

Iontophoretic Delivery of Tetracycline Hydrochloride Across Hairless Rat Skin

J.Paturi¹, C.Kolli¹, P.M.Friden² and A.K.Banga¹

¹Department of Pharmaceutical Sciences, Mercer University, Atlanta, GA 30341;

²Transport Pharmaceuticals Inc, Framingham, MA 01701.

Purpose: To study the iontophoretic transdermal delivery of tetracycline hydrochloride through hairless rat skin and compare the delivery efficiency as a function of different formulations and delivery parameters.

Methods: *In vitro* permeation studies were performed using freshly excised hairless rat skin mounted on side-by-side diffusion cells. A constant current source and silver/silver chloride electrodes were used for the delivery of current. The effect of pH (2.1, 3.0, 8.0, 9.2), current density (0.2, 0.3, 0.4 mA/cm²), and time of current application (30min, 1h, 2h) on the iontophoretic delivery of tetracycline hydrochloride was studied. Cathodal or anodal iontophoresis was used depending on the ionic state of the drug in the respective buffer media. Samples were collected at fixed time points and analyzed by HPLC.

Results: The cumulative amount of the drug delivered by passive permeation at the end of 10 h was $1.7 \pm 0.45 \mu\text{g}/\text{cm}^2$. Anodal iontophoresis (0.4 mA/cm²) for one hour at pH 3.0 enhanced the flux six fold resulting in permeation of $11.18 \pm 2.02 \mu\text{g}/\text{cm}^2$ of the drug at the end of 10 h. Cathodal iontophoresis at pH 9.2 (0.4 mA/cm²) further increased the delivery to $19.65 \pm 6.9 \mu\text{g}/\text{cm}^2$. The amount of drug permeated through the skin increased with an increase in the current density and time of application of current. An increase in current density from 0.2 to 0.4 mA/cm² increased the amount of drug permeated from $5.85 \pm 0.72 \mu\text{g}/\text{cm}^2$ to $19.65 \pm 1.91 \mu\text{g}/\text{cm}^2$. Dose response studies revealed enhanced delivery of the drug at higher donor concentrations. For a donor concentration of 10 mg/ml, $22.11 \mu\text{g}/\text{cm}^2$ of tetracycline hydrochloride permeated through the skin as compared to $8.25 \mu\text{g}/\text{cm}^2$ delivered from a donor concentration of 2.5 mg/ml.

Conclusions: The amount of drug permeated across the skin was greatest with cathodal iontophoresis at pH 9.2 followed by anodal iontophoresis at pH 3.0 and passive delivery at pH 3.0. The amount of drug permeated increased as current density increased and also as the donor concentration increased.

Acknowledgements: This study was funded by Transport Pharmaceuticals, Inc. Framingham, MA.