Journal of Chromatography A, 1218 (2011) 6498–6504

Contents lists available at ScienceDirect

Journal of Chromatography A

journal homepage: www.elsevier.com/locate/chroma

Coatings of one monomer molecularly imprinted polymers for open tubular capillary electrochromatography

Ze-Hui Wei, Xi Wu, Bian Zhang, Rui Li, Yan-Ping Huang*, Zhao-Sheng Liu**

Tianjin Key Laboratory on Technologies Enabling Development of Clinical Therapeutics and Diagnostics (Theranostics), School of Pharmacy, Tianjin Medical University, Tianjin 300070, China

ARTICLE INFO

Article history:
Received 19 April 2011
Received in revised form 27 June 2011
Accepted 1 July 2011
Available online 18 July 2011

Keywords:
Capillary electrochromatography
Molecularly imprinted polymer
OMNiMIPs
Chiral separation
Coating

ABSTRACT

One monomer molecularly imprinted polymer coatings were first synthesized in fused silica capillary columns with 2-methacrylamidopropyl methacrylate (MAM) as single functional monomer in addition to a cross-linking monomer. Since MAM may generate no or little EOF, a strategy of precursor of polymerization, which does not interfere with the formation of defined imprints, was used to introduce an ionizable functional monomer to generate a stable electroosmotic flow for electrochromatography (CEC) by post-polymerization hydrolization. The resulting MAM-based open-tubular imprinted capillary was able to separate enantiomers by means of CEC. The resolution of enantiomers separation achieved on *S*-amlodipine-imprinted capillary was up to 16.1. The strong recognition ability (selectivity factor was 3.23) and high column performance (theory plates was 26,053 plates m^{-1}) of template were obtained. The MIP coatings were also prepared using either *S*-naproxen or *S*-ketoprofen as template molecule. The resolutions of enantiomers separation were 2.20 and 4.56, respectively. The results illustrate that the synthesis of MIP using one monomer is not only an experimental-simplified process, but also an approach to producing chiral stationary phase with high efficiency and selectivity.

1. Introduction

Molecular imprinting is by now established as one of the most promising methods to construct artificial receptors that can achieve specific recognition at a molecular level [1,2]. This technique makes use of the interaction between the targeted template molecules and the functional monomers in a prepolymerization mixture, where upon polymerization in the presence of a cross-linker monomer, a recognition property toward the template can be imparted to the product polymer. The advantages that these highly selective polymers, molecularly imprinted polymers (MIPs), possess over biopolymers are low cost, good physical and chemical stability. Recently, MIPs have been found in an ever increasing range of application areas, such as enzyme-like catalysis [3], bio-mimetic sensors [4], solid-phase extraction [5], drug delivery systems [6] and chromatography [7].

Although the methodology of MIP preparation is relatively easy, the optimization of MIP formulation components is complicated by variables such as the type of functional monomers and crosslinker to use, the optimum ratio of functional monomer/cross-linker, and the optimum ratio of functional monomer/template. Even in a relatively simple molecule for MIP preparation, the optimization is complicated since these variables are dependent with each other. Although the combinatorial [8] and chemometric approach [9] can be used for the design and the evaluation of the MIPs, it is a very time-consuming and difficult task to obtain the best results for MIP formulation.

Recently, a strategy of a functional cross-linker was developed to prepare MIPs, which were referred to as *o*ne *mon*omer *m*olecularly *i*mprinted *p*olymers (OMNiMIPs) [10–14]. The structural design of the new monomers was based on a single monomer required to prepare MIPs, which incorporates the template-binding functionality with the necessary cross-linking features for molecular recognition and network formation. This approach eliminates variables such as choice of functional monomer and crosslinker, the ratio of functional monomer/crosslinker, and the ratio of functional monomer/template which normally complicate the MIP design. Furthermore, for the molecular recognition in OMNiMIPs, the incorporation of the functional monomer into the cross-linker backbone reduces not only the conformational flexibility of the binding site, but also the entropic effect associated with binding interactions. As a result, OMNiMIPs have enhanced binding and selectivity properties versus traditionally formulated ethylene glycol dimethacrylate (EDMA)/methacrylic acid (MAA) imprinted polymers [11]. However, low column efficiency, along excessive peak broadening and tailing in the chromatography of the tem-

* Corresponding author.
** Corresponding author. Tel.: +86 22 23536746; fax: +86 22 23536746.
E-mail addresses: huangyp100@163.com (Y.-P. Huang), zhaoshengliu@sohu.com (Z.-S. Liu).

0021-9673/$ – see front matter © 2011 Elsevier B.V. All rights reserved.
doi:10.1016/j.chroma.2011.07.012

plate molecule, were observed with OMNiMIPs as HPLC stationary phases.

Capillary electrochromatography (CEC) is a microcolumn separation method designed to combine the advantage of the high separation efficiency of capillary electrophoresis (CE) and high selectivity offered by HPLC [15]. Rather than using a high pressure pump, the driving force of mobile phase is electroosmotic flow (EOF) with an almost flat profile. Thus, band broadening is significantly reduced and enhanced efficiency can be obtained. Many investigations have shown that CEC-based MIPs have more efficiency than HPLC-based MIPs, i.e., a high resolving capability and short separation times. Another attraction is miniaturized format of CEC since fewer reagents will be consumed. Up to now, three formats can be used for MIP-based CEC, namely particles [16–22], monolithic columns [23–32] and capillary coatings [33–41]. MIP particles, prepared by conventional polymerization method, can be packed into a capillary with a retaining frit, or immobilized by a "trapping" medium to hold the particles in the column. However, avoiding the formation of air bubble from the column frits is rather difficult. To solve the above problems, partial filling technique based on MIP micro- or nanoparticles has been developed but inadequate resolution was often observed. The highest column efficiency can be found with the MIP coated capillary [42] due to the absence of dispersive contributions in this open tubular format. The small dimensions of a capillary, however, demand the development of novel polymer formats that can be applied to such miniaturized system.

The goal of this work is to obtain an OMNiMIPs chiral stationary phase with high column efficiency for CEC. Three chiral template imprinted capillary coating were prepared with a new single crosslinking monomer, 2-methacrylamidopropyl methacrylate (MAM). Since MAM as a functional monomer may generate little or no EOF, a strategy of precursor of polymerization, which does not interfere with the formation of defined imprints, was used to introduce an ionizable functional monomer (Fig. 1A). The characterization of EOF and the ability of enantiomer separation for the new MIP-coated capillary were investigated.

2. Experimental

2.1. Reagents and chemicals

2-Methacrylamidopropyl methacrylate (MAM) was synthesized by a previously published method [12]. 3-(Trimethoxysilyl) propyl methacrylate (γ-MPS) was from Acros (Geel, Belgium). Methacrylic acid (MAA) was obtained from Beijing Donghuan Chemical Reagent (Beijing, China). Ethylene glycol dimethacrylate (EDMA) was from Sigma (St. Louis, MO, USA). 2,2′-Azobis (2-isobutyronitrile) (AIBN) was supplied by Special Chemical Reagent Factory of Nankai University (Tianjin, China). *S*-naproxen (NAP) and *rac*-naproxen were obtained from Zhejiang Xianju Pharmaceutical Co., Ltd. (Zhejiang, China). *S*- and *rac*- amlodipine (AML) were from Hengshuo Sci & Tech Corp. (Hubei, China). *S*- and *rac*-ketoprofen (KET) were from Sigma–Aldrich (St. Louis, MO, USA). Acetonitrile (ACN, HPLC grade) was purchased from Fisher (NJ, USA). Other analytical reagents were from Tianjin Chemical Reagent Co., Ltd. (Tianjin, China). Fused-silica capillaries with 100 μm ID and 375 μm OD were purchased from Xinnuo Optic Fiber Plant (Hebei, China).

2.2. Preparation of MIP capillary columns

A fused-silica capillary was flushed with 1 mol L^{-1} NaOH solution followed by water for at least 30 min each. Then the capillary was filled with a solution of 4 μL of γ-MPS in 1 mL of 6 mmol L^{-1} acetic acid, and the solution was kept in the capillary for 1.5 h. The capillary was then flushed with water and dried with a flow of nitrogen. A pre-polymerization mixtures containing imprinted molecules (0.012 mmol), single crosslinking monomer MAM (0.048 mmol), γ-MPS (2.5 μL) and radical initiator (AIBN) 1.8 mg were dissolved in 0.457 mL toluene or toluene-isooctane (7/3 (v/v)). The pre-polymerization mixture was sonicated for 10 min then introduced to the capillary using a syringe. The capillary was sealed at both ends with a rubber septum and incubated in a water bath for polymerization. After polymerization, to remove any unreacted reagents, the capillary was immediately flushed using a hand-held syringe with acetonitrile and methanol/acetic acid (9:1 (v/v)), respectively. A detection window was created at a distance of 11.5 cm from the outlet end of the MIP-coated capillary by burning out 2–3 mm segment of the polyimide outer coating. A blank capillary column without imprinted molecule was prepared in the same way.

2.3. Capillary electrochromatography

Electrochromatographic experiments were carried out on a K1050 system (Kaiao, Beijing, China) equipped with a UV detector. A Lenovo personal computer with CXTH-3000 software for capillary electrophoresis was used. The total length of the capillary was 41.5 cm and effective length (MIP-based stationary phase) was 30.0 cm. The electrolyte was a mixture of acetonitrile and different ratios of buffer with different pH. All the buffer was made using double distilled water and filtered with 0.2 μm membrane.

The resolution (R_s) was calculated according $R_s = (t_2 - t_1)/0.5(W_2 + W_1)$ and the number of theoretical plates (N) was calculated by the equation $N = 16(t_R/W)^2$, where t_R is the retention time and W is the width at the baseline between tangents drawn to inflection points for the peak.

The degree of enantiomer separation was represented by a normalized separation index $\Delta t_R/t_{R1}$, where Δt_R is the difference in the elution times of the enantiomers at peak maximum and t_{R1} is the retention time of the first eluted enantiomer.

2.4. SEM characterization of the MIP coatings

Scanning electron microscopy (SEM) was used for the characterization of MIP-coated capillaries. The fused-silica capillary samples were cut to 2–3 mm in length, and cemented into aluminum SEM planchets. Samples were sputter-coated with gold before obtaining images. All scanning electron micrographic images were obtained using a Shimadzu SS-550 scanning electron microscope, operated at 15 kV and a filament current of 60 mA.

3. Results and discussion

3.1. Preparation of OMNiMIPs capillary

To form a successful polymer coating, the most important parameter of polymerization is porogen, which produces phase separation of the solid polymer from the liquid porogens. The density and structure of the final polymer coating is highly dependent on the nature of the porogen [36]. Successful systems of porogen to prepare MIP-coated capillary for CEC consist of toluene [33], ACN [34], and a mixture of solvents, e.g., ACN/2-propanol [37], toluene/ACN [38] and a ternary mixture of toluene/isooctane/DMSO [41]. Experiments show that only using one porogen cannot dissolve enough MAM and for binary porogens, a mixture of toluene/isooctane is better than ACN/isooctane on solubility of MAM. As a result, toluene/isooctane are used for the preparation of MAM-based MIP-coated capillary. However, high proportion of isooctane in porogens can result in lower column

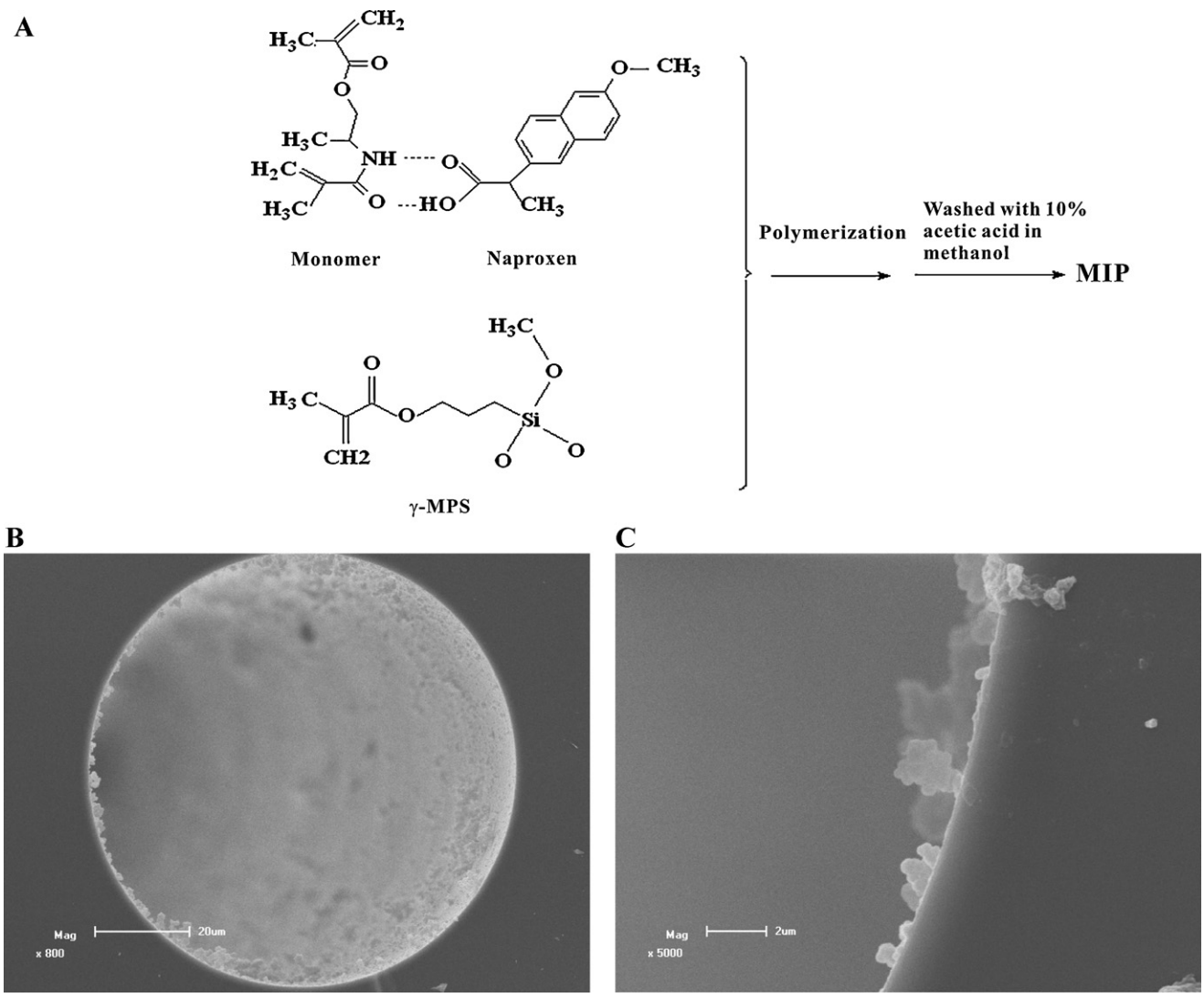

Fig. 1. Schematic representations of the preparation of OMNiMIPs-coated capillary (A); scanning electron micrograph of MIP-coated capillary prepared using *S*-AML as template molecule. The image B was under 800×; the image C was under 5000×.

efficiency due to macroporous structure of resulting coating. In this work, 30% (v/v) of isooctane in porogens is found to be optimum.

In the MIP-coated capillaries reported previously [33,34], MAA is the only ionizable monomer and thus provides the fixed charged sites for the generation of EOF that CEC needs. However, MAM-based MIP might not be expected to afford any EOF since it does not contain any ionized functionalities. 2-Acrylamido-2-methyl-1-propanesulfonic acid (AMPS), which has been widely utilized as ionizable monomer to produce EOF for CEC [42], can act as a hydrogen donor. As a result, it is harmful to introduce AMPS into the pre-polymerization mixture for preparing MIP due to the interfering interaction between AMPS and template. For support of EOF while avoiding the interfering interaction formed between the print species and the functional monomers, γ-MPS, as a polymerization precursor, has been proven to be specifically suitable for this situation [43]. Once incorporated into MIP matrix, the ester bonds (Si–O–C) of γ-MPS are easily and efficiently cleaved hydrolytically with the loss of methanol to sustain EOF by providing silanol groups.

Visualization of the microstructure of the resulting MIP films was accomplished through scanning electron microscopic investigations conducted on several capillary segments. Fig. 1B shows a SEM cross-sectional view of MIP-coated capillaries imprinted. A layer of MIP with a thickness around 1–2 μm covering the inner surface of the capillary is obtained (Fig. 1C).

3.2. EOF characterization of OMNiMIPs-coated capillary

EOF created in the stationary phase is the force that drives the mobile phase through the column. Therefore, control of EOF plays an important role in the design of the CEC column. The deprotonation of the silanol groups, derived from the hydrolysis of the ester bonds, on the surface of MAM-based MIP provides a negative surface charge under CEC running conditions. This negatively charged substrate attracted cations from the electrolyte in the mobile phase forming the electrical double layer and thereby generating a cathode EOF from anode to cathode. The dependence of the magnitude of the apparent EOF on the pH of the mobile phase was examined in the pH range 3.0–6.6 at 80% ACN on *S*-NAP-imprinted MAM-based capillary (Fig. 2). Under the experimental conditions used, a strong cathode EOF was observed as expected.

EOF in the MAM-based OT imprinted capillary was compared with an imprinted capillary that utilizes the most widely used MIP formulation, i.e., the combination of MAA and EDMA. As shown in Ref. [41], there was a considerable difference in EOF in the MAA-based and MAM-based imprinted capillaries. Thus, the EOF seems

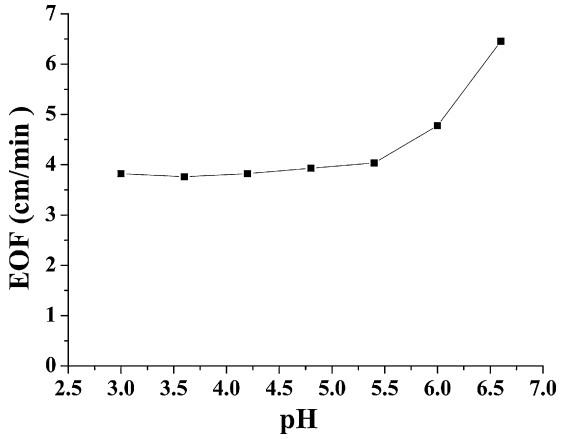

Fig. 2. Effect of the pH value in the eluent on the EOF mobility measured with thiourea as unretained marker on the *S*-NAP-imprinted coated capillary. UV detection was carried out at 254 nm and separation was performed at 10 kV. The electrolyte used was composed of ACN/0.01 mol L^{-1} acetate (pH 3.0–6.6) (80/20 (v/v)).

to be dependent on the nature of EOF promoter of respective OT-MIP capillaries. With the increase of pH in the range of 3.0–7.0, for the MAA-based MIP-coated capillary with *d*-zopiclone imprints, the ionization content of MAA increases, the EOF mobility increases. The trend of increase in EOF with the value of pH is in agreement with a polymer-based imprinted monolith in which MAA was used as an EOF promoter [29]. In contrast, for the MAM-based MIP-coated capillary, the trend shows an increase in EOF with the value of pH, which is accordance with silica-based monolithic columns [15]. It is observed from Fig. 3 that when the value of pH is 6.0, the EOF of the MIP-coated capillary reaches 8.0×10^{-8} m^2 V^{-1} s^{-1}, which is much higher than the result of Huang et al. [34].

3.3. Capillary electrochromatographic enantiomer separation

We examined electrochromatograms of the enantiomer separation of amlodipine using *S*-AML-imprinted coated capillaries. Fig. 3A and B illustrates the separation of *rac*-amlodipine by CEC depicting the characteristic elution order and the selective retention of the template. In the optimum chromatographic conditions, the resolution of two enantiomers is 16.1. Blank coated capillary that has not template molecule in the synthesis did not show any chiral separation (Fig. 3C). It should be noted that the blank column has longer retention time for *rac*-AML. The possible reason is the thicker coating of the blank column due to the shift in polymerization kinetics in absence of template molecule in reaction solution.

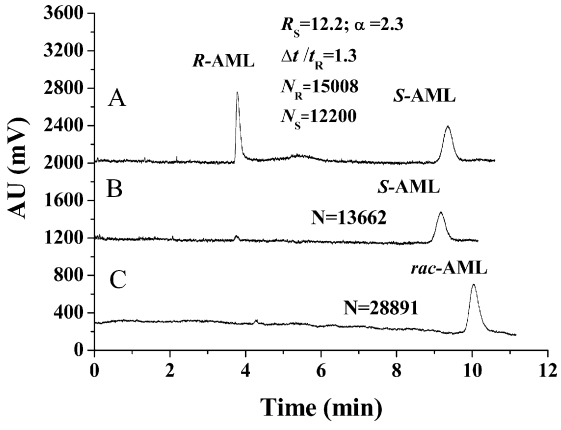

Fig. 3. Electrochromatograms of *rac*-AML (A), *S*-AML (B) on *S*-AML imprinted capillary and *rac*-AML on non-imprinted capillary (C) demonstrating the imprinting effect and identifying the peaks. Conditions: separation voltage: 12 kV; temperature: 25 °C, UV-Vis detector: 238 nm; ACN/10 mmol L^{-1} acetate (pH 4.2) (90/10 (v/v)).

Table 1
Enantiomer separations on *S*-AML-imprinted capillary at various electrolyte pH values.

pH	N_R (plate m^{-1})	N_S (plate m^{-1})	α	$\Delta t_R/t_{R1}$	R_s
3.0	10,217	7791	2.67	1.67	12.6
3.6	13,325	11,563	3.23	2.23	16.1
4.2	15,008	12,200	2.30	1.30	12.2
5.0	25,202	21,258	1.77	0.76	11.3
6.0	26,053	20,126	1.34	0.34	5.88

In order to prove the versatility of one-monomer, we also synthesized two MIP-coated columns using *S*-NAP and *S*-KET as template molecules, respectively. Baseline separation of NAP and KET can be achieved on the respective MAM-based imprinted capillaries (Fig. 4A and B). Similarly, blank coated capillary did not show any chiral separation of *rac*-NAP and *rac*-KET. The enantioselectivities of naproxen and ketoprofen are 1.20 and 1.26, respectively. It seemed that MAM, the functional cross-linker, can lead to improved enantioselectivity over the traditional formulated MIP incorporating MAA as functional monomer [29,37].

To assess the superiority of the new imprinted capillary over those prepared with two monomers, i.e., a system of MAA and EDMA, the CEC results of the corresponding *S*-NAP-imprinted monolithic capillary were evaluated comparatively with regards to efficiencies, enantioselectivities and resolution of enantiomers [29]. Indeed, the comparison of the calculated enantioselectivity value of NAP clearly indicated that MAM-based MIP is a better chiral selector. For example, enantioselectivity value of NAP from MAA-EDMA system [29] was increased from 1.05 to 1.20 (MAM-based MIP) (Fig. 4A).

3.4. Effect of pH value on chiral separation

The pH value of buffers on chiral separation is also an important aspect, since it alters the charges of the analytes and the polymers, thus affects the molecular recognition of the MIPs, electrophoretic mobility, as well as EOF. In this study, using *S*-AML-imprinted capillary, the enantiomer separation of amlodipine at different pH value in the mobile phase (from 3.0 to 6.0) was examined. The results are shown in Fig. 5 and Table 1. It is well-known that the selectivity of MIP is maximal at a pH near the pK_a value of the imprinted molecule [29,37]. In the present study, the optimized eluent pH for amlodipine was 3.6. As the pH value of the mobile phase increases, the selectivity of enantiomer, the index of chiral separation, as well as resolution, decreased gradually. The probably reason is the increased nonselective sites with increasing mobile phase pH [44].

3.5. Effect of acetonitrile contention on enantiomer separation

The effect of the content of ACN in the mobile phase on the selectivity of imprinted molecule was investigated in the range of 80–95% (v/v). When the ACN concentration was less than 75%, EOF was small and band-broadening was increased. In spite of increased column efficiency, a trend of decreased separation factors and resolution for AML enantiomers was observed when the amount of ACN was increased (Fig. 6). This result was in agreement with previous reports on MIP-coated capillaries for CEC enantiomer separation [37,40]. However, when the content of ACN increased further, bubbles formed. The highest normalized separation index was achieved at 80% ACN in the electrolyte. While the maximum EOF was obtained using high ACN content buffer, it was found that the optimized ACN volume was 95% in terms of separation time.

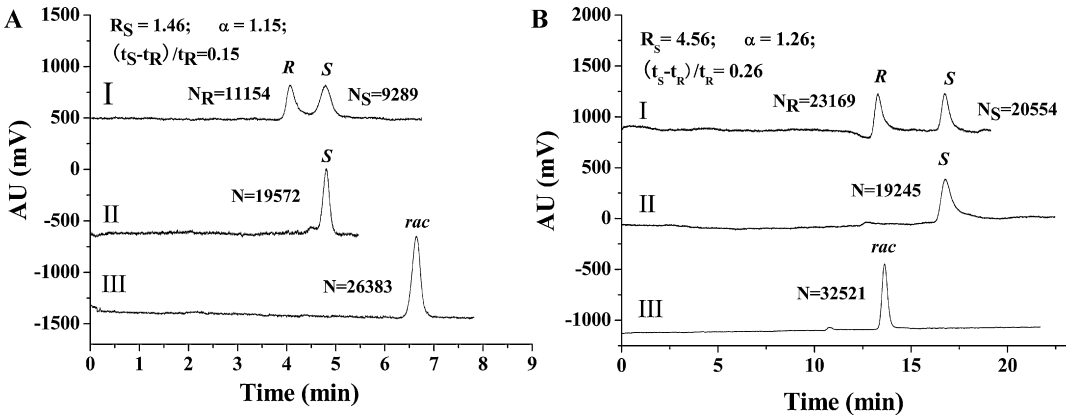

Fig. 4. (A) Electrochromatograms of *rac*-NAP (I), *S*-NAP (II) on *S*-NAP imprinted capillary and *rac*-NAP on non-imprinted capillary (III) demonstrating the imprinting effect and identifying the peaks. Conditions: separation voltage: 12 kV; temperature: 25 °C, UV-Vis detector: 254 nm; ACN/10 mmol L^{-1} acetate (pH 3.6) (90/10 (v/v)); (B) electrochromatograms of *rac*-KET (I), *S*-KET (II) on *S*-KET imprinted capillary and *rac*-KET on non-imprinted capillary (III) demonstrating the imprinting effect and identifying the peaks. Conditions: separation voltage: 12 kV; temperature: 25 °C, UV-Vis detector: 254 nm; ACN/10 mmol L^{-1} acetate (pH 3.6) (80/20 (v/v)).

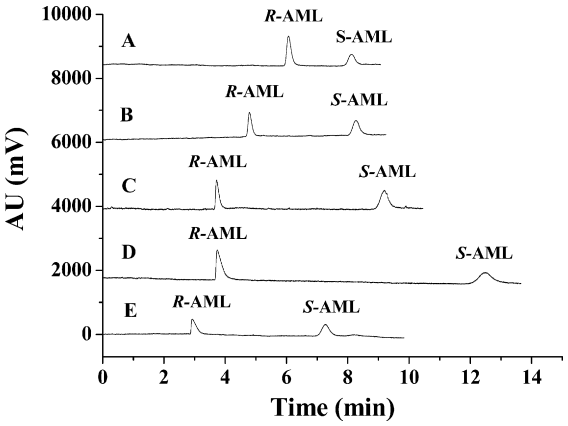

Fig. 5. Effects of the enantiomer separation of different pH value on *S*-AML imprinted capillary. Sample: *rac*-AML. Elution order: *R*-AML followed by *S*-AML. Conditions: separation voltage: 12 kV; temperature: 25 °C, UV-Vis detector: 238 nm; ACN/10 mmol L^{-1} acetate (90/10 (v/v)), (A) 6.0, (B) 5.0, (C) 4.2, (D) 3.6, (E) 3.0.

3.6. Effect of voltage on plate height

Van Deemter plot, as depicted in Fig. 7, is constructed through variations in the operating voltages (3–15 kV) on the AML-imprinted capillary by using ACN/0.01 M acetate (pH 4.2) (90/10 (v/v)) as mobile phase. The optimum in flow velocities can be found, as confirmed by the Van Deemter's theoretical plate height of thiourea versus flow velocity plots. In the case of *S*-AML on the imprinted capillary, the larger slope on Van Deemter's plot is observed than thiourea, the unretained neutral marker, indicating a significant contribution to the peak dispersion of *C*-term. This behavior is related to the mass transport resistance within the separation medium due to the higher retention on MIP-coated column.

The Golay equation (Eq. (1)) enables a calculation of the theoretical performance of OT capillary columns [45]:

$$H = \frac{2D_m}{u} + \frac{d_c^2 u}{D_m}\frac{k^2}{16(1+k)^2} + \frac{d_f^2 u}{D_s}\frac{k}{(1+k)^2} \quad (1)$$

where d_c is the inner diameter of capillary, d_f is the thickness of the porous polymer layer, u is the linear flow velocity and D_m is the diffusion coefficient in the mobile phase, which were calculated with the Wilke–Chang equation. The calculated curves fitted reasonably well with the experimental *H*–*u* data applying an estimated diffusion coefficient in the stationary phase $D_s = 3.66 \times 10^{-12}$ m^2/s.

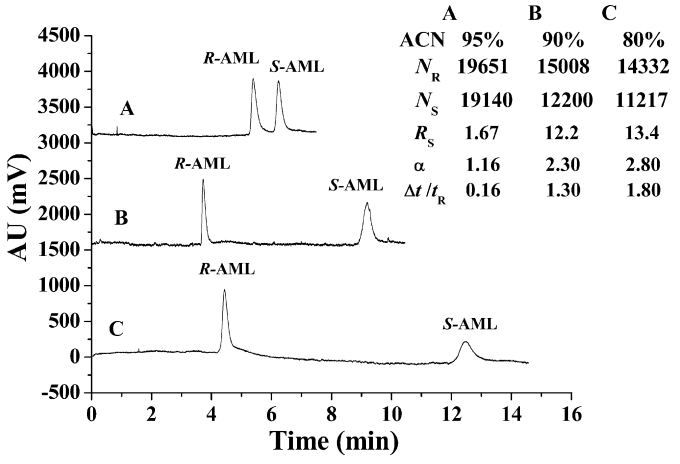

Fig. 6. Effects of the enantiomer separation of the different ACN concentration on *S*-AML-imprinted coatings column. Sample: *rac*-AML. Elution order: *R*-AML followed by *S*-AML. Conditions: separation voltage: 12 kV; temperature: 25 °C, UV-Vis detector: 238 nm; ACN/10 mmol L^{-1} acetate (pH 4.2).

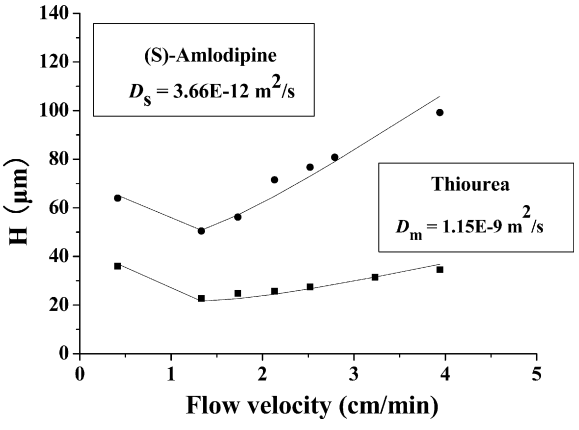

Fig. 7. Effect of voltage on the plate height (*H*) on *S*-AML imprinted coatings column. The electrolyte used was composed of ACN/acetate (pH 4.2, 10 mmol L^{-1}) (90/10 (v/v)). CEC experiments were performed by applying different voltage from 3 to 15 kV, respectively. (A): Thiourea as the unretained neutral marker. Lines calculated according to the Golay equation for $D_m = 1.15 \times 10^{-9}$ m^2/s; (B): *S*-AML. Lines calculated according to the Golay equation for $D_m = 1.88 \times 10^{-9}$ m^2/s and $D_s = 3.66 \times 10^{-12}$ m^2/s.

Table 2
Relative standard deviation (RSD) of reproducibility on OMNiMIPs-coated capillaries with *S*-AML imprints.

	Intra-capillary		Inter-capillary	
	The first peak	The second peak	The first peak	The second peak
Retention time (RSD%)	2.67%	1.18%	0.50%	0.78%
Column efficiency (RSD%)	2.33%	3.20%	2.37%	3.58%
Resolution (RSD%)	1.42%		2.86%	

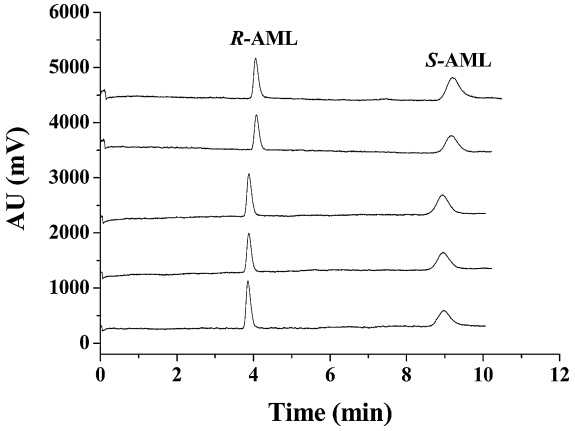

Fig. 8. Intra-column reproducibility of the enantiomer separation of AML using *S*-AML imprinted coatings column. Sample: *rac*-AML. Elution order: *R*-AML followed by *S*-AML. Separation voltage: 12 kV; temperature: 25 °C, UV-Vis detector: 238 nm; ACN/10 mmol L^{-1} acetate (pH 4.2) (90/10 (v/v)).

3.7. Reproducibility and limit of detection

The reproducibility of various CEC parameters is a critical consideration in the field of the preparation and the application of MIP coatings. In our study, a number of parameters such as retention time and R_s were measured to test the intra-column and the inter-column reproducibility of the OMNiMIPs capillaries with *S*-AML imprinting (Figs. 8 and 9). The results of retention time, column efficiency and resolution of (*R*)- and *S*-AML and R_s of two enantiomers on the different batches and the identical column are shown in Table 2. The intra-column reproducibility of a single capillary is averaged from the results of continuously repeating five injections. RSD for the resolution of two enantiomers is lower than 3%. However, RSD for the resolution from column-to-column preparation is 5% ($n = 3$). From reproducibility experiments, it seemed that the MIP coatings using one-monomer instead of conventional crosslinking agent and functional monomer on molecular imprinting had better reproducibility of preparation. The limit of detections (LODs) at S/N = 5 determined by sequential dilution were found to be 3.0 μg/mL for *S*-AML.

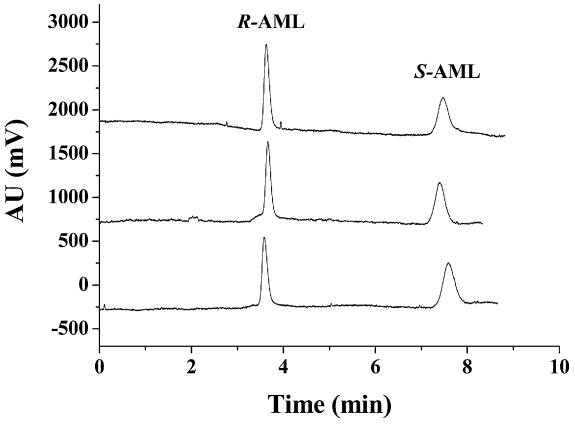

Fig. 9. Inter-column reproducibility of the enantiomer separation of AML using three different *S*-AML imprinted coatings column. Sample: *rac*-AML. Elution order: *R*-AML followed by *S*-AML. Separation voltage: 12 kV; temperature: 25 °C, UV-Vis detector: 238 nm; ACN/10 mmol L^{-1} acetate (pH 4.2) (90/10 (v/v)).

4. Conclusion

We reported here for the first time a method for in situ preparation of one-monomer molecularly imprinted polymer as thin coating inside capillaries. Chiral separations of racemic amlodipine, naproxen, and ketoprofen were achieved on the imprinted capillaries in CEC mode, in which the greatest resolution of enantiomers separation achieved was 16.1. The imprinted capillaries prepared with the one-monomer showed higher chiral separation ability and the stability of column than conventional MAA-EDMA two monomers system, suggesting that it not only simplified the experimental process, but also increased the ability of selective recognition originated from the one monomer. In view of the high performance showed above, this new approach would open new perspectives for the development on the highly selective and efficient MIPs stationary phase.

Acknowledgement

This work was supported by the National Natural Science Foundation of China (Grant No. 21075090).

References

[1] M.J. Whitcombe, I. Chianella, L. Larcombe, S.A. Piletsky, J. Noble, R. Porter, A. Horgan, Chem. Soc. Rev. 40 (2011) 1547.
[2] A. Poma, A.P. Turner, S.A. Piletsky, Trends Biotechnol. 28 (2010) 629.
[3] G. Wulff, Chem. Rev. 210 (2002) 1.
[4] K.D. Shimizu, C.J. Stephenson, Curr. Opin. Chem. Biol. 14 (2010) 743.
[5] E. Turiel, A. Martín-Esteban, J. Sep. Sci. 32 (2009) 3278.
[6] F. Puoci, F. Iemma, N. Picci, Curr. Drug Deliv. 5 (2008) 85.
[7] J. Haginaka, J. Sep. Sci. 32 (2009) 1548.
[8] D. Batra, K.J. Shea, Curr. Opin. Chem. Biol. 7 (2003) 434.
[9] A.M. Rosengren, J.G. Karlsson, P.O. Andersson, I.A. Nicholls, Anal. Chem. 77 (2005) 5700.
[10] M. Sibrian-Vazquez, D.A. Spivak, J. Org. Chem. 68 (2003) 9604.
[11] M. Sibrian-Vazquez, D.A. Spivak, J. Am. Chem. Soc. 126 (2004) 7827.
[12] J.L. Jeune, D.A. Spivak, Anal. Bioanal. Chem. 389 (2007) 433.
[13] K. Yoshimatsu, J.L. Jeune, D.A. Spivak, L. Ye, Analyst 134 (2009) 719.
[14] A.C. Meng, J.L. Jeune, D.A. Spivak, J. Mol. Recognit. 22 (2009) 121.
[15] F. Svec, E.C. Peters, D. Sýkora, J.M.J. Fréchet, J. Chromatogr. A 887 (2000) 3.
[16] X.-X. Shi, L. Xu, H.-Q. Duan, Y.-P. Huang, Z.-S. Liu, Electrophoresis 32 (2011) 1348.
[17] G. Chirica, V.T. Remcho, Electrophoresis 20 (1999) 50.
[18] J.M. Lin, K. Uchiyama, T. Hobo, Chromatographia 47 (1998) 625.
[19] J.M. Lin, T. Nakagama, K. Uchiyama, T. Hobo, Chromatographia 43 (1996) 585.
[20] P. Spégel, L. Schweitz, S. Nilsson, Electrophoresis 22 (2001) 3833.
[21] P. Spégel, L. Schweitz, S. Nilsson, Anal. Chem. 75 (2003) 6608.
[22] F. Priego-Capote, L. Ye, S. Shakil, S.A. Shamsi, S. Nilsson, Anal. Chem. 80 (2008) 2881.
[23] L. Schweitz, L.I. Andersson, S. Nilsson, Anal. Chem. 69 (1997) 1179.
[24] P. Spégel, L. Schweitz, L.I. Andersson, S. Nilsson, Chromatographia 69 (2009) 277.
[25] C. Cacho, L. Schweitz, E. Turiel, C. Perez-Conde, J. Chromatogr. A 1179 (2008) 216.
[26] M. Li, X. Lin, Z. Xie, J. Chromatogr. A 1216 (2009) 5320.
[27] H.F. Wang, Y.Z. Zhu, J.P. Lin, X.P. Yan, Electrophoresis 29 (2008) 952.
[28] J. Ou, X. Li, S. Feng, J. Dong, X. Dong, L. Kong, M. Ye, H. Zou, Anal. Chem. 79 (2007) 639.
[29] Y.L. Xu, Z.S. Liu, H.F. Wang, C. Yan, R.Y. Gao, Electrophoresis 26 (2005) 804.

[30] S. Liao, X. Wang, X. Lin, Z. Xie, Electrophoresis 31 (2010) 2822.
[31] J. He, G. Fang, Q. Deng, S. Wang, Anal. Chim. Acta 692 (2011) 57.
[32] B.Y. Huang, Y.C. Chen, G.R. Wang, C.Y. Liu, J. Chromatogr. A 1218 (2011) 849.
[33] L. Schweitz, Anal. Chem. 74 (2002) 1192.
[34] Y.C. Huang, C.C. Lin, C.Y. Liu, Electrophoresis 25 (2004) 554.
[35] S.A. Zaidi, W.J. Cheong, J. Chromatogr. A 1216 (2009) 2947.
[36] O. Brüggermann, R. Freitag, M.J. Whitcombe, E.N. Vulfson, J. Chromatogr. A 781 (1997) 43.
[37] S.A. Zaidi, K.M. Han, S.S. Kim, D.G. Hwang, W.J. Cheong, J. Sep. Sci. 32 (2009) 996.
[38] J.Z. Tan, V.T. Remcho, Electrophoresis 19 (1998) 2055.
[39] S.A. Zaidi, W.J. Cheong, Electrophoresis 30 (2009) 1603.
[40] S.A. Zaidi, K.M. Han, D.G. Hwang, W.J. Cheong, Electrophoresis 31 (2010) 1019.
[41] X. Wu, Z.-H. Wei, Y.-P. Huang, Z.-S. Liu, Chromatographia 47 (2010) 625.
[42] Y.-P. Huang, Z.-S. Liu, C. Zheng, R.-Y. Gao, Electrophoresis 30 (2009) 155.
[43] Q.L. Deng, Z.H. Lun, R.Y. Gao, L.H. Zhang, W.B. Zhang, Y.K. Zhang, Electrophoresis 27 (2006) 4351.
[44] Y. Chen, M. Kele, I. Quinones, B. Sellergren, G. Guiochon, J. Chromatogr. A 927 (2001) 1.
[45] S. Eeltink, F. Svec, J.M.J. Frécchet, Electrophoresis 27 (2006) 4249.