Wissenschaftliches Hauptprogramm Teil 1:
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The use of in vitro skin permeation testing in the development of topical drugs

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The use of in vitro permeation experiments with split thickness human skin in Franz cells is a valuable tool for the development of topical drug products such as creams, gels, sprays and patches. When properly conducted with undamaged skin samples, precise results are obtained that are predictive for in vivo skin absorption, measured as plasma levels in clinical trials. Results of in vitro skin absorption studies have been validated for a number of topically applied drugs, such as NSAIDs, antiviral and antifungal drugs and nicotine.
The rate of skin absorption depends on a number of factors such as chemical structure of the drug, pharmaceutical dosage form, concentration, excipients and skin permeation enhancers. Relative small changes in the chemical structure can have a considerable effect on the skin permeation. When comparing acyclovir 5% cream and penciclovir 1% cream, at equal quantities (5 mg/cm2), approximately 3x more penciclovir passed into the deeper layers of the skin.

The skin permeation rate can depend on the quantity of applied drug, but is sometimes complex. A linear increase in skin absorption was seen with increasing quantities of Voltaren Emulgel, from 5-20 mg/cm2, but increasing the concentration of diclofenac in the Emulgel from 1% to 2% actually lowered the skin absorption. Similarly, a 5% diclofenac formulation was less absorbed than 1% Voltaren Emulgel. Apparently, the ratio of diclofenac and excipient concentrations in a formulation are critical for efficient skin absorption.

The in vitro skin absorption assay was also successfully used in the development of Lamisil Once, a new antifungal product that treats fungal skin infections with one single treatment vs 1 or more weeks for conventional products. As fungi mainly grow in the top layers of the skin, absorption across the skin is not essential and a formulation was developed that prolongs the residence time of terbinafine in the stratum corneum. For this purpose, in vitro skin absorption experiments were complemented with a tape stripping technique that measures drug concentration in the top layers of the skin. The results of the in vitro skin technology successfully guided the pharmaceutical development with results that were confirmed in clinical PK and efficacy trials.