Oral transmucosal delivery of naratriptan

Abstract

Naratriptan (NAR) is currently used as the hydrochloride salt (NAR.HCl) for the treatment of migraine and is available in tablet dosage forms for oral administration. Buccal drug delivery offers a number of advantages compared with conventional oral delivery including rapid absorption, avoidance of first pass metabolism and improved patient compliance. We have previously prepared and characterised the base form of NAR and shown that it has more favourable properties for buccal delivery compared with NAR.HCl. This study describes the design and evaluation of a range of formulations for oral transmucosal delivery of NAR base. Permeation studies were conducted using excised porcine buccal tissue mounted in Franz cells. Of the neat solvents examined, Transcutol® P (TC) showed the greatest enhancement effects and was the vehicle in which NAR was most soluble. The mechanisms by which TC might promote permeation were further probed using binary systems containing TC with either buffer or Miglyol 812® (MG). Mass balance studies were also conducted for these systems. The permeation of TC as well as NAR was also monitored for TC:MG formulations. Overall, TC appears to promote enhanced membrane permeation of NAR because of its rapid uptake into the buccal tissue. Synergistic enhancement of buccal permeation was observed when TC was combined with MG and this is attributed to the

increased thermodynamic activity of NAR in these formulations. Significantly enhanced permeation of NAR was achieved for TC:MG and this was also associated with less TC remaining on the tissue or in the tissue at the end of the experiment. To our knowledge this is the first report where both enhancer and active have been monitored in buccal permeation studies. The findings underline the importance of understanding the fate of vehicle components for rational formulation design of buccal delivery systems.