OPTIMASI FASE GERAK METODE BIOANALISIS KARBAMAZEPIN DAN KARBAMAZEPIN 10,11-EPOKSIDA DALAM *SPIKED*-PLASMA MANUSIA SERTA UJI STABILITASNYA MENGGUNAKAN KROMATOGRAFI CAIR KINERJA TINGGI

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INTISARI

Karbamazepin (CBZ) merupakan obat antikonvulsan yang memiliki indeks terapetik sempit. Metabolit aktifnya berupa karbamazepin 10,11-epoksida (CBZ-E) dapat meningkatkan efek toksisitas. Tujuan penelitian ini adalah untuk mengetahui metode bioanalisis yang tepat serta stabilitas CBZ dan CBZ-E selama masa analisis yang digunakan dalam aplikasi TDM. Metode yang digunakan adalah kromatografi cair kinerja tinggi (KCKT) detektor DAD dengan parameter yang didasarkan pada kriteria *European Medicines Agency* (EMA) dan *Center of Drug Evaluation and Research* (CDER). Sistem yang digunakan adalah HPLC-DAD dengan panjang gelombang 210 nm, fase diam kolom C18 *reverse phase* (150 mm x 4,6 mm, 5 µm), fase gerak metanol: air (60:40, v/v), laju alir 1 mL/menit dan menggunakan pelarut metanol. Preparasi sampel menggunakan proses pengendapan protein menggunakan asetonitril dan ekstraksi cair-cair menggunakan heksan. Optimasi fase gerak yang dilakukan yaitu metanol: air (60:40 v/v), metanol: air (70:30 v/v), air: asetonotril (50:50 v/v) dan hasil fase gerak terbaik yaitu metanol: air (60:40 v/v) dengan waktu retensi CBZ 4,587 menit dan CBZE 2,730 menit. Hasil uji linearitas kurva baku CBZ dan CBZE menghasilkan nilai r = 0,998 dan r = 0,993. Berdasarkan hasil uji stabilitas diketahui bahwa larutan standar CBZ dan CBZE stabil selama 24 jam di suhu 25°C dan selama 30 hari di suhu 4°C, CBZ dalam *spiked*-plasma stabil selama 24 jam di suhu 25°C, stabil selama 30 hari pada suhu -20°C, dan stabil dalam 3 kali siklus beku cair dan pada CBZE dalam *spiked*-plasma stabil selama 6 jam di suhu 25°C, stabil selama 21 hari pada suhu -20°C dengan nilai *%diff* ± 15,00 %.

Kata Kunci: Karbamazepin, karbamazepin 10,11-epoksisa, KCKT-DAD, Uji Stabilitas.

OPTIMIZATION OF MOBILE PHASE BIOANALYSIS METHOD CARBAMAZEPIN AND CARBAMAZEPIN 10,11-EPOXIDE IN HUMAN SPIKED-PLASMA AND STABILITY TEST USING HIGH-PERFORMANCE LIQUID CHROMATOGRAPHY

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ABSTRACT

Carbamazepine (CBZ) is an anticonvulsant drugs with a narrow therapeutic index. The active metabolite is carbamazepine 10,11-epoxide (CBZ-E) can increase the effect of toxicity. The purpose of this study was to determine the appropriate bioanalytical method and the stability of CBZ and CBZ-E during the analysis period used in TDM applications. The method used is high-performance liquid chromatography (HPLC) DAD detector with parameters based on the criteria of the European Medicines Agency (EMA) and the Center of Drug Evaluation and Research (CDER). The system used is UHPLC-DAD with a wavelength of 210 nm, stationary phase column C18 reverse-phase (150 mm x 4.6 mm, 5 m), methanol: water (60:40, v/v) mobile phase, a flow rate of 1 mL/min, and using methanol as solvent. Sample preparation using protein deposition process using acetonitrile and liquid-liquid extraction using hexane. Optimization of the mobile phase carried out in methanol: water (60:40 v/v), methanol: water (70:30 v/v), water: acetonitrile (50:50 v/v), and the best mobile phase results are methanol: water (60:40 v/v) with a retention time of CBZ 4,587 minutes and CBZE 2,730 minutes. The results of the linearity test of the CBZ and CBZE standard curves resulted in the values of r = 0.998 and r = 0.993. Based on the results of the stability test, it is known that the standard solutions of CBZ and CBZE are stable for 24 hours at 25°C and 30 days at 4°C, CBZ in spiked-plasma is stable for 24 hours at 25°C, stable for 30 days at -20°C, and stable for 3 cycles of freeze-thaw and CBZE in spiked-plasma stable for 6 hours at 25°C, stable for 21 days at -20°C with a value of %diff ± 15,00 %.

Keywords: Carbamazepine, Carbamazepin 10,11-Epoxide, HPLC-DAD, Stability Test