

## Abstract

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Title of diploma thesis: Study of effects of prolonged administration of emtricitabine on expression of ABC efflux transporters in maternal and fetal organs

The aim of this thesis was to evaluate the effect of chronic administration of antiretroviral substance emtricitabine (FTC) on expression of drug efflux ABC-binding cassette (ABC) transporters in the placenta, maternal and fetal organs (brain, liver, kidney, small intestine) of pregnant rats. We focused on two most important representatives of drug efflux ABC transporters, P-glycoprotein (MDR1) and Breast Cancer Resistance Protein (BCRP). Knowledge of FTC effects on gene expression of these transporters is crucial especially when using FTC in combination therapy, known as Highly Active Antiretroviral Therapy (HAART). Changes in MDR1/BCRP expression may lead to significantly altered pharmacokinetics of concomitantly administered drugs. First, bioavailability was analyzed. AUC of FTC (3,5 mg/kg) following i.m. administration was comparable to that one after i.v. administration allowing us to use i.m. application as a route of FTC administration to rats. Subsequently, quantitative gene expression analysis of *Mdr1a*, *Mdr1b*, and *Bcrp* was carried out using reverse transcriptase polymerase chain reaction in real time (qRT-PCR). Gene expression analysis was performed in organs isolated from Wistar pregnant rats that were administered FTC (i.m.) for 10 days, half the time of pregnancy. In none of the tested tissues, maternal or fetal organs and placentas any significant change in expression of the drug efflux transporters tested was observed. Data obtained in this study contribute to the understanding of safety profile of FTC.