76g Novel Mucoadhesive Formulations Employing pH Responsive Biomaterials

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A significant amount of effort has been spent on identifying ways to slow down the GI transit of the therapeutic especially that of the small intestine, the location where the majority of absorption occurs. The two main areas of thrust for research pertaining to increasing the bioavailability of drugs possessing narrow absorption windows are retaining the dosage form in the stomach (Gastroretentive) and slowing down transit time in the small intestine (mucoadhesive). Gastroretentive dosage forms maintain the drug delivery system above the absorption window and release the drug accordingly. Mucoadhesion affords the ability to slow upper GI transit by maintaining the dosage form at the site of absorption through some type of interaction with the intestinal mucosa. The motility of the gastrointestinal tract plays a major role in appropriately engineering a dosage form. The delivery system must be designed so that it works with the digestive system to accomplish the goal of targeting the area where the narrow absorption window of the therapeutic exists.

Smart biomaterials composed of pH responsive polymers, poly((meth)acrylic acid), were synthesized using a precipitation polymerization technique. The microparticles were grafted with linear polymer chains (PEG) that are capable of complexing with the hydroxyl groups of the polyacid and interpenetrating into the mucus gel layer upon entry into the small intestine. Upon introduction of an alkaline solution, these materials imbibe a significant amount of water and create a highly viscous solution. The gelled materials serve as both a control release membrane and resist the inertial forces associated with motility, thereby effectively slowing down the transit of the dosage form. The amount and length of the linear chain were varied to investigate their effects on the release behavior of ranitidine HCl.

Formulations composed of anhydrous lactose, ranitidine HCl, Cab-O-Sil, magnesium stearate, and the pH responsive polymer microparticles were formulated into HPMC size 0 capsules. The release behavior of these capsule formulations was assessed using dissolution in both SGF and SIF. Capsules containing the aforementioned formulations were coated with Eudragit L 30D 55, and dissolution was performed in SGF for two hours followed by SIF. Thermal analysis of the formulations was performed using DSC, and the physical mixtures were evaluated using FT-IR.

Dissolution studies conducted indicated that the polymer particles are capable of controlling the release of the therapeutics which is dependent on the medium's pH. Particles containing larger amounts of PEG, released the drug at a more rapid rate due to the lowered cohesion of the individual particles. Diffusional inhibition is lowered due to the lack of the gel membrane. Enteric coated capsules were successful in preventing release in the stomach and provided a dosage form capable of releasing the therapeutic at the site of optimal absorption.

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