

Analisis asam valproat menggunakan metode dried blood spot secara kromatografi cair kinerja ultra tinggi tandem spektrometri massa = Analysis of valproic acid with dried blood spot method by ultra performance liquid chromatography mass spectrometer

Muhammad Falahuddin Malich Salaz, author

Deskripsi Lengkap: <https://lib.ui.ac.id/detail?id=20411457&lokasi=lokal>

Abstrak

Asam valproat merupakan obat anti epilepsi yang bisa digunakan pada semua tipe epilepsi dan berkembang sebagai terapi tambahan untuk penyakit bipolar. Obat ini memiliki indeks terapi sempit sehingga dibutuhkan pemantauan terapi obat menggunakan metode dried blood spot yang sederhana dan mudah dilakukan serta akurat. Tujuannya untuk memperoleh kondisi optimum dan metode tervalidasi asam valproat dalam darah total secara Kromatografi Cair Kinerja Ultra Tinggi Tandem Spektrometri Massa KCKUT SM SM Larutan kontrol kualitas dan kurva kalibrasi sampel darah dibuat dengan menotolkan masing-masing sebanyak 20 L dan dikeringkan selama lebih kurang 1 jam. Kertas DBS dipotong sekitar lebih kurang 5 mm dan diekstraksi menggunakan campuran larutan asetonitril metanol 1:3 yang mengandung baku dalam asam benzoat dengan konsentrasi 1000 g/mL. Pemisahan dilakukan menggunakan kolom Waters Acquity™ UPLC C18 1.7 μm 2.1 x 100 mm dengan fase gerak berupa campuran asam asetat 0.1 asetonitril 40:60 dengan elusi isokratik dan laju alir 0.4 mL/menit. Deteksi massa dilakukan dengan Waters Xevo TQD tipe Electrospray Ionization ESI negatif pada mode Multiple Reaction Monitoring. Pendeteksian asam valproat berada pada nilai m/z 142.95, 142.95 dan asam benzoat pada m/z 121.1, 77.1. Metode ini linear pada rentang 0.5 - 100 g/mL dengan r² 0.9991. Akurasi dan presisi baik within run maupun between run memenuhi persyaratan dengan nilai diff dan KV tidak melebihi 15 dan tidak lebih dari 20 pada konsentrasi LLOQ. Sampel DBS stabil minimal 16 hari pada suhu kamar. Metode analisis tervalidasi diaplikasikan terhadap satu subjek sehat dan diperoleh C_{max} sebesar 88.15 g/mL dan T_{max} 1.5 jam. Secara keseluruhan metode ini memenuhi persyaratan validasi menurut EMEA Guideline 2011.

.....

Valproic acid (VA) is a drug of anticonvulsant which is used to treat all types of epilepsy and has been developed as an adjuvant therapy for bipolar disorder. Valproic acid (VA) has a narrow therapeutic window index that needs therapeutic drug monitoring with dried blood spot method which is simple, easy, and accurate. This aim of this research is to develop an optimum and validated method for valproic acid in whole blood as Dried Blood Spot method using Ultra Performance Liquid Chromatography tandem Mass Spectrometry (UPLC-MS/MS). Quality control and calibration samples were obtained by pipetting 20 L onto CAMAG DBS Paper and left to dry at room temperature for 1 h before processing. Using a 5 mm punch cutter, discs were transferred to microtube and 200 L extraction solution asetonitril metanol 1:3 containing benzoic acid as internal standard. 1000 g/mL was added. Chromatographic separation was achieved by Waters Acquity™ UPLC C18 1.7 μm 2.1 x 100 mm with mobile phase consist of 0.1 acetic acid: acetonitrile 40:60 under isocratic elution and flow rate was 0.4 mL/min. Mass detection was performed on Waters Xevo TQD equipped with an electrospray ionization (ESI) source at negative ion mode in the multiple reaction monitoring (MRM) mode. Valproic acid (VA) was detected at m/z 142.95, 142.95; benzoic acid at m/z 121.1, 77.1. This method was linear in range concentration of 0.5 - 100 g/mL with r² 0.9991. This method also fulfill the acceptance of accuracy and

precision within and between run in three days by diff and coefficient of variation CV not more than 15 and not more than 20 for LLOQ concentration The DBS Card samples is stable at least for 16 days at room temperature Validation method was applied in one healthy subject was obtained C_{max} 88.15 g/mL with T_{max} 1.5 h Overall this method fulfill the acceptance criteria of validation based on EMEA Guideline 2011.