ABSTRACT

New insights into the mechanism of action of gelatine tannate for acute diarrhoea. Part 2: antibacterial activity.

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Background:

The pathogenesis of infectious diarrhoea can be osmotic or secretory. Whilst osmotic diarrhoea results from unabsorbed solutes exerting an osmotic force and driving water into the intestinal lumen, secretory diarrhoea occurs as a net secretion of water into the intestinal lumen regulated upon the effect of second messengers, thereby resulting in massive water secretion and dehydration. If the latter is caused by bacterial enterotoxins, such as cholera toxin or *E coli* heat-stable enterotoxin, osmotic diarrhoea ultimately results from epithelial damage induced by the cytotoxic effect of viruses, most commonly rotavirus. Tannins are long known to be insoluble in basic environments, thought therefore to exert a local effect on the intestinal lumen through their ability to bind proinflammatory mucoproteins. Tannins also bind bacterial toxins and inhibit bacterial growth. Nevertheless, the mechanism by which gelatine tannate may be effective against bacteria was not fully understood so far.

Aims:

We assessed the efficacy of gelatine tannate against *S typhimurium* or *E coli* adhesion in an *in vitro* intestinal epithelial model in order to determine the mechanism of action of gelatine tannate and also if it can confer additional protection against secretory diarrhoea.

Study design and methods:

The Caco-2 monolayer is a relevant, well-established model that recreates *in vitro* the intestinal mucosa deprived of mucous cells; the modified model (Caco-Goblet), including mucus-secreting goblet cells, represents a more predictive model to study ion transport and interaction with mucus. After pre-incubation with gelatine tannate 5 mg/mL for 4 hours, we tested the protective effect of gelatine tannate against intestinal adhesion following inoculation (1 hour) with either *S typhimurium* or *E coli*, both administered at the concentration of 1e+07 CFU/well, to Caco-2 and Caco-Goblet models, respectively. The invasive efficiency was expressed as the number of viable internalised bacteria by counting the colony-forming units (CFU).

Results:

We observed a significant restriction of passage of *E coli* (from 2.1e+04 to 1.45e+03 CFU/mL) and *S typhimurium* (from 2.3e+05 to 6.4e+04 CFU/mL).

Conclusions

Most interestingly, gelatine tannate showed a strong protective effect against adhesion of *S typhimurium* and *E coli* in Caco-2 and Caco-Goblet models, indeed not described so far for any other antidiarrhoeal. These results are in good agreement with film-forming properties of gelatine tannate, quantified as reduction of paracellular flux by TEER and Lucifer yellow measurements, and corroborate the hypothesis of a physical barrier formation by gelatine tannate, contributing to the growing body of evidence of its film-forming properties.