Pharmacokinetic Modeling of in vitro Diffusion Rates for Antiviral Drug Acyclovir

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Acyclovir is an antiviral drug used in the treatment of Herpes Labialis, a difficult to treat viral infection affecting over 140 million people worldwide. Traditionally, administration of Acyclovir has been by oral or intravenous route. These formulations are effective but face difficulty in clearance from the kidneys in humans with poor renal or immunological function. Topical transdermal (via skin) delivery of acyclovir by cream or gel formulations can provide direct delivery to the site of infection, thereby alleviating nerve pain, reduce viral multiplication, and facilitate clearance. Topical application of acyclovir, an antiviral drug designed to treat herpes infections, was evaluated by using gel formulations with plasma concentrations similar to generic Zovirax formulations. Invitro diffusion rates for 5% acyclovir solution were collected via vertically mounted Franz diffusion cells with a dialysis membrane mounted between donor and receptor compartments. To create an in vivo predictive model of clearance, invitro diffusion data above were modified by applying human clearance data for acyclovir from published NIH studies. The obtained data were used to simulate the drug clearance rates in patients with normal renal function and impaired renal function. Invitro diffusion rates and in vivo clearance rates calculated above were used to model output concentration and clearance variables. Neural networks modeling of data provided statistical algorithms to pair input variables (initial concentrations, release rates, plasma concentrations) with predicted output variables (output concentration, clearance rate). Results showed a dose-dependent relationship of acyclovir that can be complicated by diffusion and renal clearance mechanisms.

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