Effect of coupling medium volume on sonophoresis of proteins through rat skin

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Low-frequency ultrasound has been found to increase transdermal drug delivery; and proposed mechanisms include thermal effect, acoustic cavitation (formation and collapse of bubbles in a medium) and acoustic streaming (Lavon & Kost 2004). During the cavitation process, 2 types of cavitation can occur: stable cavitation (regular bubble formation and collapse) and inertial cavitation (violent bubble formation and collapse) (Mitragotri & Kost 2004). However, inertial cavitation is thought to increase skin permeability by the formation of microjet bubbles. In most studies, ultrasound has been applied via small volumes (e.g., 1mL) of coupling media. The disadvantages of small volumes are loss of coupling media due to splashing and excessive temperature rise. This could be remedied by increasing the volume of the coupling medium. However, ultrasound (US) wave generation and propagation in large volumes and the effects on transdermal delivery are unknown. The aimof this study was therefore to explore the relationship between coupling medium volume and transdermal protein delivery. Permeation studies using Franz cells were conducted with full-thickness rat skin as the membrane and PBS as the receptor medium. The donor compartment was filled with different volumes (10, 20, 30, 40, 50mL) of couplingmedium (water) and US was applied at 30%amplitude, probe distance of 5mmand pulse wave of 0.5 s on, 0.5 s off for a total sonication time of 2min. Following US application, the coupling medium was removed, the skin was rinsed and blotted dry and 50 _L of iodine-125 labelled bovine serum albumin (BSA) was applied onto the skin. After 24 h, the levels of radioactivity in the receptor compartment and in the skin weremeasured using a gamma counter. Gel electrophoresis on the receptor phase confirmed BSA presence. It was found that that increasing the coupling medium volume resulted in increased protein permeation into the receptor phase. There could be two possible explanations for the higher protein permeation when large volumes of coupling mediumwere used. Firstly, the effect of atmospheric pressure caused by the mass of water found on top of the skin may enhance the impact of microjets hitting the skin surface and result in deeper and greater protein penetration. Secondly, the abundance of gaseous molecules in larger volumes may result in increased inertial cavitation, air bubbles being essential for cavitation to occur. Further work must be conducted to assess the damage caused to skin by larger volumes of coupling medium to skin.

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