Enhancing pH-responsive drug release in gastrointestinal environment by alginate – CMC/CAP microbeads

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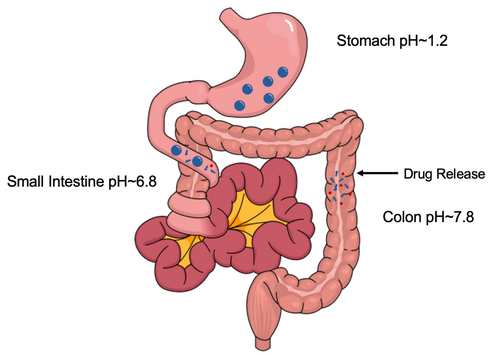
Introduction

Background

- Colon-targeted delivery maximizes local drug levels and reduces systemic effects.
- Prevention of premature drug release in stomach remains challenging.
- Sodium alginate (SA) is commonly used for oral encapsulation but lack of strong pH sensitivity.
- Carboxymethyl cellulose (CMC) and cellulose acetate phthalate (CAP) show the strong pH-dependent swelling and degradation properties.

Objectives

- Develop a pH-responsive drug delivery system.
- Analyze the drug release behavior of different type of microbeads under gastrointestinal-mimicking environment.
- Evaluate the effectiveness of polymer blending strategies to enhance colon-targeted drug release.



Sequential release of drug in gastrointestinal environment

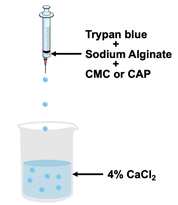
Methods

Microbeads Preparation

- Ionic gelation of SA containing 0.04% (w/v) trypan blue (TB) or 1% (w/v) Dexamethasone (DEX).
- Formulations: a) 1% CMC + 1% SA. b) 0.5% CAP (in acetone) + 1% SA. c) 1% CMC + 0.5% CAP + 1% SA.
- Drop into 4% $CaCl_2$ and crosslink for 5 min.

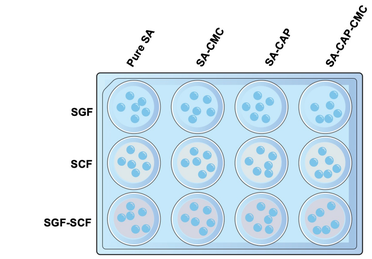
Characterization

- Optical microscopy for bead morphology.
- Drug-release testing
  - Phase a: Simulated Gastric Fluid (SGF) (pH 1.2) for 2 h.
  - Phase b: Simulated Colonic Fluid (SCF) (pH 7.8) for 2 h.
- TB quantification: Absorbance at 630 nm
- Data analysis: Fit cumulative release amount to zero-order, first-order, Higuchi, or Korsmeyer-Peppas model.



Fabrication

Characterization

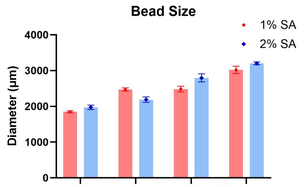


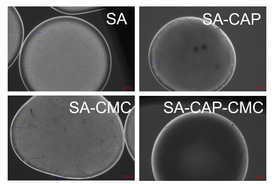
***In vitro* release**

Results

Morphology

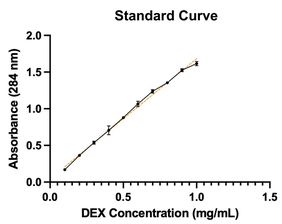
- Microbeads with different size were fabricated.
- The morphology of four kinds of microbeads were characterized.

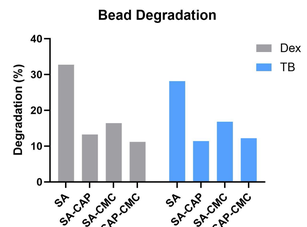




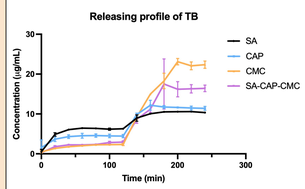
Data Analysis

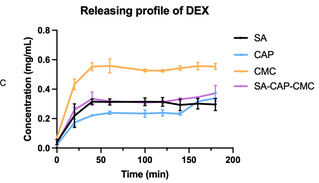
- The standard curves of Trypan Blue and DEX were created.
- Addition of CMC or CAP decelerated the degradation of SA in SGF.
- Upon transferring to SCF, SA microbeads showed a relatively slow release, while CMC-containing SA microbeads demonstrated accelerated release of drugs.





- CMC group showed the minimal release in SGF and maximum release in SCF.
- The addition of CAP to SA slightly improve the performance of SA microbeads.





Conclusion

Incorporating CMC and CAP into alginate microbeads significantly improved their pH responsiveness by reducing drug release in acidic gastric condition and enhancing targeted release in the neutral colonic environment. As compared to conventional CAP-coated strategies, this method is simpler and more practical, showing great potential for enhanced oral delivery.

References

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