

A novel strategy to assess drug delivery kinetics to epidermal targets in vivo

Magdalena Hoppel (1), M. Begoña Delgado-Charro (1), Richard H. Guy (1)

(1) University of Bath, Department of Pharmacy & Pharmacology, Bath, UK

Introduction:

It has proven difficult to quantify 'drug input' from a formulation to the viable skin because the epidermal and dermal targets of topically applied drugs are hard, if not impossible, to access in vivo. Defining the drug input function from a formulation to the viable skin with a straightforward and practical experimental approach would enable a key component of dermal pharmacokinetics to be characterised. Stratum corneum (SC) tape-stripping has been used to measure drug uptake from a formulation after a defined period of application; by delaying tape-stripping post-removal of the formulation, it is also possible to assess drug clearance from the SC. It is hypothesised that the difference between uptake and clearance measurements allows estimation of a topical drug's input function into the viable tissue [1]. This study aimed to test this idea by comparing the input of lidocaine into the viable skin, following application of commercialised patch and cream products, using SC tape-stripping in vivo with that determined more conventionally in vitro.

Methods:

Twelve healthy human volunteers participated in the in vivo SC tape-stripping study, which was approved by the Research Ethics Approval Committee for Health of the University of Bath. On separate occasions, either a Versatis® 5 mg medicated plaster or LMX4 cream (lidocaine 4% w/w) was applied to both forearms. Drug uptake into, and clearance from, the SC were measured immediately following 12 hr of patch application, and 4 hr and 8 hr post-patch removal, respectively; for the cream, the uptake time was 1 hr, the clearance times were the same as those for the patch. In vitro experiments used dermatomed, abdominal pig skin (750 µm) and Franz diffusion cells (n ≥ 6 for each formulation); the receptor solution was PBS buffered at pH 7.4.

Results and discussion:

The in vivo SC uptake and clearance data provided estimates of the lidocaine input rate into the viable skin tissue of $11.5 \pm 2.3 \mu\text{g cm}^{-2} \text{h}^{-1}$ and $5.3 \pm 2.8 \mu\text{g cm}^{-2} \text{h}^{-1}$ from the cream and patch, respectively. The significantly higher delivery of the drug from the cream compared to the patch was confirmed qualitatively and quantitatively in vitro. From the estimated steady state flux of lidocaine from the patch in vivo, and the amount of drug cleared from the SC post-removal of the formulation, the total delivery was determined to be $\sim 110 \mu\text{g cm}^{-2}$. This value agrees very well with the claimed [2] lidocaine absorption of $150 \pm 100 \mu\text{g cm}^{-2}$. In conclusion, the results support the hypothesis that drug input into the viable skin from a topical formulation can be estimated using SC tape-stripping at judiciously selected uptake and clearance times.



References:

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[2] Electronic Medicines Compendium. Versatis 5% medicated plaster. Summary of Product Characteristics. Available at www.medicines.org.uk/emc/medicine/19291 [Last accessed 06/02/2017]

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