Mucin degradation and its significance in inflammatory conditions of the gastrointestinal tract

Anthony M. Roberton and Anthony P. Corfield

9.1 MUCUS AND MUCINS

A protective mucus gel layer covers the surface of the gastrointestinal tract. The main structural component of mucus is the mucins, large, heavily glycosylated glycoproteins that form gels when sufficiently concentrated (Allen, 1981a). Native mucus gels contain 2–10% mucin (mucus glycoprotein) dry weight, most of the balance being water. Other constituents present in mucus from the surface of the gastrointestinal tract are proteins, nucleic acids, lipids, sloughed epithelial cells and bacteria (Allen and Hoskins, 1988).

9.1.1 Roles of the mucus barrier

The mucus gel is at the interface between the delicate epithelial cells lining the gut and the gut lumen, which contains many aggressive or damaging agents. One major role of the mucus is to protect the epithelium from damage by these luminal factors, the nature of which changes with each region of the gut.

In the stomach, the damaging factors include acid, pepsin and hypo- or hyperosmotic conditions. The mucus layer maintains the pH gradient
between the cell surface and the lumen acid and acts as a primary barrier. In the small intestine the mucus layer protects against damage by the pancreatic proteases and high-molecular-weight toxins if present. Pancreatic proteases are still present in the large intestine, and in addition there are large numbers of bacteria, some of which produce potentially harmful enzymes and antigens. The mucus layer is believed to protect against bacterial invasion of the host tissue, but much remains to be understood about the relationship between colonic bacteria and the colon mucus layer. The mucus in the mucus is potentially an excellent source of energy, but since excessive destruction of the mucus layer would damage the host and might destroy the habitat for the bacteria, a ‘mutualistic symbiosis’ must have evolved, resulting in ‘peaceful co-existence’ between the bacteria and the host (Luckey, 1972).

Other roles for the mucus barrier have been suggested. These include lubrication of food particles, enhanced uptake of fat digestion products by acidic mucin-mediated dissociation of mixed micelles (Shiau, Kelemen and Reed, 1990) and protection against sudden dehydration due to osmotic changes. The surface of the mucus layer is hydrophobic (Goddard, Kao and Lichtenberger, 1990) because of the association of lipids with mucins (Witas et al., 1983) and the configuration of the carbohydrate chains (Sundari, Raman and Balasubramanian, 1991). All molecules being secreted or absorbed must pass through the mucus layer and, because of the latter’s viscosity, hydrophobic properties and acidic groups, there is potential for differential rates of passage and adsorption.

Attention has recently focussed on the trefoil peptides, a family of small proteins that are secreted by the gastrointestinal mucosae (Sands and Podolsky, 1996). They are involved in the process of wound healing and mucosal restitution, and are associated with mucins in the adherent mucus gel. They may have a protective function at the intestinal mucosal surface, preserving the integrity of the mucus barrier (Sands and Podolsky, 1996). This is likely to be an area of continuing interest for understanding mucin stability. In addition, a mitogenic activity of trefoil peptides has been identified, which plays an important role in the recovery of the mucosa after damage (Dignass et al., 1994).

9.1.2 Structure and thickness of the mucus barrier

Mucus forms a continuous insoluble gel, adherent to the mucosal surface. The thickness of the mucus varies with location in the human: 50–450 μm in stomach, 10–250 μm overlying the villi in the ileum (Allen and Hoskins, 1988) and 107 ± 48 μm, 134 ± 68 μm and 155 ± 54 μm in proximal colon, distal colon and rectum respectively (Pullan et al., 1994). Isolated and purified mucins form reconstituted viscoelastic gels at similar