Effect of probe distance on sonophoresis of proteins through rat skin

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Low frequency ultrasound (US) is an effective physical enhancer in delivering various molecules through the skin. Among the mechanisms that have been proposed are heating, cavitation (formation and collapse of bubbles in a medium) and acoustic microstreaming (unidirectional flow currents of fluid caused by sound waves). Unfortunately, many important experimental parameters for optimal drug permeation have yet to be established. One of them is the probe distance fromthe skin surface. So far,most experiments have been conducted at 10mm. The aim of this study was to establish the relationship between the probe distance and protein permeation through skin. Permeation studies using Franz cells were conducted using full-thickness rat skin as the membrane. The receptor medium was phosphate buffered saline (PBS). The donor compartment was filled with 20mL of couplingmedium(eitherwater or 0.04%SLS aqueous solution) andultrasoundwas applied, using a probe placed at varying distances (5, 7.5, 10, 12.5, 15mm) fromthe skin. The ultrasound protocol was fixed at 30% amplitude and 0.5 s on, 0.5 s off pulse wave for a total sonication time of 2 min. Following US application, the coupling medium was removed, the skin was rinsed, blotted dry and 50 _L of iodine-125 labelled bovine serum albumin (BSA) was applied onto the skin. After 24 h, 400 _L samples were taken from the receptor compartment and the radioactivity level was counted using a gamma counter. Gel electrophoresis on the receptor phase confirmed the presence of BSA. Increasing the probe distance was found to result in decreased protein permeation when water was used as coupling medium. The decreased protein permeation is thought to be due to decreased damage caused by mechanical effects of US to the skin and was reflected in a reduced number of pits formed with increasing probe distance when aluminium foil was used as themembrane andUS was applied. The pits on the aluminiumfoil give an indication of indentations that may be formed in skin by US via microjet formation on skin and through which protein can permeate into the skin and then into the receptorphase. Interestinglywhen0.04%SLS aqueous solutionwas used as the couplingmedium, a different trend was observed. Increasing distance from5 to 12.5mm resulted in increased permeation; further increase in probe distance (to 17.5mm) resulted in decreased in permeation. This increased and decreased permeation with increasing probe distance reflects the increase and decrease in pitting on aluminiumfoilwhen the latterwas usedas themembrane.Although it is not clear why the presence of 0.04%SLS causes such as difference in permeation profile, this study has highlighted the importance of probe distance on permeation and the existence of different optimal distances for different coupling media.