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# THE RELEASE OF FAMOTIDINE FROM POLY(ACRYLIC ACID) MICROSPHERES

# POLİAKRİLİK ASİT MİKROKÜRELERİNDEN FAMOTİDİNİN SALIMI

**ZELİHAGÜL DEGİM**

Faculty of Pharmacy, Gazi University, 06330 Etiler, Ankara, Turkey

*Microspheres of famotidine as an anti-ulcer drug have been prepared by w/o emulsification technique using poly(acrylic acid) as a polymeric material. Drug release from the microspheres was determined at pH 1.2 simulated gastric medium using continious flow through cell. The release rate of famotidine was determined by using microspheres which have different curing times.*

*Antiasit ilaçlardan biri olan famotidinin, poliakrilik asit ile y/s emülsiyon tekniği kullanılarak mikroküreleri hazırlanmıştır. pH=1.2'lik yapay mide ortamında sürekli akış hücresi ile ilaç salımı incelenmiştir. Farklı çapraz bağlanma süreleri kullanılarak hazırlanan mikrokürelerden famotidin salımı incelenmiş ve bulunan sonuçlar karşılaştırılmıştır.*

**Keywords** : *Poly(acrylic acid); Microspheres; Curing time; Famotidine*

**Anahtar kelimeler:** *Poliakrilik asit; Mikroküre; Çapraz bağlanma; Famotidin*

## Introduction

In recent years, considerable interest has been shown in the use of mucoadhesive dosage forms with regard to enhancing the local and systemic administration of peptides and other poorly absorbed drugs from the gastrointestinal tract(1). Bioadhesive controlled release systems for drug delivery are often designed in order to target drugs in spesific areas of the body(2).

Mucoadhesive polimers have been developed for buccal, nasal, ocular, vaginal, urinary and oral applications(3).

Mucoadhesives may remain attached to the gastric mucus layer until they are removed spontaneously from the surface by various factors including natural mucin turnover. Therefore, the study of mucoadhesives may provide approaches that enable not only prolongation of the total residence time but also control of the retention time of oral dosage forms in the stomach and perhaps elsewhere in the gastrointestinal tract. In earlier studies, a large number of polymers were examined as to their bioadhesive/mucoadhesive potential in order to derive meaningful information on structural requirements for attachment. It was observed that polyanions with a high charge density, such as poly(acrylic acid), were good mucoadhesive (4-6).

Histamine2 receptor antagonists like famotidine are beneficial in the treatment of gastric and duedonal ulcers, gastroesophageal reflux and hypersecretory states. Famotidine is also helpful in the prevention of strees ulceration and recurrence of gastric and duedonal ulcers. The elimination half-life for famotidine is 2-3 h. (7).

Famotidine (20-40 mg) supresses nocturnal acid by 85% when administrated orally (8,9). Therefore microcapsules (10) or microspheres were adopted to retard its release and to reduce the number of doses required, there by reducing the amount necessary to achieve sustained action.

## Materials and Methods

*Materials*

Famotidine was obtain from Ilsan-Iltas (Turkey), poly(acrilic acid) was obtained from Aldrich Chemical Co. (U.K).

*Methods*

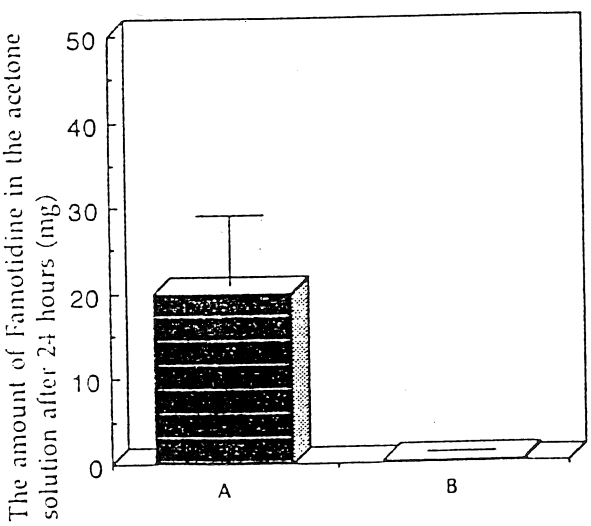
Microspheres were prepared by method of Lewis and Kellaway(11,12). A w/o emulsification technique was employed where the aqueous medium consisted of 1 g poly(acrylic acid) with 0.26 g of maltose and organic medium was 100 ml of olive oil containing 0.4 g palmitic acid. Since palmitic acid is an endogenous lipid, any residual amounts present in the microspheres should be pharmaceutically acceptable. Both the organic and aqueous mediums were placed in a wide-necked round bottomed flask and stirred 8000 r.p.m. by ultraturrax (Janke&Kunkel), within a few minutes a fine emulsion was heated to 90-105°C for 1.5-4 hours until the oil appered clear and the microspheres were cured. The cooled mixture was poured into a large beaker containing 200 ml of acetone. The flask was washed thoroughly with a further 100 ml of acetone. The supernatant phase was removed from the sedimented particles. The microspheres (15-85 μm) were washed repetedly with acetone until no traces of oil could be detected. The

microspheres were dried and stored under vacuum and sized using a Malvern Laser Diffraction Spectrometer. Then the particles were treated for 24 h. with drug in acetone for loading and acetone was evaporated under vacuum and drug was loaded into the microspheres.

The dissolution rate of famotidine microspheres were determined in triplates at pH 1.2 and 37°C at the required flow rate of continious flow through cell. The samples were analysed by HPLC using a reverse phase $C_{18}$ column. The eluent consisted of 15% methanol, 69% water, 16% 0.05 M sodium dihydrogen phosphate and the flow rate was 2 ml/min. (13).

## Results and Discussion

The acetone solution was used to load famotidine to the poly(acrylic acid) microspheres because when aqueous solution of famotidine was used all the poly(acrylic acid) microspheres swelled and sticked to each other permanently and lost their microsphere forms after the water was evaporated. The microspheres absorbed famotidine by passive diffusion over 24 h. The diffusion of famotidine into the microspheres was checked and determined by HPLC Fig. 1 shows the absorbtion of famotidine by the microspheres.




A: Famotidine in Acetone
B: Famotidine in Acetone + PAA microspheres (200 mg)

Fig.1. Amount of famotidine (mg) in the solution of acetone after 24 hours

In general drug release was sustained for at least 6 hours. Different preparation times were compared and it was evident that increased curing time gave rise to an increased rate of release of famotidine as shown in Fig. 2.

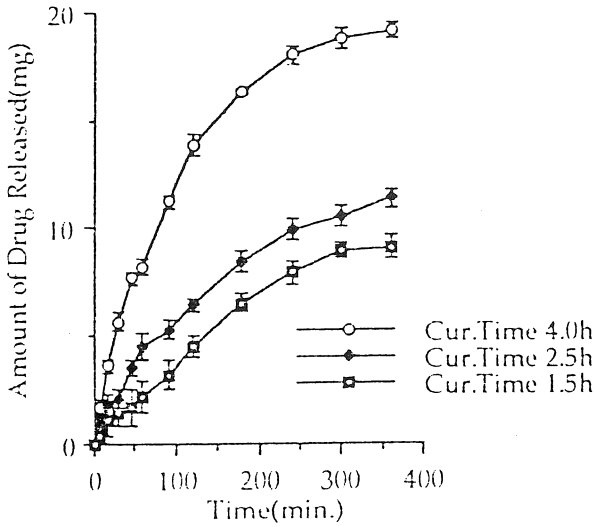



Fig.2. In vitro release of famotidine from microspheres of [Malt]:[PAA] 4.0:10.0, with different curing times

It is possible that with increased curing time the polimeric network inside the microspheres becomes heavily cross-linked. This would account for the low percentage of famotidine released from the least cured particles. The microspheres were not as critical varying the curing time for a change in the rate of release of famotidine. An increase in the curing time of the particles resulted with an increase in the release rate of drug, possibly due to the association of the famotidine on the surface of the highly cured microspheres, and not throughout the polymeric network.

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