Ekawan Yoosakul et al., Chem Sci J 2017, 8:4 (Suppl)
DOI: 10.4172/2150-3494-C1-015

Simultaneous determination of Efavirenz/Emtricitabine/Tenofovir Disoproxil Fumarate in human plasma by liquid chromatography-tandem mass spectrometry with electrospray ionization method and its application to a bioequivalence study

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Efavirenz (EFV)/Emtricitabine (FTC)/Tenofovir Disoproxil Fumarate (TDF) formulation is a combination of antiretroviral agents which is indicated for the first-line regimen for treatment of HIV-1 infection. Several LC-MS/MS methods which developed for determine EFV/FTC/TDF in biological samples has been reported using various extraction methods. A selective, precise, accurate and reproducible Liquid Chromatography-tandem Mass Spectrometry (LC-MS/MS) assay method has been developed and validated for simultaneous determination of the human plasma concentration of EFV/FTC/TDF using Efavirenz-d5, Emtricitabine [$^{2}H_{3}$-^{15}N] and Tenofovir-d7 as Internal Standards (IS). The analytes and ISs were extracted from human plasma via solid phase extraction method which validated as per the US FDA guidance for industry, bioanalytical method validation and the guideline on bioanalytical method validation of European Medicines Agency. The reconstituted samples were chromatographed on ACE5 CN column using gradient mobile phase system composed of 1 mM ammonium acetate buffer (pH 2.1):methanol and monitored in the positive ion mode by applying ESI probe. The calibration curves were linear (r^2>0.99) over the concentration range of 50.453-6074.957 ng/mL, 50.213-3015.858 ng/mL and 10.276-806.678 ng/mL of EFV, FTC and TDF, respectively. The results of intra and inter day precision and accuracy studies were within the acceptable limits. The method was successfully applied to a bioequivalence study of EFV/FTC/TDF 600/200/300 mg tablets formulation after oral administration to 52 healthy Thai volunteers under fasting condition. The 90% confidence intervals of the least squares means ratios of the test to the reference product of AUC_{0-72} and C_{max} of EFV and $AUC_{0-tlast}$, $AUC_{0-\infty}$ and C_{max} of FTC and TDF were within the bioequivalence range of 80.00-125.00%.

Biography

Ekawan Yoosakul is currently working as a Researcher in Bioequivalence Study Group, Research and Development Institute, the Government Pharmaceutical Organization (GPO), Bangkok, Thailand, responsible for method development, method validation and bioanalysis in biological fluids.

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