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In Vivo Dermis Pharmacokinetics Of Acyclovir Following Iontophoresis From a Cream Formulation

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Purpose: To study the concentration time course of acyclovir (ACV) in skin *in vivo* via microdialysis sampling following iontophoresis (cathodal and anodal) or passive delivery from a cream formulation.

Methods: Linear microdialysis probes were inserted into the upper dorsal shaved skin of tranquilized rabbits. After one hour, iontophoresis was performed at $200\mu\text{A}/\text{cm}^2$ constant current density for 60 minutes using a drug cartridge which consisted of a stainless steel electrode covered with a pad that was filled with the formulation via a syringe. Dialysate samples were collected every 6 min (flow-rate: $3\mu\text{L}/\text{min}$) for 3 hours and analyzed for ACV via a validated HPLC assay. For the passive delivery studies, a similar patch was used and left in place for six hours. Dialysate samples were collected every 30 min (flow rate: $1\mu\text{L}/\text{min}$). Retrodialysis was performed at a control site for each experiment at the same experimental conditions as at the sampling site to estimate the recovery factor.

Results: Rabbits tolerated iontophoresis well and no redness or adverse events were observed during or after the treatments. The ACV skin concentrations for both passive delivery and cathodic iontophoresis were always extremely low, near the limit of detection ($5\text{ ng}/\text{mL}$; $n=3$). ACV skin concentration increased upon anodic iontophoresis ($\text{AUC}: 15.5 \pm 3.2\text{ mg}/\text{L}\cdot\text{min}$; mean \pm SE, $n=4$). Probes recovery was $27 \pm 2\%$ (mean \pm SE, $n=4$) at $3\mu\text{L}/\text{min}$ and $79 \pm 2\%$ ($n=3$) at $1\mu\text{L}/\text{min}$.

Conclusions: Iontophoresis significantly enhanced the delivery of acyclovir in a cream formulation into the skin as compared to passive delivery. Anodal iontophoresis was more effective than cathodal, indicating that, because of the neutral pH of the cream, electro-osmosis is the primary mode of drug transport across the skin. These data suggest that anodal iontophoretic delivery of acyclovir across the skin may be a much more effective treatment for herpes lesions.