Transdermal transport of calcein through electroporated skin - preliminary results of an *ex vivo* experiments

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SUMMARY

The success of transdermal drug delivery depends on the ability of the drug to permeate the intact skin barrier in sufficient quantities to achieve its desired pharmacological effect. The greatest challenge is to surmount the limitations imposed by the outermost layer of the skin – the stratum corneum. For this purpose different enhancement methods are used, one of them being electroporation. Namely, electroporation has a potential to create aqueous pathways across the stratum corneum, to enhance transdermal drug delivery [1, 2].

Our purpose was to investigate the effect of the electrode polarity, long low voltage pulses and short high voltage pulses on calcein transport through the dermatomed pig skin.

Vertical glass Franz diffusion cells were used to study molecular transport through excised and dermatomed pigs' ear skin. The donor compartment contained calcein solution (0,1 mM) in phosphate buffer at pH 7,4. The receiver solution was a phosphate buffer (pH 7,4) termo-regulated at 37 °C. The concentration of calcein in receiver compartment after electroporation was measured with spectrofluorometer.

Firstly, electrode polarity has a great influence on calcein flux through the skin. Calcein in buffer solution is negatively charged. When the negative electrode is put in the donor and the positive one in the receiver compartment, calcein delivery is 5-fold higher than when the polarity of electrodes was reversed (Figure 1).

Secondly, the comparison of short high and long low voltage pulses shows that for successful molecular transport through the skin the use of long low voltage pulses is very important, while the molecular transport after short high voltage pulses is hardly significantly different from the control (passive diffusion) (Figure 2). Moreover – against our expectations – calcein transport after long low voltage pulses is almost 2-fold higher than after the combination of short high voltage and long low voltage pulses. This is most likely due to the changes in the buffer caused by high voltage pulses, which will be the subject of our further research work.

Transdermal drug delivery has a big potential for delivering drugs that are not suitable for administration through other routes, such as intravenous or oral. Unfortunately, transdermal flux is often too low to achieve its desired pharmacological effect. Therefore, it is necessary to temporarily reduce the skin barrier properties to ensure therapeutically significant delivery. This can be achieved by using electroporation as an effective enhancement method.

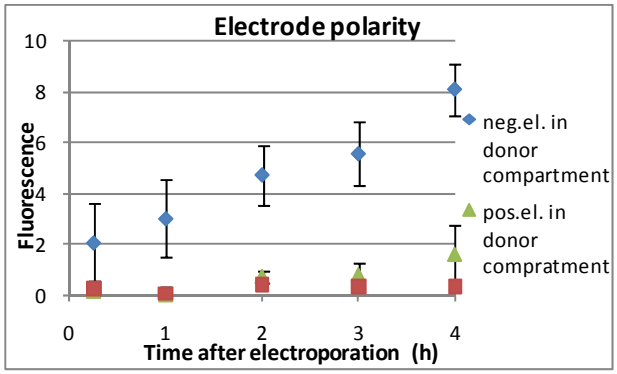

Fig. 1: The influence of the electrode polarity in the donor compartment to the transport of calcein through the skin.

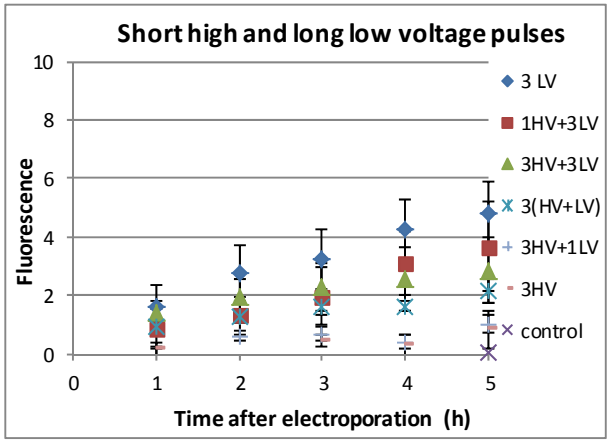

Fig. 2: Comparison of high and low voltage pulses to the flux of calcein through the skin.

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