Preparation, characterization and buccal permeation of naratriptan

Abstract

Naratriptan (NAR) is currently used for the management of migraine as the hydrochloride salt (NAR.HCl) and is administered as an oral tablet. This work evaluates the feasibility of buccal delivery of NAR in order to ensure faster onset of action and avoid the side-effects associated with conventional oral formulations. We hypothesized that the unionized form of NAR would permeate buccal tissue to a greater extent than the salt. Therefore the first stage of this work required preparation of the free base from NAR.HCl. Characterisation of the base with thermal and elemental analyses confirmed its purity; log *P* and log *D* values were also determined. The pH permeation profile of NAR was also determined in the range 7.4–10. Solubility studies in non-aqueous solvents indicated that Transcutol™ (TC) and dipropylene glycol (DPG) were suitable vehicles for the free base. Maximum amounts of NAR which permeated after 6 h were ~130 μg/cm^2. Based on the pH permeation results and studies conducted at two different doses NAR appears to permeate porcine buccal tissue via the transcellular route. Finally, estimates of likely systemic values suggest that optimised formulations should be taken forward for *in vivo* evaluation.