4cp Molecularly Designed Mucoadhesive pH Responsive Tethered Biomaterials and Their Use in Spatially Controlled Therapeutic Delivery

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Introduction

The idea of mucoadhesive delivery systems has been the focus of intense research over the last three decades, however very few materials that exhibit clinical success have been developed. Very little bioavailability data exists showing an improved pharmacokinetic profile due to the mucoadhesive nature of the delivery system. This provides clear evidence that there has been very little success in developing a truly mucoadhesive dosage form. This failure can be attributed to the assumption of developing systems that have mucin-only interacting capabilities. Many other factors must be considered in designing a superior formulation.

A need exists for the development of drug delivery system capable of following normal GI transit but possessing the capability to increase residence time in the small intestine. Through a synergistic combinatorial approach, materials capable of hydrating to control release, creating a highly viscous suspension, developing intimate contact with the mucous gel layer, and interpenetrating into the mucus to develop enhanced physical bridging have been developed to create a delivery system capable of increasing the residence time of a therapeutic.

Research Objectives

The goals of this work have been to (a) synthesize and characterize novel high viscosity-inducing hydrogel microparticles possessing the necessary surface energy characteristics and tethered structures to, upon contact, develop intimate physical bridges with the mucous gel layer; (b) formulate these particles into a dosage form capable of spatially delivering the therapeutic to the small intestine while maintaining the desired physicochemical characteristics of the mucoadhesive biomaterials; (c) investigate the ability of these systems to effectively increase bioavailability through in vitro cell-culture models and in vivo animal studies.

A properly formulated viscosity-inducing polymer, poly((meth)acrylic acid), can slow the transit of a dosage form in the small intestine. With the addition of a linear polymer chain, either nonionic (poly(ethylene glycol) (PEG) or cationic (poly(2-(dimethylamino)ethyl methacrylate) (PDMAEMA)), additional physical bridges can be formed with the creation of electrostatic interactions. Capsule formulations allow for proper gelation of the material and work with the contractile forces of the small intestine to spread the contents along the intestinal wall, effectively maximizing the contact between the formulation and the mucous gel layer. Enteric coating provides spatial targeting allowing the therapeutic to be delivered within its window of narrow absorption.