THE EFFECT OF BILE SALT AND PHOSPHATIDYLCHOLINE ON THE RHEOLOGICAL PROPERTIES OF PIG PURIFIED GASTRIC MUCUS

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In the stomach mucus is purported to contribute to the gastric mucosal barrier by forming a continuous protective gel layer adherent to the surface epithelial cells. Conflicting evidence exists as to whether bile salts break down mucus structure (Martin et al 1978; Bell et al 1985) although intragastric concentrations are known to be acutely ulcerogenic. Recently the toxicity of bile salts to the mucosal barrier has been shown to be mitigated by the presence of phosphatidylcholine (PC) (Martin et al 1985). Whether part of the protective function of PC involves a modification of bile salt action upon mucus structure has not been previously investigated. The purpose of this study is therefore to determine the effect of physiological concentrations of sodium taurodeoxycholate (STDC) on the physical properties of gastric mucus and to assess if these are altered by the presence of PC.

Samples of gastric mucus from freshly slaughtered pigs (Suis scrofa domestica) were pooled, solubilised in a protease inhibiting buffer and purified by gel filtration on Sepharose CL4B at 4°C. Following exhaustive dialysis against 0.02 M Tris HCl buffer at pH 7.4, the purified glycoprotein was concentrated to a gel by ultrafiltration and the dry weight determined. An appropriate quantity of Tris buffer was introduced by gentle mixing to give a gel of 8.8% w/w and the sample stored overnight at 4°C. Sample aliquots were subsequently adjusted with appropriate buffered test solutions to yield 8% w/w gels containing either (i) 5 mM STDC, (ii) 20 mM STDC, (iii) 5 mM STDC + 5 mM PC, (iv) 20 mM STDC + 20 mM PC, or (v) buffer alone (control). All samples were stored for 2 hours at 4°C to ensure homogeneity before conducting rheological investigations using an oscillating sphere microrheometer (James & Marriott 1982). Determinations were carried out on at least 10 samples per group.

When compared with controls both concentrations of STDC significantly reduced mucus elasticity (G') and viscosity (G") at all oscillatory frequencies within the test range 0.2 to 20 Hz. Treatment with 20 mM STDC resulted in decreases in G' and G" of 50% and 40% respectively ($p < 0.005$), whilst 5 mM STDC reduced both moduli by approximately 35% ($p < 0.05$). The decrease in viscoelasticity observed in the presence of STDC was significantly reduced ($p < 0.05$) by inclusion of equimolar concentrations of PC. This effect was more apparent at 20 mM than 5 mM, supporting results from a previous study demonstrating mitigation by PC of bile salt induced damage to the mucosal barrier as a whole (Martin et al 1985). G' and G" values of mucus treated with 20 mM STDC + 20 mM PC were not significantly different to control values, whilst treatment of mucus with 5 mM STDC + 5 mM PC resulted in an approximate 15% reduction in both parameters but these were only significantly different from control values ($p < 0.05$) at half of the frequencies tested.

These results demonstrate that bile salts are mucolytic at concentrations similar to those found in the stomach following duodenogastric reflux. Such breakdown in gel structure in vivo may seriously compromise mucus barrier function leading to an impairment in mucosal defence and subsequent ulcerative damage. Moreover, biliary phospholipid content would appear to be a major determinant of the damaging potential of refluxed bile to the mucus barrier and ultimately the underlying gastric mucosa.

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