Charles University

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Title of diploma thesis: Study of effects of antiretroviral drugs on transmembrane transport of tenofovir disoproxil fumarate across MDCKII - ABCB1 cell monolayer

Tenofovir disoproxil fumarate (TDF) - ester prodrug of tenofovir is considered as one of the most frequently used component of combination antiretroviral therapy. Several ways of application and good patients' tolerability is typical for this compound. TDF is a substrate of dug transporter such as P-glycoprotein (P-gp) therefore its efflux activity may limit the bioavailability after oral administration and distribution of TDF. As many of antiretroviral drugs are also substrates or inhibitors of P-gp, drug - drug interactions with TDF at the level of transmembrane transport could be expected.

The aim of the diploma thesis was to describe effects of co-administered antiretroviral drugs on transfer of TDF across MDCKII cell monolayer by using bidirectional transport and concentration equilibrium setups.

The results of experiments confirmed that TDF is a substrate of P-gp. High values of efflux ratio describing transmembrane transport of TDF across parental cells have been observed. This indicates the participation of canine endogenous transporters expressed by MDCKII cells. The similar effects of tested antiretroviral drugs - TDF, abacavir, indinavir and saquinavir across both of monolayers have been observed. This caused complication in the interpretation of the results. MDCKII cell line does not seem to be appropriate for determination drug - drug interactions of TDF caused on P-gp and potentially on other transporters either and the data collected from transport experiments have not provided proper information draw definite conclusions.