Talanta 89 (2012) 149–154

Contents lists available at SciVerse ScienceDirect

Talanta

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

Simultaneous and sensitive capillary electrophoretic enantioseparation of three β-blockers with the combination of achiral ionic liquid and dual CD derivatives

Yue Jin, Cheng Chen, Lingchen Meng, Jitao Chen, Meixian Li, Zhiwei Zhu*

Beijing National Laboratory for Molecular Sciences, College of Chemistry and Molecular Engineering, Peking University, Beijing 100871, PR China

ARTICLE INFO

Article history:
Received 18 October 2011
Received in revised form
25 November 2011
Accepted 1 December 2011
Available online 24 December 2011

Keywords:
Achiral ionic liquid
β-Cyclodextrin
Enantioseparation
β-Blocker

ABSTRACT

Successful simultaneous enantioseparation and sensitive determination of three β-blockers (PIN, OX and PRO), have been achieved by capillary electrophoresis using an achiral ionic liquid, [GTMA]Cl, as a modifier to cooperate with dual CDs containing DM-β-CD and TM-β-CD. The influence of aIL was investigated in details, including various aILs, the concentration of aIL and molar ratio of aIL to CD. The ratio of DM-β-CD to TM-β-CD in dual CDs was also discussed. DM-β-CD and TM-β-CD favor the enantioseparations of PIN/OX and PRO, respectively. Meanwhile, the presence of [GTMA]Cl was found to play a key role in enantioseparations, and it widened the scope of application of DM-β-CD and TM-β-CD. Furthermore, FESI as an effective on-line sample enrichment technique was developed to improve the detection sensitivity. Under the optimum conditions, the detection limits of the three pairs of enantiomers range from 0.10 to 0.65 nM, which are much lower than those in the conventional methods. Eventually, the proposed method was successfully applied to the analysis of spiked urine sample with good recoveries.

1. Introduction

Together with HPLC among the most powerful separation techniques, CE offers three unique advantages for enantioseparation over standard chromatographic techniques, the tremendous flexibility by allowing the incorporation of various chiral selectors, the use of different separation modes, and low solvent consumption [1–3]. Of all the frequently used chiral selectors in CE, CDs and their numerous derivatives are of great interest due to their structural variety and commercial availability as well as their broadest selectivity spectra among chiral selectors [4,5]. However, the utility of native CDs or their derivatives as individual chiral selector to resolve enantiomers is not always satisfactory. Hence, the utility of more than one chiral selector is very often of choice to improve the enantioseparation in recent years, including a combination of two CDs [6] or one CD with different types of chiral selectors (e.g. ILs, camphorsulfonic acid, crown ether and so on) [5].

ILs are defined as materials consisting only of ionic components with low melting points close to room temperature. Not like conventional organic solvents, ILs are environmentally benign, non-volatile and non-flammable with a high thermal stability [7]. The most important is that they can be designed by choosing specific cations and anions to meet specific requirements. Based on these advantages, ILs have been successfully used in various research areas, including replacing traditional organic solvents in organic or inorganic syntheses, solvent extractions, liquid–liquid extractions, electrochemical reactions and even a medium to enhance the sensitivity of thermal lens measurements [8–10]. In separation science, ILs have been used originally primarily as GC stationary phases and later as mobile phase additives for LC and CE. For example, ILs have shown increasing applications including pseudo-stationary phase in MEKC, support coatings on the capillary wall, background electrolytes in nonaqueous CE, and additives as CE buffers for achiral or chiral separation [11,12]. Very recently, the combined use of CD derivatives and ILs has captured the attention of the analysts for the improvement of chiral separation in CE [13–15]. These findings suggested that the addition of ILs, especially the novel chiral ILs and surfactant-tie ILs from lab synthesis [11,16], would widen the scope of application of CDs for the separation of chiral compounds. Unfortunately, the synthesis of reported chiral ILs requires rather expensive reagents and elaborated synthetic schemes, which in turn severely hinders the applications of ILs in CE [8]. So the motivation for this study is derived primarily from the anticipation of simultaneous enantioseparation of three β-blockers including PIN, OX and PRO, by using commercially available aILs to cooperate with CDs. The

Abbreviations: PIN, pindolol; OX, oxprenolol; PRO, propranolol; IL, ionic liquid; aIL, achiral ionic liquid; [GTMA]Cl, glycidyltrimethylammonium chloride; DM-β-CD, 2,6-di-O-methyl-β-cyclodextrin; TM-β-CD, 2,3,6-tri-O-methyl-β-cyclodextrin; FESI, field-enhanced sample injection; CE, capillary electrophoresis; MEKC, micellar electrokinetic chromatography; [BMIM]BF_4, 1-butyl-3-methyl-imidazolium tetrafluoroborate; [BMPYR]Cl, *N*-butyl-*N*′-methyl-pyrrolidinium chloride; [BMPIP]Cl, *N*-butyl-*N*′-methyl-piperdinium chloride; HDTM-β-CD, Heptakis(2,6-di-O-methyl)-(2,3,6-tri-O-methyl)-β-cyclodextrin; PBS, phosphate buffer solution; EOF, electroosmotic flow.

* Corresponding author. Tel.: +86 10 62757953; fax: +86 10 62751708.
E-mail address: zwzhu@pku.edu.cn (Z. Zhu).

0039-9140/$ – see front matter © 2011 Elsevier B.V. All rights reserved.
doi:10.1016/j.talanta.2011.12.005

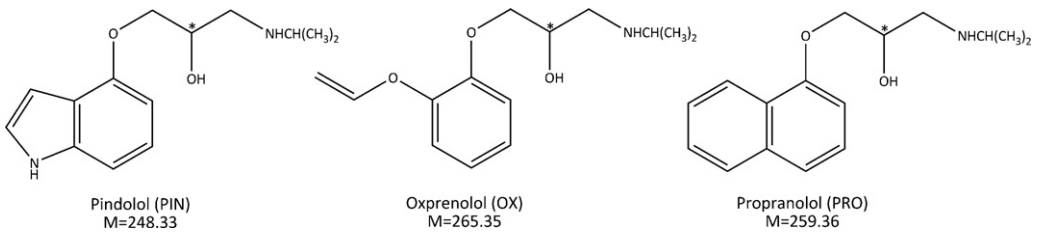

Fig. 1. Chemical structures of PIN, OX and PRO (the asterisk (*) denotes chiral center).

structures of the β-blockers studied in this paper are shown in Fig. 1. Our previous study showed that OX and PRO except PIN could be enantioseparated based on their interactions with bovine serum albumin [17]. In this paper, the combination of [GTMA]Cl and dual CDs showed great efficiency to enhance the enantioseparation of the above three β-blockers enantiomers, which indicated that the use of relatively inexpensive commercialized aIL would widen the scope of application of CDs. Meanwhile, with FESI the detection limits of the three pairs of enantiomers were also improved greatly.

2. Materials and methods

2.1. Apparatus

All experiments were performed with a P/ACE MDQ instrument equipped with a diode-array UV detector (Beckman Coulter, USA). Data acquisition and instrument control were carried out using 32 Karat software (Version 7.0). Separations were performed in 64.5 cm (56.0 cm to detector) uncoated fused-silica capillaries with 50 μm i.d. and 365 μm o.d. (Yongnian Optical Fiber Factory, China).

2.2. Materials

R,S-Pindolol (PIN), *R,S*-oxprenolol (OX) and *R,S*-Propranolol (PRO) were purchased from Acros or Sigma. [BMIM]BF_4, [BMPYR]Cl, [BMPIP]Cl and [GTMA]Cl were obtained from Fluka. HDTM-β-CD, DM-β-CD and TM-β-CD were from Sigma. Deionized water was obtained by triply distilling tap water from an all-quartz still. All the other chemicals were of analytical reagent grade and used without further purification.

2.3. Procedure

The stock solutions of racemic PIN, OX and PRO were prepared in deionized water with the concentration of 0.10 mM. The standard solutions were diluted with deionized water to the desired concentration before use. PBS was selected as the running buffer. The pH was adjusted with triethylamine. All the solutions were stored at 4 °C. Prior to separation, all electrolyte solutions were filtered through a 0.45 μm polytetrafluoroethylene membrane filter.

Prior to separation, the new capillary was flushed with 1.0 M sodium hydroxide for 10 min, then with deionized water for 10 min, and finally with running buffer for 15 min. Between consecutive analysis, the capillary was flushed with deionized water for 5 min, 1.0 M sodium hydroxide for 5 min, deionized water for 5 min, and finally with running buffer for 3 min in order to improve the reproducibility. The voltage applied in the separation was +30 kV, the capillary was held at 25 °C and the wavelength of the UV detector was maintained at 220 nm.

In FESI, injection was performed electrokinetically after a short water plug. The injection time, the injection voltage and the pre-injection of water plug were studied and optimized in this work. All measurements were carried out at least three times.The resolution was calculated as follows:

$$R_s = \frac{2(t_2 - t_1)}{w_1 + w_2}$$

where t is the enantiomer migration time, R_s is the resolution, and w is the width of the peak at the baseline. The suffixes 1 and 2 refer to the first and second migrating enantiomer, respectively.

2.4. Pre-treatment of urine sample

The spiked urine sample containing 100 μM racemic PIN, 1000 μM racemic OX and 500 μM racemic PRO was prepared by diluting the stock solutions in the urine obtained from a healthy female volunteer. One of the major reasons for not spiking the same concentration of β-blockers was to make their electrophoretic peak heights closer. The blank urine sample and the spiked human urine sample were filtered through a 0.22 μm polytetrafluoroethylene membrane filter and stored at 4 °C. The prepared samples should be tested within 24 h. The sample solutions were diluted 10,000-fold with deionized water before injection.

3. Results and discussion

3.1. Evaluation of synergistic effect between ILs and CD derivations

The stereoselective analyses of β-blockers in CE were conducted by varying the concentration of various mono-additives including four types of commercialized aILs, three native CDs and one CD derivative (Table 1), in 50 mM PBS (pH 4.4). To favor the research in aqueous solution, all of the aILs used in this work were highly miscible in water. As summarized in Table 1, upon addition of aILs, no enantioseparation was observed, but the achiral separation was improved. The addition of native CDs led to negative influence on the achiral separation except for γ-CD. Best results were obtained by using HDTM-β-CD as chiral selector, which exhibited reasonable enantioselectivity for PIN and OX, but it was less successful for the PRO enantiomers. In each case the *S* enantiomers were migrating faster, indicating that these enantiomers should have weaker

Table 1
Selection of the chiral selector in a mono-additive system.

Additives (5–20 mM)	Results
[BMIM]BF_4, [BMPYR]Cl, [BMPIP]Cl, α-CD, β-CD	The migration time increases with the additive concentration. No improvement was obtained.
[GTMA]Cl, γ-CD	The migration time increases with the additive concentration. The resolutions of the three β-blockers were improved without enantioseparation.
HDTM-β-CD	The migration time increases with the additive concentration rapidly. Chiral separations of PIN and OX were obtained except for PRO.

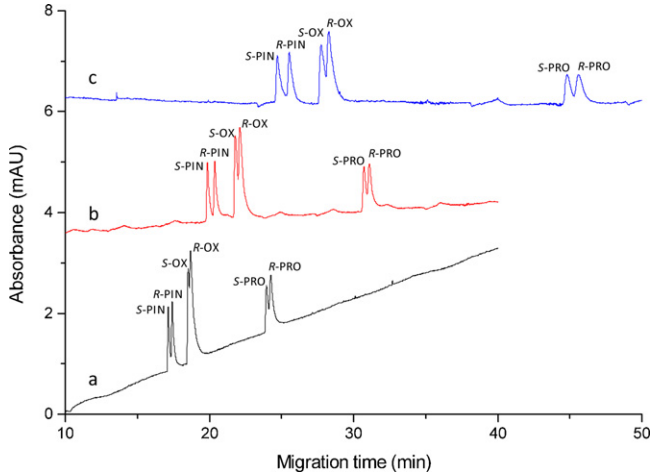

Fig. 2. Effect of the HDTM-β-CD concentration. HDTM-β-CD concentration (mM): (a) 5; (b) 10; (c) 15. Concentration of β-blockers (μM): racemic PIN, 300; racemic OX, 700; racemic PRO, 500. Experimental conditions: 50 mM phosphate buffer, pH 4.4; injection by pressure, 0.5 psi; injection time, 5 s; separation voltage, +30 kV.

interaction with the CDs. With the increasing of HDTM-β-CD concentration, the migration times as well as chiral resolutions of PIN and OX were increased. Nevertheless, the enantiomers of PRO still could not be enantioseparated even though the concentration of HDTM-β-CD was further increased. To enhance the enantioseparation, in particular for PRO, an additional chiral selector was required to provide the three-point interactions needed for chiral separations.

Since HDTM-β-CD had been chosen as a part of multi-additive system, the next step was to find another one. The aILs including [BMIM]BF_4, [BMPYR]Cl, [BMPIP]Cl and [GTMA]Cl with the concentration from 5 mM to 20 mM, were examined whether to improve chiral resolutions of the above β-blockers. Both of [BMPYR]Cl and [BMPIP]Cl played negative roles in the enantioseparation, and even counteracted the effect of HDTM-β-CD. As for [BMIM]BF_4, it had few effects as if they did not exist. Fortunately, the alteration of selectivity and improvement of either chiral or achiral resolutions of the above β-blockers were obtained by the addition of [GTMA]Cl. This indicated that some sort of synergistic effect should exist between [GTMA]Cl and HDTM-β-CD in a way.

3.2. *Effect of [GTMA]Cl and HDTM-β-CD concentration on chiral resolution and migration time*

The effect of HDTM-β-CD concentration was investigated by fixing the concentration of [GTMA]Cl at 20 mM. As shown in Fig. 2, it can be seen that the decrease in HDTM-β-CD concentration results in a baseline distortion. Meanwhile, the higher concentration of HDTM-β-CD leads to wider peak and longer migration time. However, the continuous increase in concentration of HDTM-β-CD (higher than 15 mM) brings about the poor peak efficiency and extremely long migration time mainly due to the high viscosity of CD and the formation of CD-analyte complexes. Accordingly, the 10 and 15 mM HDTM-β-CD were chosen as fixed concentration to estimate the effect of [GTMA]Cl concentration as a compromise consideration between the resolution and analysis time. The influence of the ratio of aIL to CD, namely the concentration of [GTMA]Cl at two different HDTM-β-CD concentrations, was investigated by adding various concentrations of [GTMA]Cl to the both of the two CE buffers containing 10 or 15 mM HDTM-β-CD, respectively. Fig. 3A and B shows that the chiral resolutions of PIN and OX at either 10 or 15 mM HDTM-β-CD increase with increasing [GTMA]Cl concentration as a whole. However, the case of PRO is a bit different. When the ratio of aIL to CD is high enough (such as 4:1), the resolution of

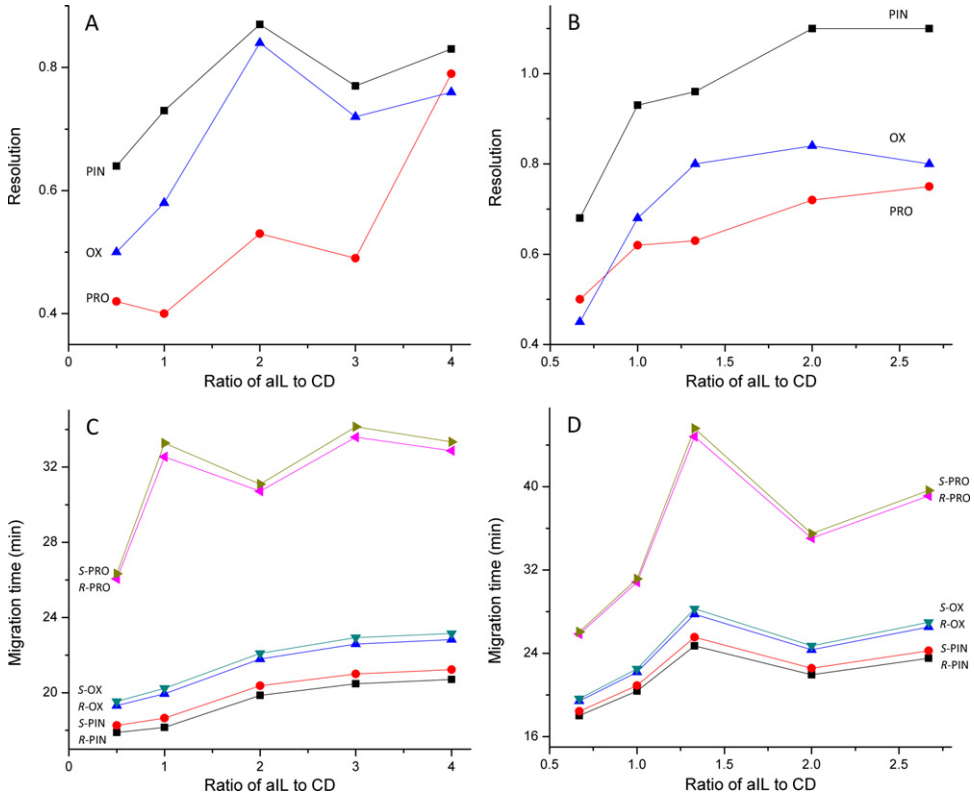

Fig. 3. Effect of the ratio of [GTMA]Cl to HDTM-β-CD on chiral resolution (A and B) and migration time (C and D). Concentration of HDTM-β-CD (mM): (A and C) 10; (B and D) 15. Other conditions are the same as in Fig. 2.

PRO can reach 0.79 that even exceeds OX. But it's a pity that such a higher ratio results in worse reproducibility and longer migration time. Considering both of resolution and migration time, 30 mM [GTMA]Cl and 15 mM HDTM-β-CD, as the ratio of aIL to CD is 2:1, were chosen as the optimum concentrations. In addition, for each β-blocker there is a maximum of migration time (corresponding to the ratio of 4:3) over the studied range (Fig. 3D). This interesting phenomenon will be discussed in next section.

3.3. Hypothesis of enantioseparation mechanism using [GTMA]Cl and HDTM-β-CD

It has been reported that the cationic β-CD synthesized with [GTMA]Cl and β-CD can be used to modify the surface of zeolite to prepare a novel and effective sorbent for removal of p-nitrophenol from aqueous solution [18]. So the above interesting phenomenon seems to involve association between [GTMA]Cl and HDTM-β-CD. During the separation, the capillary is filled with the CE buffer containing three major species: the positively charged [GTMA] cation, the neutral chiral selector HDTM-β-CD, and positively charged or neutral β-blockers (PIN, $pK_a = 9.21$; OX, $pK_a = 9.13$; PRO, $pK_a = 9.14$) [19]. Hence, the interactions among these species might include hydrogen bonding, hydrophobic interactions and ion-dipole/ion-induced-dipole, which mainly exist in the complexes of [GTMA]Cl-CD and β-blockers-CD as well as β-blockers-[GTMA]Cl-CD. Under the low concentration of [GTMA]Cl, the most of [GTMA] cations are first covalently coated onto the capillary wall, which leads to a surface charge reversal and thus reduces the EOF. As a consequence of this, few free [GTMA] cations in buffer can combine with CD. This can be explained that both of the chiral resolution and migration time increase with [GTMA]Cl concentration, until the ratio of aIL to CD reaches 1:1. At this stage, the enantioseparations of PIN and OX are primarily dependent on the interaction between enantiomers and CD. One of the major reasons for low resolution of PRO is that its enantioseparation is based on the interaction between enantiomers and [GTMA]Cl-CD complex, which is concluded from the comparison between the mono-additive system and multi-additive system. In other words, it is the extent of association of β-blocker with CD that dictates the β-blockers-[GTMA]Cl-CD association. Not like PIN and OX being completely or partially included in the CD cavities, PRO with larger size that cannot be included in the CD cavities has rather strong association with the [GTMA] cations in the running buffer or [GTMA]Cl-CD complex [20]. With the concentration of [GTMA]Cl increased, more and more [GTMA] cations are free in the buffer and thus combine with CD. When the ratio is increased to 2:1, the concentration of [GTMA]Cl-CD complexes might reach a saturation point. At that moment, the enantioseparations of three β-blockers are mainly based on the interaction between enantiomers and [GTMA]Cl-CD complex, which leads to the improvement on the chiral separation and decrease in migration time. Because the positively charged [GTMA]Cl-CD complex migrates faster than the CD alone, the migration time of β-blockers-[GTMA]Cl-CD is shorter than β-blockers-CD. On the other hand, the higher ionic strength would be a predominant factor resulting in the increase of migration time if the concentration of [GTMA]Cl further being increased (Fig. 3C and D). In general, the roles of a variety of ILs applied in CE are no more than the following: (*i*) single pseudostationary phase or separation medium; (*ii*) binary pseudophase in combination with micelles or CDs; (*iii*) support coating on the capillary wall; (*iv*) BGE in nonaqueous CE; (*v*) micelle forming surfactant for both achiral and chiral separations [9]. Obviously in this system, the [GTMA]Cl acts as either role *ii* or role *iii*. However, the further study is needed for an understanding of the molecular level of the chiral recognition between these β-blockers and [GTMA]Cl-CD complex.

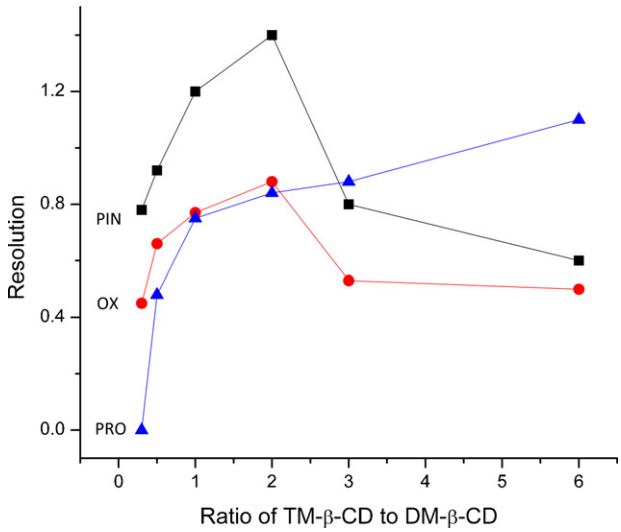

Fig. 4. Effect of the ratio of TM-β-CD to DM-β-CD on chiral resolution. The total concentration of CDs: 15 mM. Other conditions are the same as in Fig. 2.

3.4. Effect of dual CDs on resolution

Basically, HDTM-β-CD is impurities which are over-methylated homologs, primarily DM-β-CD and TM-β-CD. It is well known that the composition of chiral selectors plays a key role in the chiral separation and reproducibility. In order to investigate the effect of the composition of chiral selectors and to avoid reproducibility problems which may be inherent with randomly substituted CD derivatives, HDTM-β-CD was replaced with dual-CD system consisting of DM-β-CD and TM-β-CD. This mixture containing the same components as HDTM-β-CD primarily does, has almost the same influence on the migration time and chiral resolution. Herein only the effect of TM-β-CD/DM-β-CD ratio was investigated upon the fixed total concentration of CDs (15 mM). As shown in Fig. 4, the increasing ratio of TM-β-CD/DM-β-CD has

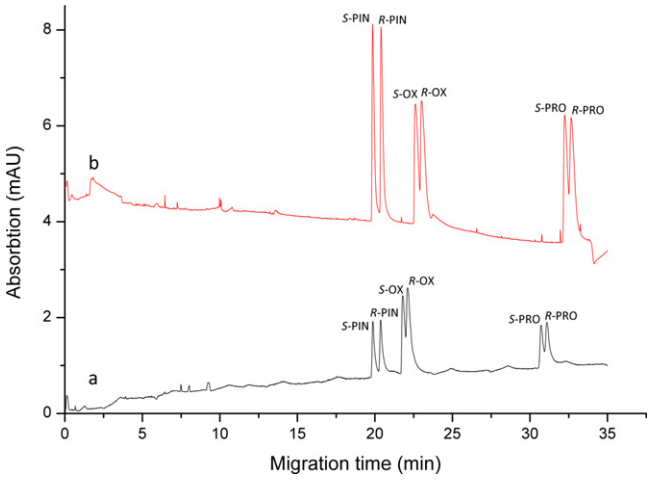

Fig. 5. Comparison of the electropherograms of the enantiomers of the three β-blockers between the conventional method (a) and the FESI method (b). Concentration (μM): (a) racemic PIN, 300; racemic OX, 700; racemic PRO, 500; (b) racemic PIN, 0.05; racemic OX, 0.5; racemic PRO, 0.1. The conditions in the conventional method are the same as in Fig. 2. Experimental conditions in the FESI method: 50 mM phosphate buffer, pH 4.4; injection by voltage, +10 kV; injection time, 5 min; water plug, 10 s at 0.5 psi; separation voltage, +30 kV.

Table 2
Results of regression analysis on calibration, the detection limits and enhancement factors with FESI.

Component	Calibration curves[a] $A=a+bc$	Correlation coefficient	RSD of migration time (%, $n=5$)	RSD of peak area (%, $n=5$)	Detection limit (nM)	Linear range (nM)	Enhancement factor
R-PIN	$A=3.5\times10^3+1.6\times10^3c$	0.9991	0.60	4.7	0.11	$0.63–1.2\times10^2$	7.3×10^4
S-PIN	$A=4.0\times10^3+1.9\times10^3c$	0.9991	0.30	2.6	0.10	$0.63–1.2\times10^2$	8.0×10^4
R-OX	$A=2.0\times10^3+1.7\times10^2c$	0.9990	0.20	3.8	0.40	$0.75–7.5\times10^2$	1.7×10^5
S-OX	$A=3.1\times10^3+2.4\times10^2c$	0.9995	0.51	3.8	0.65	$0.75–7.5\times10^2$	6.2×10^4
R-PRO	$A=4.4\times10^2+9.0\times10^2c$	0.9982	0.44	3.2	0.10	$0.12–1.2\times10^2$	2.0×10^5
S-PRO	$A=5.0\times10^2+9.9\times10^2c$	0.9972	0.80	3.5	0.12	$0.12–1.2\times10^2$	8.0×10^4

[a] A: peak area, 10^{-6} Au s; c: concentration of analyte, nM.

a significant influence on the chiral resolution of PRO, while the highest chiral resolutions of PIN and OX were obtained at ratio of 2:1. It is reasonable that the enantioseparation of PIN and OX are primarily based on the interaction between enantiomers and [GTMA]Cl–DM-β-CD complex, while the enantioseparation of PRO on the interaction with [GTMA]Cl–TM-β-CD complex. In our work, the ratio of 2:1 was recommended as a compromise consideration among chiral resolutions of PIN, OX and PRO. Under the optimum conditions, the typical electropherogram is shown in Fig. 5a.

3.5. Optimization of field-enhanced sample injection system

To improve the detection sensitivities, FESI was introduced in this system. The dependence of the peak intensity on injection time and injection voltage was investigated. More injection time generally favors higher sensitivity, while overloading may cause peak broadening [21]. Considering both of sensitivity and efficiency, 5 min under +10 kV injection voltage was chosen as the optimum injection time. The presence of water plug during the long FESI step was proved to be favorable to the improvement of the total focusing effect. Moreover, it could improve the reproducibility. Herein, a short of water plug (0.5 psi × 10 s) which induced the best peak shape was introduced into the capillary to obtain good reproducibility. Under the optimum conditions, the typical electropherogram is shown in Fig. 5b. The results of regression analysis on calibration, the detection limits and enhancement factors with FESI are summarized in Table 2. Compared with either the conventional injection in this system or Huang's FESI method with detection limit for PRO of 0.5 μg/mL (about 2 μM) [22], the enhancement of the sensitivity is greatly improved with at least 4 orders of magnitude for these β-blockers.

3.6. Applications

To evaluate the enantioseparation efficiency of [GTMA]Cl/TM-β-CD/DM-β-CD as well as FESI techniques, the proposed methods were applied to the analysis of spiked human urine sample. Because the electrolyte of the sample solution strongly influenced the FESI concentration efficiency, also thanks to its high sensitivity, the final human urine sample solution could be diluted 10,000-fold before injection. Representative electropherograms for the analysis of spiked samples are illustrated in Fig. 6. The quantitative results and the recoveries of this method are listed in Table 3. The good recoveries between 96% and 114% indicate the great accuracy of the proposed method. However, there is a little matrix interference leading to the migration time of analytes being advanced by about 2.5 min compared with standard solution. Fortunately, there have few changes for the relative migration time among the analytes, which means each of these analytes can be regarded as an internal standard. Consequently, under optimal separation conditions, the trace-level β-blocker enantiomers in the human urine sample can be identified sensitively by the proposed method.

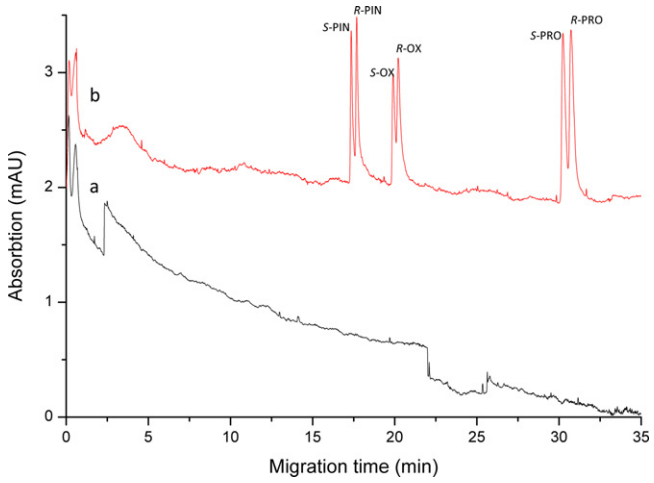

Fig. 6. Electropherograms of urine sample and spiked urine sample under optimum FESI condition. Spiked concentration (μM): (a) 0; (b) racemic PIN, 100; racemic OX, 1000; racemic PRO, 500. Other conditions are the same as the FESI method in Fig. 5.

Table 3
Results for the determination of the four components in urine sample ($n=3$).

Component	Original amount (μM)	Added (μM)	Found (μM)	Recovery (%)
R-PIN	–	50	48	96
S-PIN	–	50	49	98
R-OX	–	500	505	101
S-OX	–	500	570	114
R-PRO	–	250	243	97
S-PRO	–	250	266	106

4. Conclusions

Baseline separation, high efficiencies, and symmetrical peaks of three β-blockers were obtained by using an aIL as modifier to cooperate with dual CDs. Compared with [BMIM]BF_4, [BMPYR]Cl and [BMPIP]Cl, [GTMA]Cl is more effective for the improvement of enantioseparation of β-blockers, which indicates that the combined use of [GTMA]Cl with β-CD as a binary electrolyte system should provide a suitable alternative for a rapid identification of β-blocker enantiomers. Additionally, the high sensitivity, with LODs in range of 0.10–0.65 nM, was obtained by FESI as an on-line sample stacking technique, which was much lower than those of the conventional methods. The good recoveries may allow the success of this technique in the detection of β-blocker enantiomers in human urine sample.

Acknowledgements

This work was jointly supported by the National Natural Science Foundation of China (NSFC, No. 21175006; 20975003 and 20735001) and the National High Technology Research and Development Program of China (No. 2009AA035200).

References

[1] S. Fanali, P. Catarcini, G. Blaschke, B. Chankvetadze, Electrophoresis 22 (2001) 3131–3151.
[2] S. Fanali, J. Chromatogr. A 735 (1996) 77–121.
[3] B. Preinerstorfer, M. Lammerhofer, W. Lindner, Electrophoresis 30 (2009) 100–132.
[4] Z. Juvancz, R.B. Kendrovics, R. Ivanyi, L. Szente, Electrophoresis 29 (2008) 1701–1712.
[5] G.K.E. Scriba, J. Sep. Sci. 31 (2008) 1991–2011.
[6] E. Lipka, C. Danel, S. Yous, J.P. Bonte, C. Vaccher, Electrophoresis 31 (2010) 1529–1532.
[7] M. Koel, Crit. Rev. Anal. Chem. 35 (2005) 177–192.
[8] K. Bica, P. Gaertner, Eur. J. Org. Chem. (2008) 3235–3250.
[9] S.A. Shamsi, N.D. Danielson, J. Sep. Sci. 30 (2007) 1729–1750.
[10] Y.F. Zhao, Y.Q. Gao, D.P. Zhan, H. Liu, Q. Zhao, Y. Kou, Y.H. Shao, M.X. Li, Q.K. Zhuang, Z.W. Zhu, Talanta 66 (2005) 51–57.
[11] M. Borissova, K. Palk, M. Koel, J. Chromatogr. A 1183 (2008) 192–195.
[12] T.F. Jiang, Y.L. Gu, B. Liang, J.B. Li, Y.P. Shi, Q.Y. Ou, Anal. Chim. Acta 479 (2003) 249–254.
[13] L. Huang, J.M. Lin, L.S. Yu, L.J. Xu, G.N. Chen, Electrophoresis 30 (2009) 1030–1036.
[14] B. Wang, J. He, V. Bianchi, S.A. Shamsi, Electrophoresis 30 (2009) 2812–2819.
[15] B. Wang, J. He, V. Bianchi, S.A. Shamsi, Electrophoresis 30 (2009) 2820–2828.
[16] C.D. Tran, I. Mejac, J. Chromatogr. A 1204 (2008) 204–209.
[17] G.Q. Yang, Y.F. Zhao, M.W. Li, Z.W. Zhu, Q.K. Zhuang, Talanta 75 (2008) 222–226.
[18] X.H. Li, K. Zhu, X.K. Hao, Water Sci. Technol. 60 (2009) 329–337.
[19] C. Akbay, S.A.A. Rizvi, S.A. Shamsi, Anal. Chem. 77 (2005) 1672–1683.
[20] L. Gagyi, A. Gyeresi, F. Kilar, J. Biochem. Biophys. Methods 70 (2008) 1268–1275.
[21] Y. Jin, L.C. Meng, M.X. Li, Z.W. Zhu, Electrophoresis 31 (2010) 3913–3920.
[22] L. Huang, J.M. Lin, L.S. Yu, L.J. Xu, G.N. Chen, Electrophoresis 29 (2008) 3588–3594.