

Abstract for AAPS 2006

## **Pharmacokinetics Of Acyclovir In Rabbit Dermis From Iontophoresis Of Cream, Gel And Solution Formulations**

Chinmay Shukla<sup>1</sup>, Phillip Friden<sup>2</sup> and Grazia Stagni<sup>1</sup>

<sup>1</sup>Arnold and Marie Schwartz College of Pharmacy, Long Island University, Brooklyn, NY;

<sup>2</sup>Transport Pharmaceuticals, Inc; Framingham MA

**Purpose:** To characterize *in vivo*, via microdialysis sampling, the iontophoretic delivery of acyclovir to the dermis from the following formulations: i) 5% cream (pH=6, anodal current); ii) soluble fraction of the same cream (pH=6, anodal current); iii) pH 11 solution (cathodal current); iv) 4% gel formulation (pH 11, cathodal current).

**Methods:** Custom made linear microdialysis probes were inserted into the upper dorsal shaved skin of tranquilized rabbits. Iontophoresis was performed at a constant current density of  $200\mu\text{A}/\text{cm}^2$  for 60 minutes using a cartridge, which consisted of a stainless steel electrode covered with a pad containing the formulation. Microdialysis was performed at a flow-rate of  $3\mu\text{L}/\text{min}$  for 3 hours. Dialysate samples were collected every 6 min; and analyzed for ACV via a validated HPLC assay. Retrodialysis was performed at a control site to estimate the recovery factor.

**Results:** Rabbits well tolerated the iontophoretic treatments and no redness or adverse events were observed during or after the experiments. Microdialysis probes recovery was  $54.5 \pm 0.7\%$  (mean  $\pm$  SE). The average AUCs were (mean  $\pm$  SE):  $15.6 \pm 4.2\ \mu\text{g}\cdot\text{min}/\text{mL}$  for the 5% cream;  $10.3 \pm 1.5\ \mu\text{g}\cdot\text{min}/\text{mL}$  for the soluble fraction of the same cream;  $337 \pm 163\ \mu\text{g}\cdot\text{min}/\text{mL}$  for the pH 11 solution;  $184 \pm 82\ \mu\text{g}\cdot\text{min}/\text{mL}$  for the 4% gel pH 11 formulation.

**Conclusions:** Cathodal iontophoresis of the gel (pH 11) and of the solution (pH 11) was more efficient than anodal iontophoresis of the cream (pH 6) indicating that electro-repulsion is a more effective mechanism of drug transport across the skin as compared to electro-osmosis for the iontophoretic system tested. There is no significant difference between the iontophoretic delivery from the cream and the soluble fraction of the same cream showing that most of the acyclovir delivered from the cream is located in the water phase.