J. Control. Release, 66, 149-158 (2000).

Analysis of skin permeation-enhancing mechanism of iontophoresis using hydrodynamic pore theory

Eiichiro Manabe（真鍋栄一郎）, Sachihiko Numajiri（沼尻幸彦）, Kenji Sugibayashi（杉林堅次）, Yasunori Morimoto（森本雍憲）

Faculty of Phrmaceutical Sciences, Josai University, 1-1 Keyakidai, Sakado, Saitama 350-0295, Japan

The effects of constant DC iontophoresis (0-1.5 mA/0.966 cm^2) on the permeation of three hydrophilic compounds, antipyrine (ANP, M.W. 188.23), sucrose (SR, M.W. 342.30) and *l*-kestose (KT, M.W. 506.73), through excised hairless rat skin were evaluated using hydrodynamic pore theory. The electro-osmotic flow caused by iontophoresis was measured using deuterium oxide (D_2O). The penetration-enhancing mechanism of iontophoresis was found to increase solvent flow through electro-osmosis and pore enlargement and/or new pore production in the skin barrier, together with enhancement of electrochemical potential difference across the skin. These effects were closely related to the strength of the current applied. The electro-osmotic flow of D_2O (J_{D2O}) greatly enhanced the skin permeation clearance of all hydrophilic penetrants (CL_{drug}). Pore production was classified into reversible and irreversible processes, which resulted from lower (0-0.5 mA/0.966 cm^2) and higher (0.5-1.5 mA/0.966 cm^2) currents, respectively. Thus, the enhancing effects of iontophoresis on skin permeation of nonionic hydrophilic compounds can be explained by increase in pore size and higher solvent flow.