**Monitoring of Tamoxifen, Endoxifen, and 4-Hydroxytamoxifen in Dried Blood Spots of Breast Cancer Patients using Liquid Chromatography-tandem Mass Spectrometry**

**Callista Andinie Mulyadi1**, Yahdiana Harahap1,2, Baitha Palanggatan Maggadani1, Denni Joko Purwanto3

1 Faculty of Pharmacy, Universitas Indonesia, Depok, Indonesia

2 Faculty of Military Pharmacy, the Republic of Indonesia Defense University, Bogor, Indonesia

3 Functional Medical Staff of Surgical Oncology, Dharmais Cancer Hospital, Jakarta, Indonesia

**Background and aims.** Tamoxifen is a Selective Estrogen Receptor Modulator (SERM) that is used as an adjuvant therapy for ER+ breast cancer. Upon administration, tamoxifen is metabolized to two main metabolites: endoxifen which is responsible for its therapeutic effect and 4-OHT which can increase the risk of endometrial cancer according to some researches. Efficacy of tamoxifen therapy can be assessed from clinical threshold of endoxifen, in which patients with endoxifen level above 3,3 ng/mL have a 26% lower recurrence rate. This research aims to analyze tamoxifen, endoxifen and 4-hydroxytamoxifen in dried blood spots (DBS) from breast cancer patients who received tamoxifen as an adjuvant therapy.

**Methods.** DBS samples are extracted by protein precipitation method and are analyzed using UPLC-MS/MS. The method was clinically applied to 29 breast cancer patients who received tamoxifen to evaluate the effectivity of the therapy received by patients.

**Results.** This method is partially validated and linear within range of 5 – 200 ng/mL for tamoxifen, 1 – 40 ng/mL for endoxifen, and 0.5 – 20 ng/mL for 4-hydroxytamoxifen. The result on 29 breast cancer patients showed that tamoxifen levels were in the range of 30.29 and 188.63 ng/mL for tamoxifen, 1.45 and 28.77 ng/mL for endoxifen, 0.21 and 11.28 ng/mL for 4-hydroxytamoxifen.

**Conclusion/Discussion.** This method has met the validation criteria in accordance with EMA and FDA guidelines. It was effectively used to quantify tamoxifen, endoxifen, and 4-hydroxy-tamoxifen in dried blood spots (DBS) from ER+ breast cancer patients. The levels of tamoxifen and its metabolites varied significantly among patients, with two individuals showing endoxifen concentrations below the established clinical threshold.

**References:**

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