Pharmaceutical applications : *in vitro* using diffusion cells

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SUMMARY :

Academia and industry have been used extensively *in vitro* techniques to assess skin drug penetration and permeation because they are appropriate to predict human dermal penetration, give results quickly, are time- and cost-saving, and generally show better reproducibility of results. Moreover, these experiments can be performed using either human or other mammalian skin samples. However, the experiments should be performed following the "OECD Guideline for the Testing of Chemicals. Draft New Guideline 428: Skin Absorption in vitro method"

The most common methods for evaluating in vitro skin penetration employ diffusion cells, and a rich literature confirms the suitable performance of these experiments. A pontial disadvantage of the *in vitro* studies is the lack of information regarding effects of blood flow on drug permeation, since the in vivo sink conditions cannot be completely reproduced.

Diffusion cell design may vary from a simple two compartment “static” or a more complex “flow-through” system. The static cells are composed of two compartments, the donor and the receiver, and are usually vertical (Franz cells) or side-by-side. They can vary in size, and diffusional surface.

Excised skin specimens or are sandwiched as a barrier between the two compartments, with the SC side facing the donor compartment and the formulation is applied on the skin surface. The receiver contains an appropriate fluid that simulates the blood flow and is continuously mixed by a stir bar. The ideal receiver fluid should well simulate the in vivo situation of permeation and guarantee sink conditions. Indeed, it is generally recognised that if the drug water solubility is less than 10 µg/ml, the water receiver fluid must be added of solubilizers such as alcohol, albumin, or cyclodextrin. The receiver fluid must be thermostated to ensure that the skin surface temperature is kept at the in vivo conditions (32±1°C). The drug permeating from the donor to the receiver is determined as a function of time by receptor fluid removal from the sampling port at regular intervals. To ensure sink conditions, the removed solution must be replaced with an equivalent amount of fresh receptor fluid. A rich literature regarding diffusion cell design and use is available.

Flow-through cells can be useful when the permeant has very low solubility in the receptor medium.

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