CYCLODEXTRIN-MODIFIED MICELLAR ELECTROKINETIC CHROMATOGRAPHY FOR THE ENANTIOSEPARATION OF IMIDAZOLE AND VINPOCETINE DRUGS

SITI MUNIRAH BINTI ABD WAHIB

UNIVERSITI TEKNOLOGI MALAYSIA

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Universiti Teknologi Malaysia

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"……Act! Allah will behold your actions, and (so will) His messenger and the believers, and ye will be brought back to the Knower of the Invisible and the Visible, and He will tell you what ye used to do" (A Taubah: verse 105)

This Thesis is dedicated to my beloved family.

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ABSTRACT

In the present work, cyclodextrin-modified micellar electrokinetic chromatography (CD-MEKC) method was developed and applied for enantioseparation of three imidazole drugs and vinpocetine. The three imidazole drugs namely tioconazole, isoconazole and fenticonazole were simultaneously separated for the first time by MEKC technique using dual cyclodextrin (CD) approach. A combination of two neutral CDs; 2-hydroxypropyl-γ-CD (HP-γ-CD) and heptakis (2,6-di-*O*-methyl)-β-CD (DM-β-CD) (35 mM: 10 mM) in background electrolyte (BGE) containing 35 mM phosphate buffer (pH 7.0), 50 mM sodium dodecyl sulfate (SDS) and 15% (v/v) acetonitrile at 27 kV and 30^{o}C gave the best separation of six stereoisomers of imidazole drugs with resolutions, R_s 1.90-27.22 and peak efficiencies, N > 180 000 in less than 15 min. The samples were injected electrokinetically at 3 kV for 3 s and detection was carried out at 200 nm. The method was linear over the concentration range of 25-200 mg/L ($r^2 > 0.998$) and the detection limits (S/N = 3) of the three imidazole drugs were found to be 2.7-7.7 mg/L. The CD-MEKC method was successfully applied to the determination of the three imidazole drugs in spiked human urine to give mean recoveries ranging from 72.3 to 107.5% (RSD < 6%, n = 3). The method was also applied to the analysis of commercial cream formulation of tioconazole and isoconazole. Good mean recoveries were obtained, ranging from 93.6-100% (RSD < 7%, n = 3). The best chiral separation of vinpocetine that gave four resolved peaks was achieved using 40 mM HP-β-CD in 50 mM phosphate buffer (pH 7.0) consisting of 40 mM SDS and 10% v/v acetonitrile at a separation temperature of 25^{o}C and separation voltage 25 kV. Samples were injected electrokinetically at 5 kV for 7 s. Vinpocetine detection was accomplished using diode array detector at 200 nm. The complete vinpocetine separation was achieved in less than 15 min with peak resolution, R_s 1.40-5.80.

ABSTRAK

Dalam kajian ini, kaedah kromatografi elektrokinetik misel terubahsuai siklodekstrin (CD-MEKC) telah dibina dan diaplikasikan untuk pemisahan enantiomer tiga dadah imidazol dan vinposetin. Tiga dadah imidazol iaitu tiokonazol, isokonazol dan fentikonazol telah dipisahkan secara serentak untuk pertama kalinya menggunakan teknik MEKC dengan dua siklodektrin (CD). Kombinasi dua CD neutral; 2-hidroksipropil-γ-CD (HP-γ-CD) dan heptakis(2,6-di-*O*-metil)-β-CD (DM-β-CD) (35 mM: 10 mM) dalam latarbelakang elektrolit yang mengandungi 35 mM larutan penimbal fosfat (pH 7.0), 50 mM natrium dodesil sulfat (SDS) dan 15% v/v asetonitril pada 27 kV dan 30°C telah memberikan pemisahan terbaik bagi enam stereoisomer dadah imidazol dengan resolusi, R_s 1.90-27.22 dan kecekapan puncak, N > 180 000 dalam masa kurang daripada 15 min. Sampel disuntik secara elektrokinetik pada 3 kV selama 3 s pada pengesanan panjang gelombang 200 nm. Kaedah ini adalah linear dalam julat kepekatan 25-200 mg/L (r^2 > 0.998) dan had pengesanan (S/N = 3) tiga dadah imidazol yang diperoleh ialah 2.7-7.7 mg/L. Kaedah CD-MEKC ini telah diaplikasikan dengan jayanya bagi penentuan tiga dadah imidazol dalam sampel air kencing dengan purata perolehan semula dalam julat 72.3 hingga 107.5% (RSD < 6%, n = 3). Kaedah ini juga telah diaplikasikan kepada analisis krim formula komersial tiokonazol dan isokonazol. Purata perolehan semula yang baik telah diperoleh dalam julat 93.6-100% (RSD < 7%, n = 3). Pemisahan kiral terbaik vinposetin yang memberikan empat puncak diperoleh menggunakan 40 mM HP-β-CD dalam 50 mM larutan penimbal fosfat (pH 7.0) yang mengandungi 40 mM natrium dodesil sulfat (SDS) dan 10% v/v asetonitril pada suhu pemisahan 25°C dan voltan pemisahan 25 kV. Sampel disuntik secara elektrokinetik pada 5 kV selama 7 s. Vinposetin dikesan menggunakan pengesan susun atur diod pada panjang gelombang 200 nm. Pemisahan lengkap vinposetin telah diperoleh dalam masa kurang daripada 15 minit dengan resolusi puncak yang baik, R_s 1.40-5.80.