The dermapharmacokinetics approach suggested by the FDA proposes to evaluate the level of a topically applied drug in the stratum corneum (SC) during its uptake and clearance so as to calculate classic pharmacokinetic parameters [1].

**Assumption:** SC concentration-time curves are directly related to concentration-time curves in the epidermis and dermis.

Previous studies [2,3] have characterized the uptake phase of ibuprofen into the SC from a propylene glycol (PG) vehicle.

The goal of this work was to study the clearance phase of ibuprofen from the SC after 30 minutes of infinite dose application.

### IBUPROFEN CONCENTRATION PROFILES AFTER 30 MINUTES OF APPLICATION OF A SATURATED SOLUTION

\[
C_x = K C_{con} \left(1 - \frac{x}{L}ight) \exp \left(-\frac{D}{L^2} n^2 t^2\right)
\]

### RESULTS

#### Experimental curves [4]

![Graph showing experimental curves for ibuprofen concentration in the SC](image)

**Theoretical curves (4)**

\[
\dot{C} = 2 \sqrt{\gamma} \frac{C_{con}}{\rho} \int_0^\infty \frac{1}{n^2 \exp \left(\frac{n^2 \tau^2}{L^2}\right)} \cos(\lambda e) \exp \left(-\lambda(n^2 + 1)\right) \frac{1}{\alpha^2} \left(\cos^2(\alpha e) - \cos^2(\alpha t)\right) \lambda = (2n + 1)\pi/2
\]

\[
\dot{C} = CK C_{con} \left(1 - \frac{x}{L}\right) \exp \left(-D \frac{x^2}{L^2}\right)
\]

#### Appropriate solution of Fick’s second law of diffusion

\[
D/L^2 (h^{-1}) = 0.21 \pm 0.04
\]

\[
K = 2.99 \pm 0.66
\]

\[
AUC (M) = 0.059 \pm 0.017
\]

### IBUPROFEN CLEARANCE IN THE PRESENCE OF OCCLUSION

#### Hypothesis:

Rapid diffusion and/or evaporation of PG [5] results in the, at least transient, maintenance of a saturated ibuprofen concentration at the SC surface even after removal of the original formulation.

### ATR-FTIR ANALYSIS OF PG ELIMINATION FROM SC

**Delay = 0:** Steep PG concentration gradient

- Delay = 30 min occluded: PG profile decreased

- Delay = 30 min unoccluded: Altered profile shape; significantly less PG in the surface SC layers

### CONCLUSIONS

- Ibuprofen clearance from the SC after 30 minutes of infinite dose application of a saturated solution in PG:H2O (75:25) was very slow.

- ATR-FTIR analysis demonstrated that PG clearance from the SC is very rapid and it is due to both diffusion and evaporation.

- PG clearance could cause ibuprofen precipitation in the outermost layers of the SC, thus maintaining a saturated drug concentration after formulation removal.

- The role of excipients in topical delivery and topical drug bioavailability deserves further investigation.

### REFERENCES


