



Development and evaluation of a swellable and floatable gastro-retentive delivery system

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Introduction

Gastro-retentive dosage forms have been the topic of interest in recent years as a practical approach in drug deliveries to the upper GI tract for release prolongation and absorption (figure 1). Drug candidates for these delivery systems include drugs that are absorbed mainly in the stomach or upper small intestine, or drugs that are unstable in basic environment of distal intestine and colon or those with low solubility at elevated pH conditions. Various strategies to achieve gastric-retention have been proposed and some successfully commercialized.

Objectives

Design, release evaluation and characterization of a swelling and floating delivery system for alfazosin and combination of tetracycline/metronidazole and colloidal bismuth subcitrate.

Methodology

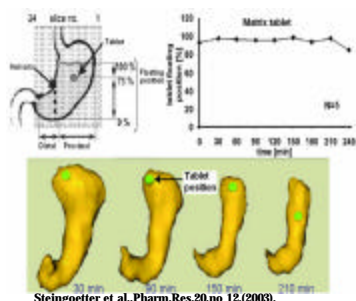
Polyethylene oxide, HPC and HPMC were used as matrix former, while microcrystalline cellulose and various excipients were used to facilitate manufacturing process. Two and three layered matrices containing various drugs within each polymeric layer in a composite system were manufactured and analyzed for drug release, floatation, and swelling and erosion behavior under acidic conditions. The hydrodynamic conditions during dissolution were also controlled by insertion of a mesh along with standard USP 27 paddle method at 50 and 100 rpm. Spectroscopy (UV) and HPLC were used for analysis of drug release for each drug and drug combinations respectively. A texture analyzer was used to calculate swelling dimensions and changes in rheological properties of the swollen matrices. System) were used

Results and Discussion

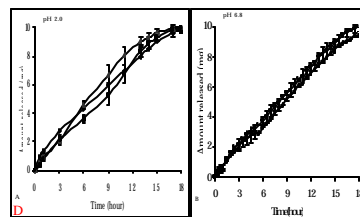
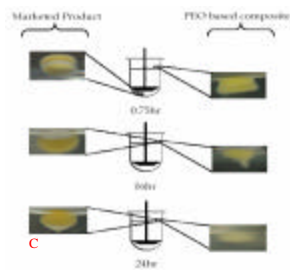
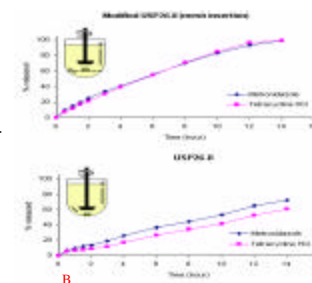
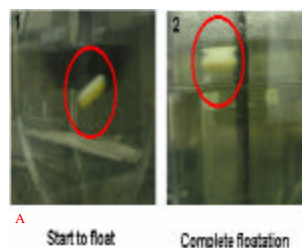
All developed composite systems (three-layer tablets) demonstrated rapid swelling with no lag time for floatation. All systems showed floatation within the upper 1/3rd of the dissolution vessels in < 15 minutes. Drug release from the delivery systems depended on erosional and swelling properties of the polymers used irrespective of compression force or tablet shape. Extent of swelling was controlled by combination of low and high molecular weight polymers with appropriate amounts of release retarding excipients. Rate and textural characteristics of matrix swelling during dissolution were determined. Hydrodynamic effect appeared to have little effect on drug release and five fold increases in overall matrix dimension due to swelling was easily achievable (figure 2, A-G).

Conclusions

Controlled release delivery of single and drug combinations in an acid environment under different hydrodynamics resembling stomach condition are shown. For gastro-retentive purposes rapid swelling and floatation in an in-vitro experimentation in either 500 ml or 1000 ml acid buffer was achieved. Extent of swelling and eventual erosion/dissolution of the entire delivery system was polymer dependent and could easily be manipulated. The delivery design provides opportunity for further investigation of drug combinations for either local effect in stomach or for drugs that have narrow window of absorption. Zero-order drug delivery and composite swelling dynamics offer a novel approach for GRDDs design.

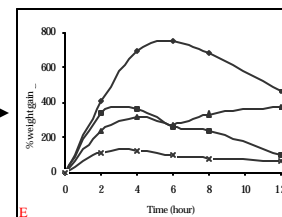


Steingoetter et al. Pharm.Res.20.no 12.(2003).
Figure 1. Coronal view of stomach illustrating calculation of the intra-gastric tablet position and 3D-MRI visualization of stomach volume



Marketed product (?), H/HM7 (?), PEO M6 (?)

Figure 2. Typical evaluation of gastro-floatable composite systems. Relative location of the delivery system in the vessel, release profiles and swelling behavior are shown. Note that once front synchronization is established zero-order kinetics can be achieved.



Layer 1 of PEO M6 (?), layer 3 of PEO M6 (?), PEO M6 (?), two layer composite based on HPMK/HPMC (?).

