

# A simple chiral separation method using capillary electrophoresis with UV detection for analysis of enantiomers of drug compounds

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## A simple chiral separation method using capillary electrophoresis with UV detection for analysis of enantiomers of drug compounds

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### Abstract

A rapid and simple method for separation of enantiomers of a variety of compounds is desirable as information regarding the enantiomeric composition may not be provided by the chemical suppliers especially chemical drug compounds. These drugs are commercially available with no information regarding whether they are pure enantiomers or racemic mixtures. Each enantiomer may have different pharmacological activity. Thus the information of chirality is important. This work aims to employ a capillary electrophoresis with UV detection as a simple and rapid method for separation of enantiomers to determine the compound chirality. The developed method has been applied for separation of different functional chemicals of drugs, such as  $\beta$ -blockers and neurotransmitter, by using a single capillary electrophoresis method. The buffer conditions for the capillary method were optimized with regards to the chiral selector type and concentration for improving the efficiency of enantiomer separation. The optimum condition of buffer was phosphate buffer (20.0 mM, pH 2.7) containing CM- $\beta$ -CD (4.0 mM). The single method was applied to the separation of four different drug compounds, viz. atenolol, propranolol, octopamine, and ibuprofen, to demonstrate the effectiveness of the developed method.

**Keywords:** Capillary electrophoresis, Chiral separation, Chiral selector, Drug chemical structure

### Introduction

Separation of enantiomer compounds is becoming the focus of researchers. It is well-known that enantiomeric compounds are closely related to their pharmacology. Enantiomers have the same chemical formula and chemical properties but differences in terms of pharmacodynamics,

pharmacokinetics and toxicology. Although chirality of compound is important, many times chemical supplier and manufacturer of the drugs do not provide any information about the chirality of the compounds. Many suppliers sell their drugs with lack of chiral information.

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Determination of enantiomers employs separation methods, such as gas chromatography (GC), high performance liquid chromatography (HPLC), and capillary electrophoresis (CE), for qualitative and quantitative analysis. These techniques have been successfully applied to separation of enantiomer compounds [1-4]. Capillary electrophoresis technique is a powerful method of separation of enantiomer compounds. It is simple, rapid, employs very low volume of sample and reagent, and with high efficiency of separation. Various CE modes have been employed, including capillary zone electrophoresis (CZE), micellar electrokinetic chromatography (MEKC), capillary electrochromatography (CEC), and gel capillary electrophoresis (GCE). Chiral separation by CZE technique is performed by adding a chiral selector to the running buffer. Various chiral selectors have been used, such as amino acids [5, 6], antibiotics [7], and cyclodextrins (CDs) [8-10]. Although various chiral selectors were successfully applied, cyclodextrins are desirable as a chiral selector in view of their low cost, solubility in water, and UV transparency. They come in different properties (e.g. nonpolar, polar, and charged), so it can be selected suitable for the target compound. Cyclodextrins are synthetic macrocyclic oligosaccharides that have basic structure of six, seven, or eight glucopyranose, representative of  $\alpha$ ,  $\beta$ , and  $\gamma$  CD. The interior and exterior of CDs have different properties (hydrophobic and hydrophilic), generating formation of a complex between CD, as the host molecule, and an enantiomer, as guest molecule [11]. It was reported that the dimensions of  $\beta$ -CD was effective to induce inclusion complexes

with molecules composed of hydroxyl groups and one or two condensed aromatic groups. Such inclusion-complexation mechanism is useful for increasing selectivity of enantiomeric separation [12].

The goal of this work is to employ a single capillary electrophoresis with UV detection system as a simple and rapid method for enantiomeric separation for drugs with different chemical structures (see Table 1). UV detection is the most common detection method for capillary electrophoresis. It is efficient and convenient for detection of drugs having a chromophore in the UV-visible region. The single system was successfully applied for chiral separation of three different drugs, viz. atenolol, propranolol and octopamine. The separation of enantiomers of these drugs by employing a single capillary electrophoresis method has not been previously reported.

## Material and Methods

### Reagents and materials

Racemic mixtures of atenolol, propranolol, and ibuprofen were kindly provided by Assoc. Prof. Chutima Phechkrajang, Faculty of Pharmacy, Mahidol University. A racemic mixture of octopamine hydrochloride (analytical grade) was purchased from Sigma (Steinheim, Germany). Orthophosphoric acid (85%, analytical grade) was supplied by Ajax (Victoria, Australia). Sodium hydroxide (analytical grade) and anhydrous caffeine ( $\geq 99\%$ , HPLC grade) were purchased from Fluka (St. Louis, MO, USA). The chiral selectors, carboxymethyl- $\beta$ -cyclodextrin (CM- $\beta$ -CD) and heptakis (2,3,6-tri-O-methyl)- $\beta$ -cyclodextrin (TM- $\beta$ -CD), were obtained from



Cyclolab (Budapest, Hungary). Deionized water (ultrapure 18.0 M $\Omega$ -cm) was obtained from Siemens Ultra Clear™ TWF EDI (Evoqua Water Technologies, PA, USA). Stock solutions of atenolol (1,000  $\mu$ M), propranolol (1,000  $\mu$ M), octopamine (1,000  $\mu$ M), ibuprofen (2,000  $\mu$ M) and caffeine (1,000  $\mu$ M, as EOF marker) were prepared in deionized water.

Phosphate running buffer (20.0 mM) was prepared by diluting 2.0 mL of 500 mM orthophosphoric acid with deionized water to the final volume of 50 mL. Sodium hydroxide (1.0 M) was used to adjust pH to 2.7. The chiral selector was dissolved in the running phosphate buffer to concentrations of 4.0, 5.0, and 6.0 mM, respectively.

#### Instrumentation

The capillary electrophoresis system was constructed in-house. It comprised a UV detector (Applied Biosystems, 785A UV detector, CA, USA), a high voltage (HV) power supply (Spellman CZE1000R, Hauppauge, USA), and a tray for the sample and buffer vials. A plexiglass safety box was designed and constructed to house the system. It has a toggle switch to turn on or off the high voltage when the CE instrument is operating. The absorbance signal was recorded using data acquisition software from eDAQ (Denistone, NSW, Australia). A fused-silica capillary tubing (Polymicro Technologies, Phoenix, AZ, USA) was utilized as the separation column. The capillary has a total length of 57.4 cm, effective length of 36.0 cm, OD 360.0  $\mu$ m and ID 50.0  $\mu$ m. The capillary column was conditioned with NaOH solution (0.1 M), ultrapure water (18.0 M $\Omega$ -cm), and running buffer daily before use. Electrokinetic injection was performed by applying 15.0 kV for 2.0 s

for sample introduction. Then an electrical field of 348.4 V cm<sup>-1</sup> was applied to the running buffer for electrophoretic separation of the enantiomers. Detection wavelength was set at 225 nm. The temperature of the capillary column was not controlled since it was an in-house instrument. However the CE instrument was operated at the room temperature of 25°C.

#### Results and discussion

The CE method was developed for enantiomeric separation. A chiral selector was added to the running buffer. This work describes the effect of the chiral selector and the choice of suitable concentration of the selected chiral selector for chiral separation of various types of drugs.

#### Selection of chiral selector

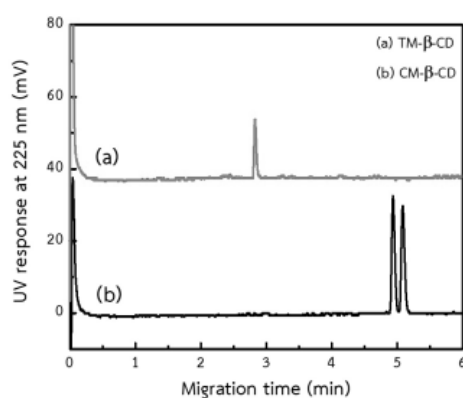
The criteria for the selection of chiral selector are charge, molecular size, inner cavity, and functional group of target enantiomeric compounds. Native CD has been described to have ability to separate chiral compounds, such as amino acids and  $\beta$ -blockers, but few applications for other groups of compounds, such as NSAIDs [13]. Two synthetic chiral selectors, CM- $\beta$ -CD and TM- $\beta$ -CD, were tested for their ability for enantiomeric separation of octopamine (see Figure 1). Neutral and anionic cyclodextrins were used for separation in this work.

Figure 1 shows electropherograms of separation of enantiomers of octopamine using two types of chiral selectors. As previously investigated by our research group, CM- $\beta$ -CD was used for the

successful separation of enantiomers of methamphetamine, pseudoephedrine, and ephedrine [14]. In this research, it was observed that CM- $\beta$ -CD was successful for the separation of octopamine into its two enantiomers. These results agreed with our previous work [14]. This is because CM- $\beta$ -CD has anionic property and therefore migrates towards the anode against the direction of the electro-osmotic flow. Thus CM- $\beta$ -CD provides

slower mobility of the enantiomers of each analyte and so make them separable [15, 16].

Another chiral selector TM- $\beta$ -CD was reported as a suitable selector for enantiomer compound containing a carboxylic group [17]. However octopamine and ephedrine are similar in terms of a benzene ring attached to the chiral center. Thus CM- $\beta$ -CD was selected for further investigation.

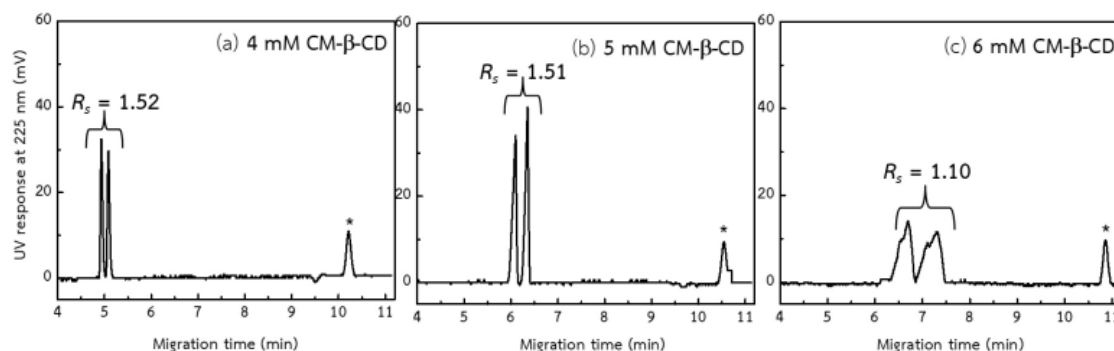


**Figure 1.** Electropherograms of racemic mixture of chiral octopamine at concentration of 25.0  $\mu$ M. CE conditions: phosphate buffer (20.0 mM, pH 2.7) with addition of (a) 4.0 mM TM- $\beta$ -CD and (b) 4.0 mM CM- $\beta$ -CD, electrokinetic injection for 2.0 s at 261.3 V  $\text{cm}^{-1}$ , applied electrical field strength of 348.4 V  $\text{cm}^{-1}$  and UV detection at 225 nm.

#### Concentration of chiral selector

The concentration of chiral selector in the running buffer is important for optimization of enantiomeric separation. High concentration of chiral selector will lead to both enantiomers of the

compounds to fully form inclusion complexes within the inner cavity of cyclodextrin giving no separation [18]. Thus optimization of CM- $\beta$ -CD concentration was investigated.



**Figure 2.** Electropherograms of enantiomers of octopamine at 25.0  $\mu\text{M}$ , containing caffeine 250.0  $\mu\text{M}$ , and with different concentration of CM- $\beta$ -CD (a) 4.0 mM, (b) 5.0 mM, and (c) 6.0 mM. CE conditions: phosphate buffer (20.0 mM, pH 2.7), electrokinetic injection for 2.0 s at 261.3  $\text{V cm}^{-1}$ , applied electrical field strength of 348.4  $\text{V cm}^{-1}$  and UV detection at 225 nm. \*Caffeine, as EOF marker.

Figure 2 shows the effect of separation for concentrations of CM- $\beta$ -CD of 4.0 mM (Figure 2a), 5.0 mM (Figure 2b), and 6.0 mM (Figure 2c), respectively. Each electropherogram in Figure 2 was selected from three replicate injections. Precision of migration time was less than 2 %RSD for all peaks. Calculation of  $R_s$  (peak resolution) was from the equation  $R_s = 1.18 \left( \frac{t_2 - t_1}{\sum W_{1/2}} \right)$ , where  $t_1$  is migration time of the first enantiomer,  $t_2$  is migration time of the second enantiomer, and  $W_{1/2}$  is summation of peak width at half height. The  $R_s$  values between two peaks of enantiomers when employing 4.0 mM and 5.0 mM CM- $\beta$ -CD were  $1.52 \pm 0.06$  and  $1.51 \pm 0.4$ , respectively. Increasing CM- $\beta$ -CD concentration to 6.0 mM could affect the velocity of electroosmotic flow (EOF) (see caffeine peaks, the EOF marker, in

Figure 2). This effect was similarly observed in the previous reports (15, 18). Therefore 4.0 mM CM- $\beta$ -CD was chosen for separation of drugs with different chemical structures (see Table 1) since 4.0 mM gave more reproducible migration times (less than 1.2% RSD) compared to the use of 5 mM CM- $\beta$ -CD (up to 1.7% RSD, results are not shown). In addition, decreasing the CD concentration lowers the final analysis cost of the developed method.

#### Application of enantiomeric separation of chiral drugs by single CE-UV method

Four different chiral drugs (atenolol, propranolol, octopamine, and ibuprofen) were tested using the single CE method. Their chemical structures are shown in Table 1





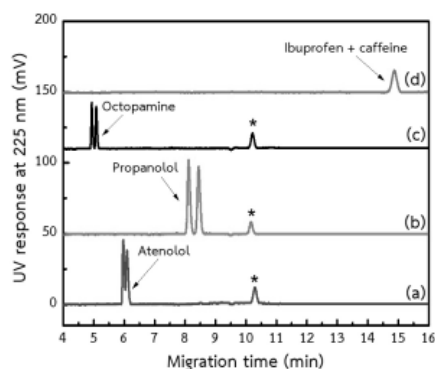
Table 1 Chemical properties of target enantiomeric compounds

Enantiomer compound	Chemical name	Chemical structure	Molecular weight (g/mol)	pKa
<b>β-blockers</b>				
Atenolol (C <sub>14</sub> H <sub>22</sub> N <sub>2</sub> O <sub>3</sub> )	2-[4-[2-hydroxy-3-(propan-2-ylamino)propoxy]phenyl]acetamide		266.34	9.60
Propranolol (C <sub>16</sub> H <sub>21</sub> NO <sub>2</sub> )	1-naphthalen-1-yloxy-3-(propan-2-ylamino)propan-2-ol		259.35	9.42
<b>Neurotransmitter</b>				
Octopamine (C <sub>8</sub> H <sub>11</sub> NO <sub>2</sub> )	4-(2-amino-1-hydroxyethyl)phenol		153.18	9.64
<b>NSAID</b>				
Ibuprofen (C <sub>13</sub> H <sub>18</sub> O <sub>2</sub> )	2-[4-(2-methylpropyl)phenyl]propionic acid		206.28	4.91

Figure 3 shows the electropherograms of the four compounds; atenolol (Figure 3a), propranolol (Figure 3b), octopamine (Figure 3c) and ibuprofen (Figure 3d). The separation of these drug compounds were carried out using a single CE condition (running buffer condition was phosphate buffer (20.0 mM, pH 2.7) containing 4.0 mM CM-β-CD). However separation was not successful for Ibuprofen. This may be due to ibuprofen being a weak acid ( $pK_a=4.91$ ) and its ionization is suppressed at pH 2.7 of the running buffer. Therefore it may migrate the same velocity as caffeine (see Figure 3d). TM-β-CD was reported as a suitable selector for enantiomeric compound containing a carboxylic group. As discussed by Zhu et al. [17], separation of *S* and *R* enantiomers of ibuprofen was achieved by employing TM-β-CD chiral selector in the running buffer (0.10 M, pH 4.92) with 0.1% HPMC. However

in our work we did not use TM-β-CD since we wish to employ a single buffer system for capillary electrophoresis. Thus separation of enantiomers of ibuprofen could not be achieved when employing CM-β-CD.

Separation of enantiomers by adding a chiral selector, such as cyclodextrin, is achieved by formation of a complex with the selector due to the inclusion of enantiomer as guest into the hydrophobic cavity of cyclodextrin as host. This interaction is due to Van der Waals and hydrophobic interaction. The equilibrium or thermodynamic complexation is characterized by a binding constant or distribution constant,  $K$ . The different affinities of enantiomers give rise to different values of  $K$  (i.e.,  $K_S \neq K_R$ ). This causes different mobility of each enantiomer leading to different migration time of enantiomers [19-23].



**Figure 3.** Electropherogram of chiral compounds, (a) atenolol, (b) propranolol, (c) octopamine (25.0  $\mu\text{M}$ ), (d) ibuprofen (1000.0  $\mu\text{M}$ ) containing 250.0  $\mu\text{M}$  caffeine. CE conditions: phosphate buffer (20.0 mM, pH 2.7) containing CM- $\beta$ -CD (4.0 mM), electrokinetic injection for 2.0 s at 261.3 V  $\text{cm}^{-1}$ , applied electrical field strength of 348.4 V  $\text{cm}^{-1}$  and UV detection at 225 nm. \*Caffeine 250.0  $\mu\text{M}$  as EOF marker.

## Conclusion

We report a single method for separation of enantiomers by employing capillary electrophoresis with UV detection. The method was used for separation of various racemic drugs, such as atenolol and propranolol ( $\beta$ -blocker drugs), octopamine (neurotransmitter drug) and Ibuprofen (NSAID drug). These compounds are commercially available and their chirality are not provided. Therefore investigation of the chiral property will be useful for possible future chirality applications. This work employed CM- $\beta$ -CD (4.0 mM) as a chiral selector in the running phosphate buffer (20.0 mM, pH 2.7). The CE method has an analysis time of only 12.0 min. The chiral separation of different three groups of drugs (*viz.* beta-blockers, neurotransmitters, NSAID drugs) was presented. This method has already been applied to amphetamine, methamphetamine, ephedrine, and pseudoephedrine [14].

Application of this CE-UV method may be applied to other drugs, such as arotinolol, clenbuterol, terbutaline sulfate, sotalol and other cardiovascular agents and bronchiectasis drugs to demonstrate the method performance [16].

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## References

1. Lloyd DK, Ahmed A, Pastoré F. A quantitative relationship between capacity factor and selector concentration in capillary electrophoresis and high performance liquid chromatography: evidence from the enantioselective resolution of benazoin using human serum albumin as a chiral selector. *Electrophoresis* 1997;18(6):958-64.
2. Potier I, Tamisier-Karolak SL, Morin P, Megel Taverna M. Comparison of native, alkylated and charged cyclodextrins for the chiral separation of labetalol stereoisomers by capillary electrophoresis. *J Chromatogr A* 1998;829(1-2):341-9.
3. Paik MJ, Nguyen DT, Kim KR. N-Menthoxycarbonylation combined with trimethylsilylation for enantioseparation of  $\beta$ -blockers by achiral dual-column gas chromatography. *J Chromatogr A* 2006; 1103(1):177-81.
4. Lv L, Wang L, Zou Y, Chen R, Yu J. Chiral separation by nonaqueous capillary electrophoresis using L-sorbose-boric acid complexes as chiral ion-pair selectors. *RSC Advances* 2016;6(106):104193-200.
5. Su Y, Mu X, Qi L. Development of a capillary electrophoresis system with Mn(II) complexes and  $\beta$ -cyclodextrin as the dual chiral selectors for enantioseparation of dansyl amino acids and its application in screening enzyme inhibitors. *RSC Advances* 2015;5(36):28762-8.
6. Mavroudi MC, Kapnissi-Christodoulou CP. Combined use of L-alanine tert butyl ester lactate and trimethyl-beta-cyclodextrin for the enantiomeric separations of 2-arylpropionic acids nonsteroidal anti-inflammatory drugs. *Electrophoresis* 2015;36(19):2442-50.
7. Lebedeva MV, Prokhorova AF, Shapovalova EN, Shpigun OA. Electrophoretic enantioseparation of profens in water-methanol solutions using eremomycin as a chiral selector. *Mosc Univ Chem Bull* 2013;68(5):215-8.
8. Maruszak W, Trojanowicz M, Margasińska M, Engelhardt H. Application of carboxymethyl- $\beta$ -cyclodextrin as a chiral selector in capillary electrophoresis for enantiomer separation of selected neurotransmitters. *J Chromatogr A* 2001;926(2):327-36.
9. Kong D, Yang W, Duan K, Cui Y, Xing S, Zhang X, et al. Capillary electrophoretic enantioseparation of m-nisoldipine using two different beta-cyclodextrins. *J Sep Sci* 2009;32(18):3178-83.
10. Machin R, Isasi JR, Vélaz I.  $\beta$ -Cyclodextrin hydrogels as potential drug delivery systems. *Carbohydr Polym* 2012;87(3):2024-30.
11. Weinberger R. Practical capillary electrophoresis. Second ed. New York: Academic Press; 2000. 459 p.
12. Fanali S. Identification of chiral drug isomers by capillary electrophoresis. *J Chromatogr A* 1996;735(1-2): 121-77.



13. Podar A, Suciu S, Oprean R. Review-Recent enantiomer separation strategies of nonsteroidal anti-inflammatory drugs (NSAIDs) by capillary electrophoresis. *Farmacia* 2016;64(2):159-70.
14. Tophan P. Simple capillary electrophoresis system for chiral analysis of illicit drugs. M.Sc. Thesis, Mahidol University. Thailand; 2014.
15. Saz JM, Marina ML. Recent advances on the use of cyclodextrins in the chiral analysis of drugs by capillary electrophoresis. *J Chromatogr A* 2016;1467:94-79.
16. Fang L, Du Y, Hu X, Luo L, Guo X, Yu J. Carbocymethyl- $\beta$ -cyclodextrine as chiral selector in capillary electrophoresis: enantioseparation of 16 basic chiral drugs and its chiral recognition mechanism associated with drugs's structural features. *Biomed Chromatogr* 2017;31:e3991.
17. Zhu X, Lin B, Epperlein U, Koppenhoefer B. Enantiomeric resolution of some nonsteroidal antiinflammatory and anticoagulant drugs using  $\beta$ -cyclodextrins by capillary electrophoresis. *Chirality* 1999;11(1):62-5.
18. Schmitt T, Engelhardt H. Derivatized cyclodextrins for the separation of enantiomers in capillary electrophoresis. *J High Resolut Chromatogr* 1993;16(9):525-9.
19. Zhu Q, Scriba GKE. Advances in the use of cyclodextrins as chiral selectors in capillary electrokinetic chromatography: fundamentals and applications. *Chromatographia* 2016;79(21):1403-35.
20. Ranzuglia GA, Manzi SJ, Gomez MR, Belardinelli RE, Pereyra VD. An analytical model for enantioseparation process in capillary electrophoresis. *Physica A* 2017;487:153-63.
21. Lancioni C, Keunchkarian S, Castells CB, Gagliardi LG. Enantiomeric separations by capillary electrophoresis: theoretical method to determine optimum chiral selector concentration. *J Chromatogr A* 2018;1539:71-7.
22. Pang N, Zhang Z, Bai Y, Liu H. A study of the interaction between enantiomers of zolmitriptan and hydroxypropyl-beta-cyclodextrin by capillary electrophoresis. *Anal Bioanal Chem* 2009;393(1):313-20.
23. Al Azzam KM, Saad B, Aboul-Enein HY. Determination of the binding constants of modafinil enantiomers with sulfated  $\beta$ -cyclodextrin chiral selector by capillary electrophoresis using three different linear plotting methods. *Electrophoresis* 2010;31(17):2957-63.

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