

Analisis Tamoksifen dan Metabolit Aktifnya dalam Volumetric Absorptive Microsampling Pasien Kanker Payudara Menggunakan Kromatografi Cair Kinerja Ultra Tinggi-Spektrometri Massa = Analysis Of Tamoxifen and Its Active Metabolites in Volumetric Absorptive Microsampling of Breast Cancer Patients by Ultrahigh Performance Liquid Chromatography-Mass Spectrometry

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Abstrak

Tamoksifen merupakan salah satu antiestrogen golongan Selective Estrogen Receptor Modulator yang telah dijadikan standar utama dalam mengobati kanker payudara ER+. Tamoksifen akan mengalami metabolisme membentuk tiga metabolit aktif, diantaranya: N-desmetiltamoksifen, 4-hidroksitamoksifen, dan endoksifen, metabolit yang memberikan efek terapi. Konsentrasi endoksifen > 3,3 ng/mL pada sampel darah kering memiliki tingkat kekambuhan 30% lebih rendah. Dalam analisis kadar tamoksifen dan metabolitnya, pengambilan sampel darah dapat dilakukan melalui fingerprick dengan teknik biosampling Volumetric Absorptive Microsampling (VAMS). Penelitian ini bertujuan untuk menganalisis kadar tamoksifen dan metabolit aktifnya pada 35 pasien kanker payudara dalam sampel VAMS untuk memantau kadarnya dalam darah dengan mengaplikasikan suatu metode analisis senyawa. Metode ultrasound-assisted liquid extraction digunakan untuk preparasi sampel VAMS dan dianalisis menggunakan Kromatografi Cair Kinerja Ultra Tinggi-Spektrometri Massa (KCKUT-SM/SM) dengan baku dalam propranolol. Metode analisis yang digunakan untuk penelitian ini telah divalidasi parsial dan telah memenuhi persyaratan serta linear pada rentang konsentrasi 2,5 – 200 ng/mL untuk tamoksifen; 2,5 – 40 ng/mL untuk endoksifen; 3 – 30 ng/mL untuk 4-hidroksitamoksifen; dan 2 – 600 ng/mL untuk N-desmetiltamoksifen. Hasil yang diperoleh dari 35 sampel VAMS ialah rentang kadar tamoksifen terukur 16,16 ng/mL hingga 160,82 ng/mL, kadar endoksifen 3,37 ng/mL hingga 28,09 ng/mL, kadar 4-hidroksitamoksifen 1,55 ng/mL hingga 24,08 ng/mL, dan kadar N-desmetiltamoksifen 206,01 ng/mL hingga 590,79 ng/mL. Semua sampel VAMS pasien yang dianalisis memiliki kadar endoksifen di atas 3,3 ng/mL melebihi ambang batas.

.....Tamoxifen is one of the antiestrogens of the Selective Estrogen Receptor Modulator class that has become the main standard in treating ER+ breast cancer. Tamoxifen is metabolized into three active metabolites, including: N-desmethyltamoxifen, 4-hydroxytamoxifen, and endoxifen, metabolites that provide therapeutic effects. Endoxifen concentrations above 3.3 ng / mL in dried blood spot have a 30% lower recurrence rate. In the analysis of tamoxifen levels and their metabolites, blood sampling can be done with biosampling technique, Volumetric Absorptive Microsampling (VAMS). This study aims to analyze the levels of tamoxifen, endoxifen, 4-hydroxytamoxifen, and N-desmethyltamoxifen in 35 breast cancer patients in VAMS samples to monitor their levels in the blood by applying a compound analysis method. Ultrasound-assisted liquid extraction method was used to extract VAMS samples and analyzed using UPLC-MS/MS with propranolol as internal standard. The analytical method used for this research has been partially validated and has met the requirements as well and linear with the linearity range of 2.5 – 200 ng/mL for tamoxifen; 2.5 – 40 ng/mL for endoxifen; 3 – 30 ng/mL for 4-hydroxytamoxifen; and 2 – 600 ng/mL for N-desmethyltamoxifen. The result on 35 VAMS samples showed that tamoxifen levels were in

the range of of 16.16 ng / mL to 160.82 ng / mL; 3.37 ng / mL to 28.09 ng / mL for endoxifen; 1.55 ng / mL to 24.08 ng / mL for 4-hydroxytamoxifen; and 206.01 ng / mL to 590.79 ng / mL for N desmethytamoxifen. All VAMS samples of patients analyzed had endoxifen levels above 3.3 ng / mL exceeding the threshold.