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 are developing a semiautomated skin penetration system (SPS) that can collect samples from the receptor fluid automatically. This skin exposure module is a prototype. We developed its precursor 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 through different skin thicknesses (700 µm, 1000 µm and full thickness pig skin) using caffeine and benzophenone-3 in the precursor system (Fig. 1). After successful comparison we are currently developing a semiautomated modul that is able to take samples from the receptor fluid automatically.

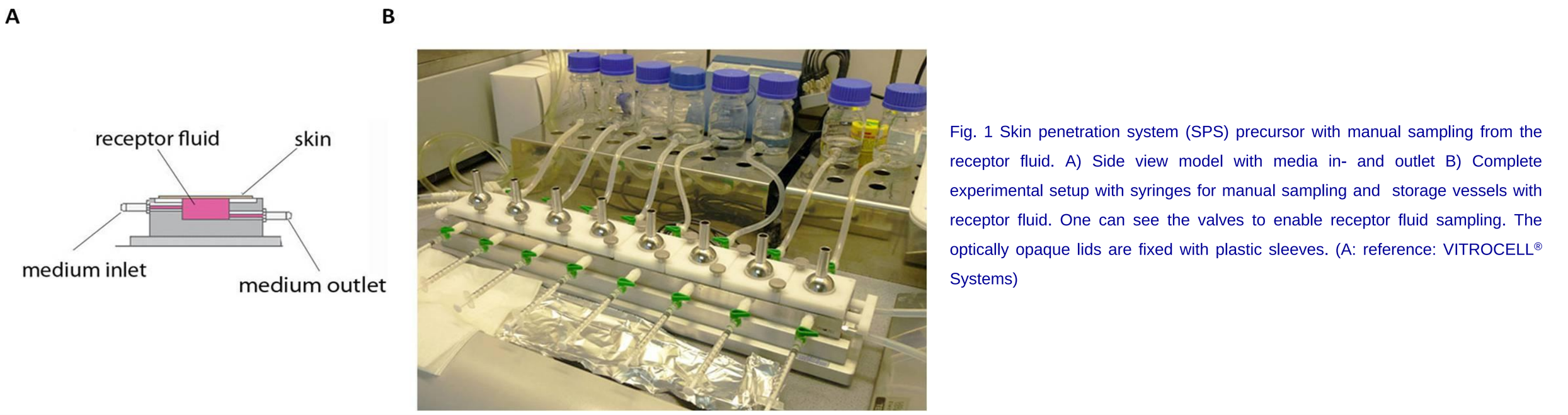

Fig. 1 Skin penetration system (SPS) precursor with manual sampling from the receptor fluid. A) Side view model with media in- and outlet B) Complete experimental setup with syringes for manual sampling and storage vessels with receptor fluid. One can see the valves to enable receptor fluid sampling. The optically opaque lids are fixed with plastic sleeves. (A: reference: VITROCELL® Systems)

Results and conclusion

We could show that a significantly higher amount of each substance was found in the receptor fluid of 700 µm and 1000 µm split-thickness pig skin than in full thickness pig skin (Fig. 2). There were no significant differences in the amount of test substance in the receptor fluid between 700 and 1000 µm dermatomed skin. These results were similar for both systems. Because less benzophenone-3 was found dermally absorbed and in total in full thickness skin it is possibly metabolized by enzymes within the dermis. Percutaneuous penetration of caffeine seems to be faster in dermatomed skin. Therefore more test substance is found in the receptor fluid after 24 h.

In conclusion, the new SPS is highly comparable to glass diffusion cells. We observed a different percutaneous penetration for full-thickness and split-thickness skin. To further investigate the penetration of caffeine and record a complete toxicokinetic profile we are currently developing a semiautomated SPS with the advantage to allow sampling from the receptor fluid automatically.

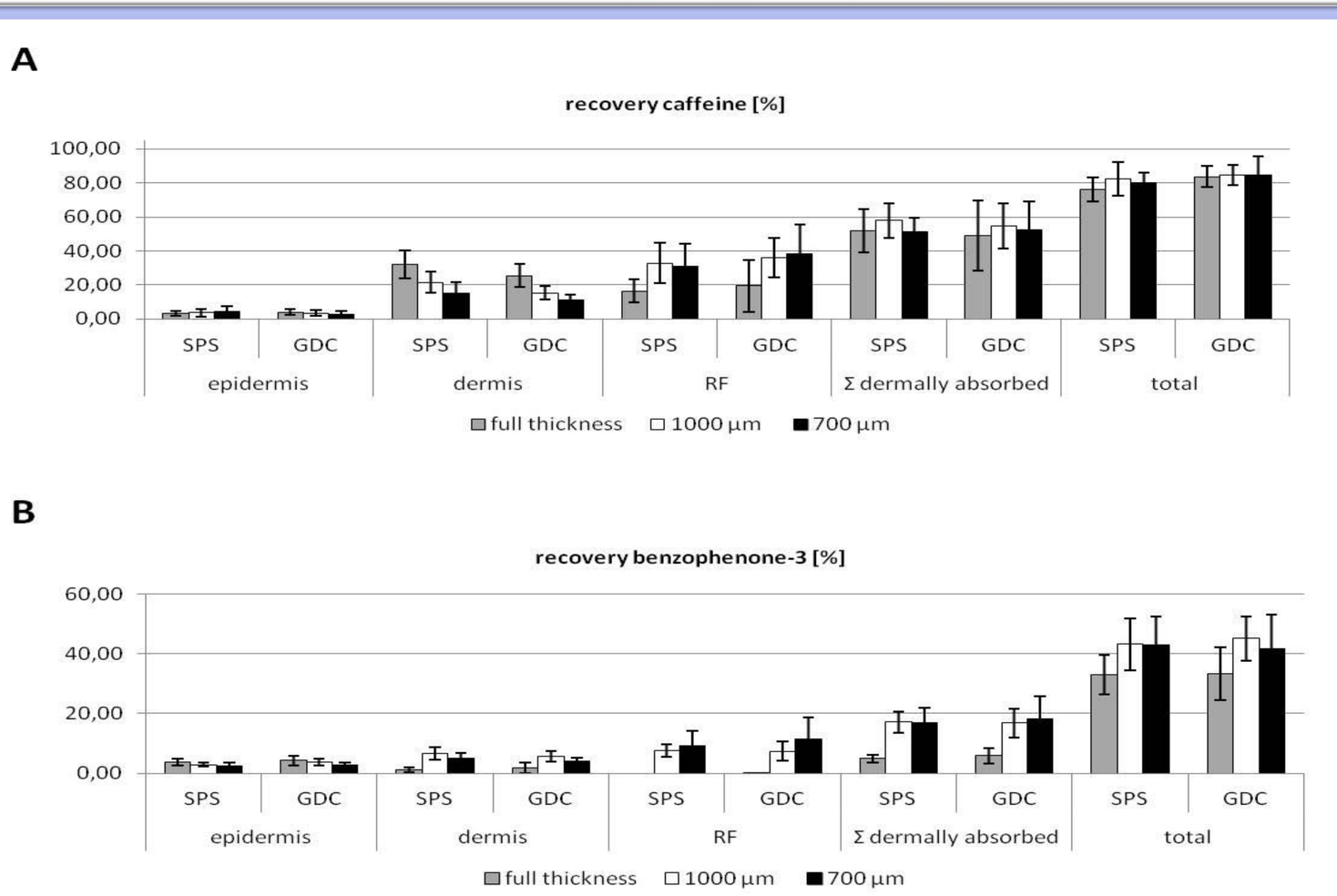

Fig. 2 Comparison of the penetration of caffeine (A) and benzophenone-3 (B) in the skin penetration system (SPS) and glass diffusion cells (GDC) after 24h. Different skin thicknesses (full thickness,1000 µm and 700 µm) were used. The thicker the skin is, the less substance is found within the receptor fluid. Benzophenone-3 seems to be metabolically converted by enzymes of the dermis because less benzophenone-3 is found in total in full thickness skin. Caffeine seems to be kept behind by the dermis. Percutaneous penetration seems to occour slower in full thickness than in dermatomed skin. Nevertheless the overall recovery of caffeine is comparable for all skin thicknesses. Penetration results are highly comparable between SPS and GDC. RF: receptor fluid.

Reference

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