Description of transdermal transport of hydrophilic solutes during low-frequency sonophoresis based on a modified porous pathway model

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Abstract
Application of low-frequency ultrasound has been shown to increase skin permeability, thereby facilitating delivery of macromolecules (low-frequency sonophoresis). In this study, we sought to determine a theoretical description of transdermal transport of hydrophilic permeants induced by low-frequency sonophoresis. Parameters such as pore size distribution, absolute porosity, and dependence of effective tortuosity on solute characteristics were investigated. Pig skin was exposed to low-frequency ultrasound at 58 kHz to achieve different skin resistivities. Transdermal delivery of four permeants [mannitol, luteinizing hormone releasing hormone (LHRH), inulin, dextran] in the presence and absence of ultrasound was measured. The porous pathway model was modified to incorporate the permeant characteristics into the model and to achieve a detailed understanding of the pathways responsible for hydrophilic permeant delivery. The slopes of the log kpp versus log R graphs for individual solutes changed with solute molecular area, suggesting that the permeability-resistivity correlation for each permeant is related to its size. The tortuosity that a permeant experiences within the skin also depends on its size, where larger molecules experience a less tortuous path. With the modified porous pathway model, the effective tortuosities and skin porosity were calculated independently. The results of this study show that low-frequency sonophoresis creates pathways for permeant delivery with a wide range of pore sizes. The optimum pore size utilized by solutes is related to their molecular radii. J Pharm Sci 92:381-393, 2003
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