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Comparison of a new skin penetration system containing a toxicokinetic modul with Franz diffusion cells

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Introduction

Critical endpoints in *in vitro* testing of cosmetic ingredients are the determination of the bioavailability of test substances in different skin layers and the examination of the toxicokinetic profile. Skin penetration studies are so far performed in Franz diffusion cells using pig skin[1]. Unfortunately with these cells an automated toxicokinetic determination is not receivable. To record a full toxicokinetic profile we developed a semiautomated skin penetration system (SPS) that collects samples from the receptor fluid automatically. This skin exposure module is a prototype. We developed it on the basis of a penetration cell from VITROCELL® Systems and tested it for comparability to Franz diffusion cells.

Methods

To perform toxicokinetic studies, we developed the SPS with eight parallel running diffusion cells. To substitute the glass diffusion cells with the SPS it is important to compare both systems in terms of performance and reproducibility. Therefore we investigated the penetration of caffeine and benzophenone-3 after 24 h through full-thickness pig skin using normal glass diffusion cells (GDC) and the SPS (Fig. 1). In total 16 skin discs from 3 different pigs where investigated in each system. After successful comparison of the penetration we recorded a full toxicokinetic profile of caffeine. Currently we are refining the SPS for liberation studies.

Results

We could show that the recovery rates of caffeine and benzophenone-3 recorded by SPS are highly comparable to those in GDC. No significant differences could be observed. While caffeine penetrated percutaneously, benzophenone-3 remained mainly on the surface (Fig. 2 a, b). It is also possible to take samples from the receptor fluid automatically . Fig. 2 c shows a toxicokinetic profile of caffeine. One can see that the samples taken from different cells within the SPS are reproducible. Percutaneous penetration of caffeine is observable after a lag time of approx. 7 h.

Conclusion

In conclusion, the new SPS is highly comparable to glass diffusion cells. We observed percutaneous penetration for caffeine after 7 h. Sampling from the receptor fluid of different penetration cells within the SPS leads to reproducible results. The SPS has the advantage that manual sampling from the receptor fluid is no longer necessary. Therefore one can record a full toxicokinetic profile, even over night.

Currently we are refining the SPS in terms of liberation studies. This means the determination of the liberation of a test substance from different formulations could be tested semi automatically.

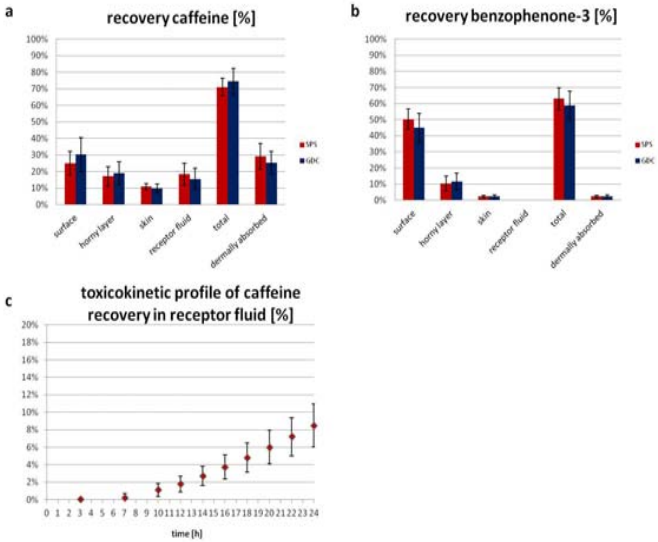

Fig. 2 Comparison of the penetration of caffeine (a) and benzophenone-3 (b) in the skin penetration system (SPS) and glass diffusion cells (GDC) after 24h. Both assays are highly comparable for hydrophilic and lipophilic substances. 16 skin discs from three pigs were used in each penetration assay. c) Recovery of caffeine in the receptor fluid in a time dependent manner. The toxicokinetic profile has been recorded with the SPS using 16 skin discs from two pigs. It shows a good reproducibility between different diffusion cells within the SPS.

Fig. 1 Semiautomated skin penetration system (SPS) for toxicokinetic studies. a) Complete overview b) Inside view showing the experimental setup with syringes, Franz cells and storage vessels for receptor fluid c) Enlargement of experimental setup showing HPLC vials, receptor fluid in- and outlet and integrated Franz diffusion cells.

Reference and Acknowledgement

[1]W. Diembeck, H. Beck, F. Benech-Kieffer, P. Courtellemont, J. Dupuis, W. Lovell, M. Paye, J. Spengler, W. Steiling: Test guidelines for in vitro assessment of dermal absorption and percutaneous penetration of cosmetic ingredients. Food Chem Toxicol. 1999, 37(2-3):191-205.

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