In Vivo Investigation of Protein Skin Penetration in Irritant Contact Dermatitis
M. Abdel-Mottaleb¹, A. Lamprecht ²
¹ Universite de Franche-Comte, ² University of Bonn

Purpose
Protein drugs are now very important for the treatment of various diseases such as diabetes, osteoporosis and cancer. Transdermal protein delivery offers an appealing alternative to the parenteral route but its efficacy is limited by the limited permeability of the skin to the hydrophilic macromolecules. One of the important factors affecting the transcutaneous delivery of peptides is disease states like dermatitis. The present investigation aimed at clearly investigating the effect of irritant contact dermatitis on the barrier properties of the skin especially the penetrability to proteins.

Methods
The study was performed using the model of dithranol induced dermatitis in mice and rats ears. Insulin solution (50U/Kg) was applied to healthy and inflamed skin of rats’ ears and blood glucose levels were measured. Results were compared to untreated animals, subcutaneous insulin injected animals (1U/Kg) and animals with tape-striped skin as a current model for disrupted skin barrier over a period of 24 hours. In parallel, fluorescently labelled dextrans (av mol wt 4,400) were applied to both healthy and inflamed mice skin and penetration was visualised by confocal microscopy.

Results
The results obtained from the tracking of the fluorescent protein penetration through inflamed and healthy skin by confocal microscopy showed that the penetration pattern of dextran was similar in both cases where macromolecules accumulated on the skin surface without any deeper penetration. Similarly, insulin penetration in rats did not exhibit blood glucose level changes after application of insulin to healthy and inflamed skin. On the other side blood glucose levels were reduced in case of stripped skin showing that the barrier disrupted skin permits the penetration of proteins. However, the effect was limited and shorter compared to the SC injection where tmin was 0.5h and 2h with a 72% and 46% reduction in blood glucose levels for the stripped skin and the SC injection respectively.

Conclusion
Results have shown that proteins could not penetrate the irritant dermatitis skin and their penetration behaviour was similar between healthy and inflamed skin. Penetration through stripped skin was significantly different from dermatitis indicating that it can’t be used as a skin inflammation model.