresis 23 (2002) 3511.
[25] G. Chen, J. Wang, Analyst 129 (2004) 507.
[26] G. Chen, L.Y. Zhang, J. Wang, Talanta 64 (2004) 1018.
[27] J. Wang, G. Chen, A.J. Muck, G.E. Collins, Electrophoresis 24 (2003) 3728.
[28] J. Wang, G. Chen, A.J. Muck, Anal. Chem. 75 (2003) 4475.
[29] W.R. Vandaveer, S.A. Pasas-Farmer, D.J. Fischer, C.N. Frankenfeld, S.M. Lunte, Electrophoresis 25 (2004) 3528.
[30] A.T. Woolley, K. Lao, A.N. Glazer, R.A. Mathies, Anal. Chem. 70 (1998) 684.
[31] R.S. Martin, K.L. Ratzlaff, B.H. Huynh, S.M. Lunte, Anal. Chem. 74 (2002) 1136.
[32] J. Wang, M. Pumera, M.P. Chatrathi, A. Escarpa, R. Konrad, A. Griebel, W. Dorner, H. Lowe, Electrophoresis 23 (2002) 596.
[33] H.L. Lee, S.C. Chen, Talanta 64 (2004) 210.
[34] H.L. Lee, S.C. Chen, Talanta 64 (2004) 750.
[35] Y.Y. Wu, J.M. Lin, R.G. Su, F. Qu, Z.W. Cai, Talanta 64 (2004) 338.
[36] J. Wang, B. Tian, E. Sahlin, Anal. Chem. 71 (1999) 5436.
[37] W.Z. Lu, R.M. Cassidy, A.S. Baranski, J. Chromatogr. 640 (1993) 433.
[38] A. Hilmi, J.H.T. Luong, Anal. Chem. 72 (2000) 4677.
[39] J. Lichtenberg, N.F. de Rooij, E. Verpoorte, Electrophoresis 23 (2002) 3769.
[40] D. Kaniansky, M. Masar, J. Bielcikova, F. Ivanyi, F. Eisenbeiss, B. Stanislawski, B. Grass, A. Neyer, M. Johnck, Anal. Chem. 72 (2000) 3596.
[41] M. Galloway, W. Stryjewski, A. Henry, S.M. Ford, S. Llopis, R.L. McCarley, S.A. Soper, Anal. Chem. 74 (2002) 2407.
[42] F. Laugere, G.W. Lubking, J. Bastemeijer, M.J. Vellekoop, Sens. Actuators B 83 (2002) 104.
[43] J. Wang, M. Pumera, G. Collins, F. Opekarc, I. Jelínekc, Analyst 127 (2002) 719.
[44] J. Lichtenberg, N.F. de Rooij, E. Verpoorte, Talanta 56 (2002) 233.
[45] J. Wang, M.P. Chatrathi, B. Tian, Anal. Chim. Acta 416 (2000) 9.
[46] J. Wang, G. Chen, M.P. Chatrathi, M. Musfatafa, Anal. Chem. 76 (2004) 298.
[47] D.C. Shin, D.A. Tryk, A. Fujishima, A. Muck, G. Chen, J. Wang, Electrophoresis 25 (2004) 3017.
[48] J. Wang, G. Chen, Talanta 60 (2003) 1239.
[49] J. Wang, M.P. Chatrathi, B.M. Tian, P. Ronen, Electroanal. 12 (2002) 691.
[50] A. Hilmi, J.H.T. Luong, Environ. Sci. Technol. 34 (2000) 3046.
[51] J. Wang, M. Pumera, G.E. Collins, A. Mulchandani, Y. Lin, K. Olsen, Anal. Chem. 74 (2002) 1187.
[52] J. Wang, M. Pumera, Anal. Chem. 74 (2002) 5919.
[53] J. Wang, M.P. Chatrathi, A. Mulchandani, W. Chen, Anal. Chem. 73 (2001) 1804.
[54] J. Wang, M. Pumera, G.E. Collins, A. Mulchandani, Anal. Chem. 74 (2002) 6121.
[55] J. Wang, G. Chen, A.J. Muck, M.P. Chatrathi, A. Mulchandani, W. Chen, Anal. Chim. Acta 505 (2004) 183.
[56] J. Wang, J. Zima, N.S. Lawrence, P.C. Madhu, A. Mulchandani, G.E. Collins, Anal. Chem. 76 (2004) 4721.
[57] G. Deng, E. Collins, J. Chromatogr. A 989 (2003) 311.
[58] G.E. Collins, Q. Lu, Anal. Chim. Acta 436 (2001) 181.
[59] J.E. Prest, S.J. Baldock, P.R. Fielden, N.J. Goddard, B.J. Treves Brown, J. Chromatogr. A 990 (2003) 325.
[60] J.E. Prest, S.J. Baldock, P.R. Fielden, N.J. Goddard, B.J. Treves Brown, Anal. Bioanal. Chem. 376 (2003) 78.