AN ASSESSMENT OF THE INFLUENCE OF CERTAIN BILE COMPONENTS UPON ACUTE GASTRIC MUCOSAL DAMAGE INDUCED IN THE CONSCIOUS RAT

R.S. Newbery, G.P. Martin, B.E. Loveday, *R.C. Machling, Department of Pharmacy, Brighton Polytechnic, Moulsecoomb, Brighton BN2 4GJ, *Department of Histology, Royal Sussex County Hospital, Brighton BN2 5SE

The generation of acute gastric ulcers by physiological concentrations of bile salts and the mitigation of this damage by phosphatidylcholine (PC) has previously been demonstrated using an ex vivo rat gastric chamber technique (Martin et al 1985). In this model however anaesthesia and surgical trauma could exacerbate lesion formation by influencing gastric mucosal blood flow as well as imposing other stress factors. The purpose of this investigation was to develop a model whereby the mucosal damaging potential of certain bile components could be examined using an intact, relatively untraumatised, in vivo gastric preparation in the conscious animal.

Male Wistar rats were anaesthetised with halothane and a polypropylene cannula (external diameter 2 mm) was positioned in the proximal forestomach and exteriorised at the back of the neck. After a post operative recovery period of at least 4 days, animals were permitted only 5% w/v glucose solution for up to 48 hours pre-experimentation, and were unrestrained during the study. Stomachs were perfused with saline for a 30 minute control period followed by either i) saline containing sodium taurodeoxycholate (STDC), ii) saline containing STDC + PC, or iii) saline alone (control) for 6½ hours. The gastric perfusion rate throughout was 1.5 ml per hour. After the initial control period 20 mg/kg dimaprit dihydrochloride, an H_2 receptor agonist was injected subcutaneously and then infused at a rate of 70 mg/kg/hr to promote acid secretion during the remainder of the experiment. The animals were then killed by cervical dislocation and the stomachs removed and photographed. Gross mucosal injury was assessed visually, and histology conducted upon gastric sections exhibiting maximal damage.

Three groups of 12 rats were employed: Group A weighed 450-500 g, Group B weighed 200-250 g and Group C, also weighing 200-250 g but in which the cannula was introduced in the glandular mucosa near the border zone with the rumen. Experiments conducted in Group A were abandoned because of the retention of solid food and hair in the stomach, despite metaclopramide treatment during the prior fasting. No obvious mucosal damage was visible in this Group upon 20 mM STDC perfusion, although buffering of intragastric acid and bile salt binding by the matted bezoar was of probable significance. In Groups B and C gastric stasis was not observed, however the site of cannulation proved critical in determining the degree of damage. In Group B 40 mM STDC was the minimum concentration necessary to elicit perceptible damage, whereas in Group C the same concentration of STDC induced haemorrhagic gastritis. In the latter Group the severity of mucosal injury was inversely proportional to the length of time the rats were permitted to recover following surgery, illustrating the importance of surgical stress factors in the potentiation of gastric damage induced by bile salts. In all experiments concomitant administration of equimolar PC:STDC attenuated the severity of damage and substantially reduced mucus release from the glandular epithelium as assessed both visually and by selective histological staining. PC generally reduced desquamation and columnar cell erosion caused by STDC and also protected against depletion of mucus stores both in the surface epithelium and within the gastric glands.

The results from these studies demonstrate that in less traumatised animal models higher, physiologically unrealistic, concentrations of bile salt are often necessary to overcome mucosal defences and induce significant damage.

Martin, G.P. et al (1985) Gastroenterol. Clin. Biol. 9: 80-83