

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

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Abstrak

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 m 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 ndash 100 g mL dengan r 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 Cmax sebesar 88 15 g mL dan Tmax 1 5 jam Secara keseluruhan metode ini memenuhi persyaratan validasi menurut EMEA Guideline 2011

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ABSTRACT

Valproic acid VA is drug of anticonvulsant which used to treat all types of epilepsy and be developed as an adjuvant therapy for bipolar disorder Valproic acid VA has a narrow of therapeutic window index that need 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 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 Disc 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 m 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 121.11 77.1 This method was linear in range concentration of 0.5–100 g/mL with r 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