Physiologically-based pharmacokinetic model of topical intra-vaginal HIV prevention

Authors: Katherine Kay¹, Lisa C. Rohan², Dhavalkumar Shah¹, Robert Bies¹

Affiliations: (1) State University of New York at Buffalo; (2) University of Pittsburgh

Objectives: A physiologically-based pharmacokinetic (PBPK) model of the vaginal space was developed with the aim to optimizing the probability of success of the vaginally administered dapivirine (DPV) for HIV prevention was developed. We focus on vaginal delivery using either a ring [1] and film [2].

Methods: The physiological structure of the vaginal space was described mathematically as a PBPK model and implemented in MATLAB. Literature reviews provided estimates of the physiological and physiochemical parameters. Drug concentration-time profiles were simulated in luminal fluids, vaginal tissue and plasma after administration of ring or film. Patient data was extracted from published clinical trials [1, 2] and used to test the model predictions.

Results: The DPV ring simulations of the two reported dosing regimens [1] resulted in predictions that were in close agreement with reported DPV concentrations in luminal fluids and plasma. The DPV film study [2] reported drug concentration at only a single time point per patient, the simulated profiles pass through the reported concentration range.

Conclusions: HIV continues to be a major public health issue and vaginal microbicides have the potential to provide a crucial, female-controlled option for protection. The PBPK model successfully simulated a realistic representation of drug PK. This provides a reliable, inexpensive and accessible platform where the potential effectiveness of new compounds and the robustness of treatment modalities can be evaluated.