The influence of chemical enhancers and pH on naratriptan permeation in porcine buccal mucosa

Abstract

Purpose The objectives of this research were, firstly, to investigate the effect of different vehicles on naratriptan permeation through porcine buccal tissue and, secondly, to study the influence of pH on naratriptan permeability parameters. Methods The permeability studies were carried out in static Franz-type diffusion cells using dermatomed porcine buccal tissue at 37±1°C for 6 h. Naratriptan (25mg/mL) was applied in the donor compartment in single vehicles including Transcutol P® (TC), dipropylene glycol (DPG), propylene glycol (PG), polyethylene glycol 200 (PEG 200), polyethylene glycol 400 (PEG 400), and oleic acid (OA), as well as in a ternary system of TC-DPG-Miglyol® (MG). In addition, the permeability of naratriptan was determined in isotonic phosphate buffer solutions (PBS) in the pH range from 7.4 to 10. The receptor compartment consisted of PBS (pH 7.4). Samples were withdrawn from the receptor compartment at designated times and replaced with fresh PBS. Results Naratriptan was delivered to a significantly higher extent from TC and DPG (with a steady state flux (Jss) of 2.35 ± 0.87 and 0.68 ± 0.42 μg/cm2/min, respectively) compared with PG, PEG 200 and PEG 400. OA did not promote naratriptan delivery across buccal tissue compared with the other vehicles. Application of naratriptan in the ternary system (TC-DPG-MG) resulted in Jss of 3.35 ± 0.72 μg/cm2/min. Furthermore, a seven-

fold increase in the buccal permeability coefficient was observed over the investigated pH range. Conclusion Buccal penetration of naratriptan has been reported for the first time. Both TC and DPG were identified as suitable vehicles for buccal delivery of naratriptan. A ternary vehicle in which TC was incorporated with both DPG and MG resulted in high permeation of naratriptan suggesting a possible synergistic effect. Elucidating the reasons for these findings will be the focus of future efforts. Moreover, pH appears to be an important factor to consider when formulating this drug for BDD. Naratriptan therapeutic plasma level ranges from 5.9-10.7 μg/ml. Extrapolating the flux values to the in vivo setting is predicted to result in naratriptan plasma concentration of 8 μg/L for a dosage form applied to an area of 1 – 6 cm2.