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Evaluation of Bile Acids and Fusidate Derivative as Nasal Absorption Enhancers Using an Electrophysiological Technique

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The present study was carried out to investigate the reversibility of the action of two nasal absorption enhancers, bile acids and fusidate derivative, on nasal membrane resistance. The nasal mucosa was isolated from rabbit nasal septum and mounted in a Ussing-type chamber to allow the monitoring of the membrane resistance and flux of fluorescein isothiocyanate-labeled dextran (FD10, M.W. 9400). Membrane resistance was reduced by 46% following treatment with 0.5% (w/v) sodium taurodihydrofusidate (STDHF) for 10 min and then gradually returned to the control level after being wash. The resistance was restored to 76% of the control level following a 30 min treatment with 0.5% (w/v) STDHF. However, there was no recovery of resistance following treatment with 0.5% (w/v) STDHF for 120 min or 1% (w/v) STDHF for 10 min. Concurrently, FD10 transport was enhanced while membrane resistance was reduced. Treatment with 0.5% (w/v) sodium deoxycholate (DC) for more than 10 min showed no reversible action and marked FD10 transport enhancement, whereas a 10-30 min treatment with 0.5% (w/v) sodium glycocholate (GC) or sodium taurocholate (TC) resulted in the rapid recovery of membrane resistance without any enhancement of FD10 permeation. STDHF transport across the nasal mucosa was ~2-fold faster than that of DC, GC, and TC. The accumulation of STDHF in the nasal mucosa was 2-fold lower than that of DC and 1.7-fold higher than that of GC and TC after 30 min treatment. The rank order of hydrophobicity determined by reverse-phase HPLC was: DC > STDHF > GC > TC. These results

suggest that the reduction in membrane resistance and its reversibility appear to be due to a balance between the accumulation and clearance of STDHF.