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Synthetic zeolites for drug delivery

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Abstract

Ibuprofen was encapsulated into synthetic zeolites by a soaking procedure. Drug-loaded matrices were then characterized for entrapped drug amount. The total amount of ibuprofen (800 mg) was encapsulated in 2 g of matrix. By using UV-Visible spectrophotometric measurements, ibuprofen release studies were done at different pH conditions so as to mimic gastrointestinal fluids. The absence of release in acid conditions and a double phased release, at two different pH values (5 and 6.8), suggest that after activation these materials offer good potential for a modified release delivery system of Ibuprofen.

Key words: zeolites; ibuprofen; drug delivery

Introduction

Zeolites and related microporous materials have a viable potential for drug delivery systems. Moreover, synthetic materials have the advantage of a bigger degree of purity, checked composition, and, most important, the opportunity to improve the essential biological and mechanical properties of drug delivery[1].

In the wake of this burgeoning research, the aim of our study was to verify the possibility of exploiting synthetic zeolites as delivery systems for targeted release in the gastrointestinal tract. An activated 13x zeolite was considered for the encapsulation of ibuprofen because of their pore structure. The choice of ibuprofen as a model drug, for this study, was justified by its short half-life, low bioavailability, and local or systemic disturbance in the gastrointestinal tract[2,3]. Accordingly, this drug was first



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encapsulated into these materials, by a soaking procedure, and then its release was studied at different pH conditions mimicking gastrointestinal fluids.

Materials

Zeolite samples, activated 13x zeolite was supplied by SPAG, Iran. Ibuprofen was purchased from Daru-Pakhsh Iran. Other chemicals and solvents were of reagent grade and were used without further purification.

Drug loading

Ibuprofen loading into the zeolites was achieved as follows: 2 g of zeolite were soaked, for two days, at room temperature, under continuous stirring, in a solution of 800 mg of ibuprofen in ethanol (30 mL).

Finally, the solvent was removed by filtration and the samples were dried by rotoevaporation under vacuum, at 30°C. The amount of drug contained within zeolites and on the surface was determined by gravimetry. Each experiment was repeated in triplicate and deviation standard was calculated.

Drug release studies

In vitro release studies of ibuprofen from zeolites were carried out as follows: 10 mg of each matrix, loaded with the drug in 40 mL of a 0.1N HCl solution (pH 1.0 simulated gastric juice), was kept at 37°C for 90 min under magnetic stirring. Then, 26.7 mL of a mixture of Na₂HPO₄ 0.2M and NaOH 0.1N was added to adjust the pH to 5.0 and, after 60 min, another 15.8 mL of buffer was added to reach pH 6.8, a condition simulating the pH gradient and the ionic condition along the gastrointestinal tract. Every 15 min, samples were filtered and analyzed by UV-spectrophotometry at 280nm. Calibration curve was determined using six different ibuprofen concentrations (100, 20, 5, 2, 1, 0.5mg/ml).

Results

Characterization

Demonstration of ibuprofen loading was indicated by IR experiments. Some characteristic adsorption peaks of ibuprofen, indicated were observed both in ibuprofen/zeolite samples, confirming that the drug was successfully loaded into the zeolites (figure 1).

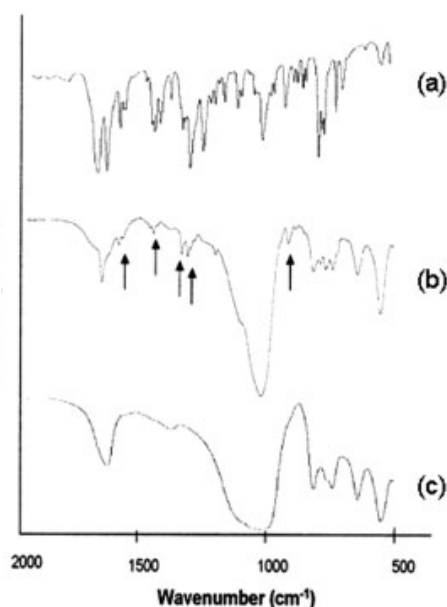


Figure 1. IR spectra of (a) Ibuprofen, (b) Ibuprofen/Zeolite (c) Zeolite

Loading of drug

The actual loading of ibuprofen into the zeolites was determined by gravimetry, which is a technique that weighs the powder after the solvent has evaporated. The total amount of ibuprofen (800 mg) was encapsulated in 2 g of matrix (28.5% of drug impregnated with respect to the impregnated zeolite).

Drug delivery profiles

Figure 2 shows the time-dependent release rates of ibuprofen. As elucidated in the experimental section, the analysis was carried at different pH levels and time periods so as to simulate gastrointestinal fluids. During the first 90 min, the pH level had the value of 1; during the following 60 min, the pH level had the value of 5.0 and then it was increased to 6.8. These data, expressed as percentages, indicated that whereas a very small quantity of the drug was released under low acid conditions, it was totally annihilated when the pH reached the higher value of 6.8 at a later time period. The interesting result was represented by the fact that ibuprofen release began at pH 5.0. An explanation for this phenomenon could be that the formation of a great amount of dissociated ibuprofen molecules, occurring at almost neutral pH, may have promoted their release from the zeolites. Since pathological conditions of the gastrointestinal tract cause a decrease of pH value, a



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double phased release at two different pH values (5.0 and 6.8), makes these systems useful for the treatment of inflammatory bowel diseases[2] .

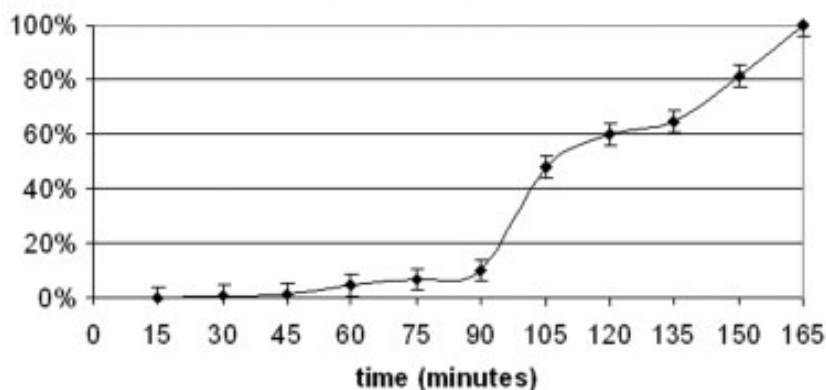


Figure 2. Time-dependent Ibuprofen release from activated from activated activated 13X zeolite at pH 1, pH 5 (90 min) and pH 6.8 (135 min).

Conclusion

Synthetic zeolites were studied to verify their ability to encapsulate and release an anti-inflammatory drug as ibuprofen. What makes this specific matrix highly suitable to create efficacious drug delivery carriers is the fact that in this study a simple soaking procedure was able to entrap ibuprofen. Drug loading was indeed confirmed by IR spectra. We found that less than 10% of the drug was released at the gastric level, a result that clearly indicates the effectiveness of this system in reducing the adverse effects commonly accompanying oral administrations of NSAIDs.

References

- [1] Cavallaro G, Pierro P, Palumbo FS, Testa F, Pasqua L, Aiello R. Drug delivery devices based on mesoporous silicate. *Drug Deliv* 2004; 11: 41-46.
- [2] Friend DR. New oral delivery systems for treatment of inflammatory bowel disease. *Adv Drug Deliv Rev* 2005; 57: 247-265.
- [3] Üner M, Gönüllü U, Yener G, Altınkurt T. A new approach for preparing a controlled release ibuprofen tablets by using beeswax. *Farmaco* 2005; 60: 27-31.