Colon specific delivery system based on ethylcellulose-alginates microspheres loaded with mesalazine

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Abstract:
The effectiveness of any medical therapy is determined not only by the therapeutic agent's pharmacokinetic and pharmacodynamic activity, but also, to a significant part, by its bioavailability at the site of action in the human system. Orally administered nano/micro drug systems (Novel Drug Delivery Systems: NDDSs) exhibit their higher effectiveness in colon therapy, particularly for bowel diseases such as Crohn's disease, ulcerative colitis, colon cancer by augmenting drug bioavailability through the protection of the drugs molecules from the acidic area and increasing penetration into the intestinal membrane. The aim of the present work was to prepare and characterize mesalazine (5-aminosalicylic acid) loaded microspheres consisting of different ratios of sodium alginates (ALG) and ethylcellulose (EC) using emulsion solvent evaporation method for intestinal release. Properties of the microspheres such as surface morphology and size, FT-IR, DTA, TGA, drug content, drug release behavior, percentage drug entrapment, percentage yield of in vitro drug release were evaluated to investigate the more suitable preparation parameters. Drug release studies were carried out in acidic medium (pH=1.2) for 2h and in phosphate buffer solution (pH=6.8) up to 8h. Ideal slow release of (5-ASA) was highly affected by this coating. Mesalazine had low dissolution ratio in acidic gastric conditions and microspheres exhibited less than 20% of active ingredient released in gastric solution, while more than 50% was released over 7h in the intestinal conditions medium. The results showed that the sustained release systems thus prepared are suitable for vectorized delivery of the drug if they are administered for colon therapy.

Key words: mesalazine, solvent evaporation method, microencapsulation, NDDSs system.

Introduction
Pharmaceutical invention and research are increasingly focusing on delivery systems which enhance desirable therapeutic objectives while minimizing side effects. Oral drug delivery system represents one of the frontier areas of drug delivery systems. Such a dosage form changes common concern which exists in areas of core dosage form, patient compliance, optimum drug delivery and bioavailability[1]. Carrier technology offers an intelligent approach for drug delivery by employing the drug to a carrier particle such as microspheres, nanoparticles… which modulates the release and absorption characteristics of the drug[2]. Microspheres constitute an important part of this particular drug delivery system because of their small size and efficient carrier characteristics. However, the success of this novel drug delivery system is limited due to their short residence time at the patient compliance, optimum drug delivery and bioavailability.

Results and discussion
Determination of drug content
Table 1: Determination of drug content of all formulations in pH=1.2

Release kinetics in the gastric medium
Fig 6: Release profiles of 5-ASA from microspheres in pH=1.2

Mathematical modeling of release profiles in the gastric medium
Fig 8: The release kinetics and mathematical modeling studies of batches 6, 8 and 9

Conclusion
The colon-targeted microspheres 5-ASA were prepared by emulsion solvent evaporation technique. Based on the results of the physicochemical characterization and in vitro drug release studies:

- The dual cross-linked alginate-ethylcelulose formulations were developed as a sustained release multi-particle delivery system that may be effective to achieve desired targeted specificity.
- The release kinetics and mathematical modeling studies carried out for optimized formulations showed that the optimized formulations were of non-filmation mechanism that was governed by both diffusion and erosion controlled.
- The system fulfilled Hansotte and Konzenoy or pyramal model fittings that interpreted for sustained and controlled drug releases. In conclusion, this work presents possible approaches for the modified release of conventional drug into newer system with a potential for colonic drug delivery and treatment of inflammatory bowel diseases.

References

Fig 1: 5-ASA microspheres preparation
Fig 2: FTIR spectrum of pure (5-ASA, ALG, EC)
Fig 3: FTIR spectra of microspheres
Fig 4: TGA/TDA of microspheres
Fig 5: Optical microscopy of microspheres (batch 08)
Fig 7: Release profiles of 5-ASA from microspheres in pH=6.8
Fig 9: Release profiles of 5-ASA from microspheres in pH=1.2