

Characterisation of *in vitro* Permeation of Ibuprofen

OBJECTIVE

Characterisation of *in vitro* permeation of Ibuprofen (IBU) using Labskin to evaluate uses as an alternative to human or animal experimentation.

METHOD

- Labskin was mounted in static glass Franz diffusion cells and equilibrated at $32^{\circ}\text{C} \pm 1^{\circ}\text{C}$. PBS was used as the receptor phase. Figure 1.
- Excess surface water was removed and TEWL measurements taken using an AquaFlux AF200 (Biox Systems).
- Infinite dose: 1 mL of saturated IBU solution in propylene glycol (PG) was tested. Receptor fluid was replaced after each sample.
- Finite dose: 3.6 μL of IBU solution (1.5% w/v in 5% PG : 95% isopropyl alcohol) was added to the donor compartment. 200 μL samples were collected and replaced by fresh PBS.
- All experiments were conducted for 24h and samples assayed by UV-HPLC.

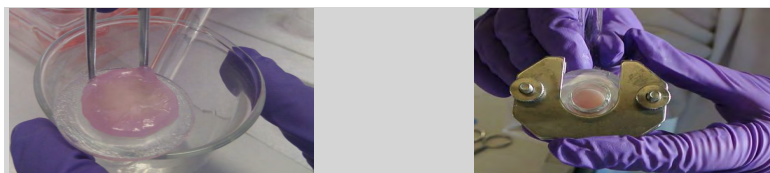


Figure 1. - Mounting in the receptor compartment of a Franz diffusion cell & Franz diffusion cell final assembly.

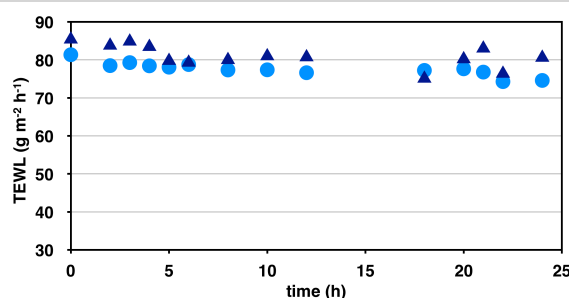


Figure 2 - TEWL values measured on Labskin, no formulation control for 24h infinite (●) and finite (▲) dose study.

RESULTS

- TEWL for Labskin remained constant over the time-course of the experiments. (Figure 2).
- Labskin demonstrates less variability (Figure 3) than typically observed for human or porcine skin and other human skin equivalent tissue culture models (Netzlaff, F., et al., European Journal of Pharmaceutics and Biopharmaceutics, 2005. 60: p.167-178)
- The flux values observed for the infinite dose study (Figure 4) were approximately 1.5 times higher for Labskin compared with human epidermis (Watkinson, R.M., et al., Skin Pharmacology and Physiology, 2009. 22: p. 225-230)
- The total amount of IBU permeated across Labskin after application of 3.6 μL of the formulation was $46.2 \mu\text{g cm}^{-2}$ compared to $17 \mu\text{g cm}^{-2}$ across human epidermis (Figure 5)

Figure 3 - Cumulative amount of ibuprofen permeated from a saturated solution of IBU in PG for 24h across Labskin at 32°C

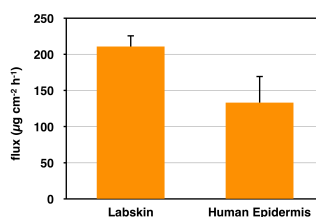


Figure 5 - Cumulative amount IBU permeated from 95:5:1.47 (IPA:PG:IBU) solution over 24h across Labskin (■) and human epidermis (◆) at 32°C (n=5, Mean \pm SD)

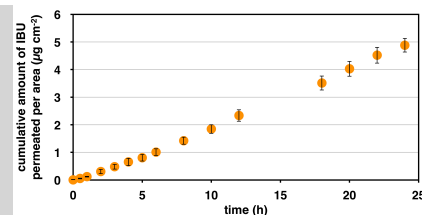
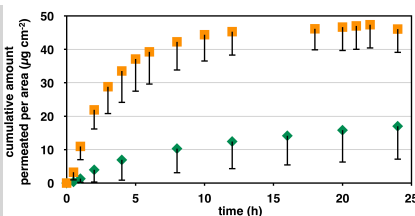


Figure 4 - Steady-state fluxes of ibuprofen through different membranes from saturated solutions in PG (mean \pm SD)



SUMMARY

Although IBU permeated through Labskin more quickly than human skin *in vitro*, permeability is comparable to porcine ear tissue - currently the closest animal model to human skin.

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