

Chitosan and Crosslinked Chitosan for Colonic Specific Drug Delivery

Purpose: Chitosan has been proposed for bacterially triggered targeted drug release to the ~~colon~~colon; however, its degradation by human colonic microflora has never been shown; ~~it has been suggested that these bacteria may not be capable of chitosan digestion.~~ The purpose of this study is to establish this fact, and investigate further factors pertinent to colonic drug delivery; pancreatic digestion and swelling of chitosan in aqueous conditions. Furthermore, we examine the effects of crosslinking on chitosan.

Methods: Chitosan films were prepared by dissolution of chitosan into 5% acetic acid in water, and casting onto Teflon plates, with/ without the addition of crosslinking agents. The films were incubated in 10% human faecal material (in pH 6.8 phosphate buffered saline [PBS]), pancreatic enzymes (porcine, USP, in PBS pH 6.8) or control conditions (PBS pH 6.8), under anaerobic conditions, at 37°C for 4 or 18 hours. The extent of digestion was assessed by measuring the weight loss. Swelling of the films was assessed over a 24 hour period, by incubation in phosphate buffered saline (pH 6.8) or hydrochloric acid (~~0.1N~~, pH 1.2), with weighing at intervals to establish water uptake.

Results

Chitosan (uncrosslinked) showed complete digestion by human faecal bacteria. Crosslinking chitosan with tripolyphosphate did not reduce the amount of digestion, but crosslinking with glutaraldehyde was able to significantly inhibit digestion at 4 hours. When developed as a dosage form, these materials must avoid degradation in the upper gastrointestinal tract by dissolution or pancreatic enzymatic digestion. Chitosan (uncrosslinked) showed acid dissolution, high swelling at pH 6.8 and was digested by pancreatic enzymes. Chitosan crosslinked with tripolyphosphate showed less water uptake, and at high crosslinker concentrations acid dissolution was prevented. Pancreatic enzymatic digestion was also avoided at 4 hours. Glutaraldehyde crosslinked chitosan had very low swelling and avoided pancreatic digestion.
~~Uncrosslinked Chitosan was completely digested by human faecal microflora and pancreatic enzymes in 4 hours. Covalent crosslinking (glutaraldehyde) inhibited colonic and pancreatic digestion at 4 hours. Ionic crosslinking (tripolyphosphate) inhibited pancreatic digestion, but not faecal. full digestion in faecal material was seen at 4 hours. The resistance to digestion by crosslinked chitosan is cross linker concentration dependent, and related to the polymeric network density. This can be seen with concentration and crosslinker dependent swelling; noncrosslinked chitosan swells the most at pH 6.8 and dissolves at pH 1.2. Glutaraldehyde crosslinked chitosan shows least swelling at either pH, and no acid dissolution. Tripolyphosphate crosslinked chitosan falls between these.~~

Conclusion. Colonic ~~microflora bacteria~~ are capable of digesting chitosan. However, chitosan alone, or chitosan crosslinked with glutaraldehyde do not show appropriate digestion/ swelling profiles necessary for colon specific release. Chitosan, crosslinked with tripolyphosphate may show some potential as a colonic drug carrier; further investigation is warranted.

Comment [CU1]: Unclear. Clarify chitosan concentration and cross linker concentration, or is it molecular weight of chitosan?

Comment [CU2]: Can you rewrite the results paragraph? A little unclear.

