SURFACTANT-MODIFIED NATURAL CLINOPTILOLITE AS A CARRIER FOR CONTROLLED RELEASE OF ASPIRIN

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ABSTRACT

In this study, clinoptilolite-rich natural zeolite (NZ) from south region of Serbia has been investigated as a carrier for controlled release of aspirin. In order to modify the adsorption ability of clinoptilolite, NZ was pretreated with cationic surfactant - benzalkonium chloride (BC). It has been found that the NZ with bilayer BC coverage (NZ-BC) exhibits the highest aspirin uptake. Aspirin release from the NZ-BC displays two stages. The first stage occurs within first 15 minutes whereas the second one proceeds gradually over 6 hours. Release profile indicates that the delivery is controlled by a diffusion process in the first stage and by the electrostatic interaction between the drug and surfactant in the second stage.

Keywords: clinoptilolite, cationic surfactant, aspirin, drug delivery.

INTRODUCTION

The natural and synthetic zeolites have emerged as exciting materials for medical applications in the recent years [1]. One of the many potential pharmacological applications of zeolites is the possible encapsulation and/or adsorption of different ions and organic molecules and the subsequent delayed release. The adsorption of surfactants on the zeolite surface may modify its properties and favor the uptake of molecules which do not adsorb onto the solid in the absence of surfactants. This phenomenon is known in the literature as the surface solubilization, adsolubilization or co-adsorption [2].

The aim of this work was an investigation of the natural zeolite from south region of Serbia with high amount of clinoptilolite (70 wt.%) as a potential carrier for molecules of pharmaceutical interest. For this purpose, modification of the zeolite surface was performed using benzalkonium chloride as a cationic surfactant. BC is considered as a safe for human use and is widely employed in the pharmaceutical industry as preservative for drugs and in several cleaners and disinfectants [3]. Obtained composite zeolite/surfactant was used for additional investigation of aspirin as a model drug. The composites zeolite/surfactant and zeolite/surfactant/drug were characterized using different techniques.

EXPERIMENTAL

The material used was the natural clinoptilolite (NZ) from Zlatokop deposit (Vranje, southern Serbia). In order to improve NZ modification, NZ was previously converted to Na-rich form (NaNZ) by treating of NZ with 1 M NaCl solution. The suspension was shaken at about 100 rpm for 24 h in a thermostated water bath (Memmert WPE 45). The obtained NaNZ was then washed by distilled water and dried at 105 ºC. NaNZ (2.0 g) was mixed with 100 cm^3 of BC (p.a., Fluka) aqueous solution of different concentrations for 24 h at room temperature. The obtained composite NZ-BC was then washed by distilled water and dried at 60 ºC.

The liquid phase adsorption of the aspirin was carried out at different drug concentrations (500 and 1000 $\mu g\ cm^{-3}$). 0.5 g of the composite NZ-BC was treated with 50 cm^3 of the drug solution. The experiments took place at room temperature under agitation

at 600 rpm with a magnetic stirrer. The system was equilibrated for 4 h and then centrifuged. The obtained composites NZ-BC-drug were then dried at room temperature over the night.

The drug desorption was performed by soaking of 0.1 g of composites NZ-BC-drug in 40 cm^3 phosphate buffer (pH = 7.0) under constant stirring at 100 rpm and 37 ºC in a thermostated water bath.

RESULTS AND DISCUSSION

For characterization of the composites NZ-BC and NZ-BC-drug different techniques were used. X-ray powder diffraction (XRPD) analysis showed that modification of NaNZ by BC and aspirin sorption do not effect the clinoptilolite crystalinity.

Amount of the adsorbed BC was determined by C,H,N and thermal analyses (TGA). It is known that when the concentration of surfactant is equal to external cation exchange capacity (ECEC) of the zeolite, a general model of sorption is the formation of monolayer at the solid-aqueous interface via strong ionic bonds. The sorbed surfactant creates an organic-rich layer changing the charge of zeolite surface from more to less negative or even positive with increasing of the surfactant concentration [4]. The C,H,N analysis indicated that on the zeolitic sample treated to 100% of ECEC by BC, a monolayer of BC is formed. When the zeolite sample is treated with BC to 500% of ECEC, the amount of adsorbed BC is doubled compared to 100% of ECEC, indicating formation of a bilayer. This is supported by TGA data.

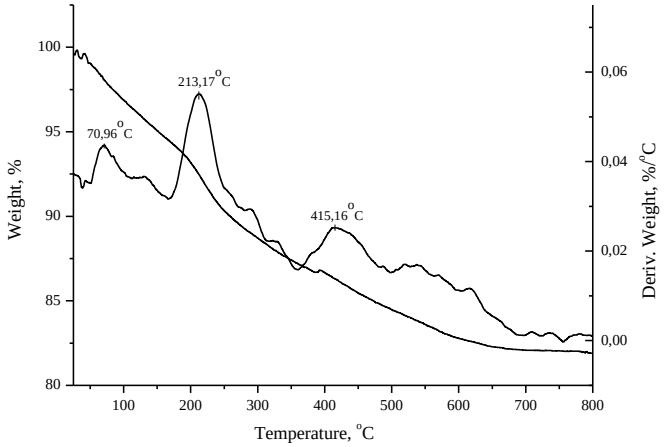

Figure 1. TG/DTG curves of the composite NZ-BC.

TGA provides information on the amount of energy required to remove surfactant molecules from the zeolite surface. The energy depends on whether the surfactant is present as a mono- or bilayer on the zeolite surface [5]. The mass loss below 170 ºC is attributed to unbound (physisorbed) water (Figure 1). The mass loss between 170 and 350 ºC accompanied by a derivative curve (DTG) peak centered at 213 ºC belongs to the BC from lower energy bonding sites. The third loss with the DTG peak centered at 415 ºC indicates the presence of strongly bonded BC most likely due to the electrostatic binding of the ammonium cation head group of BC to the electronegative zeolite surface.

FTIR spectra of NaNZ and composite NZ-BC are shown in Figure 2. Peaks at 3620, 3420, and 1640 cm^{-1} are characteristic bands of the clinoptilolite lattice connected to acidic hydroxyls Si–O(H)–Al, hydrogen-bonding hydroxyl groups, and bending vibration of absorbed water, respectively. On the spectrum of NZ-BC, three new bands appear showing the presence of BC. Two bands, at 2925 and 2855 cm^{-1}, are assigned to the C–H stretching

vibrations of the hydrocarbon chain, and third one at 1465 cm^{-1}corresponds to the C–H bending of the methyl groups [6].

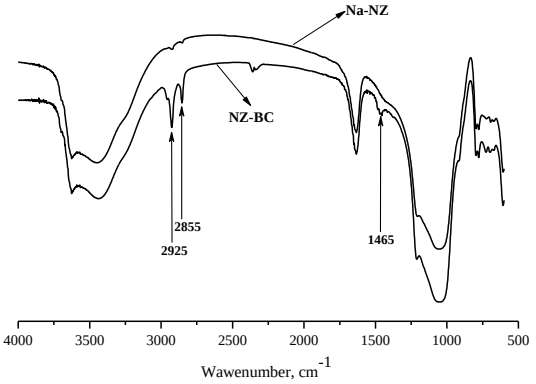

Figure 2. FTIR spectra of NaNZ and composite NZ-BC.

Solid state ^{1}H-^{13}C CPMAS NMR analysis was used to get an insight to the drug-surfactant interactions. The spectra are given in Figure 3. Only a peak at 30 ppm is evident indicating the presence of BC. It seems that the concentration of aspirin is not high enough to enable that peaks characteristic to aspirin are evident from ^{1}H-^{13}C CPMAS NMR spectra.

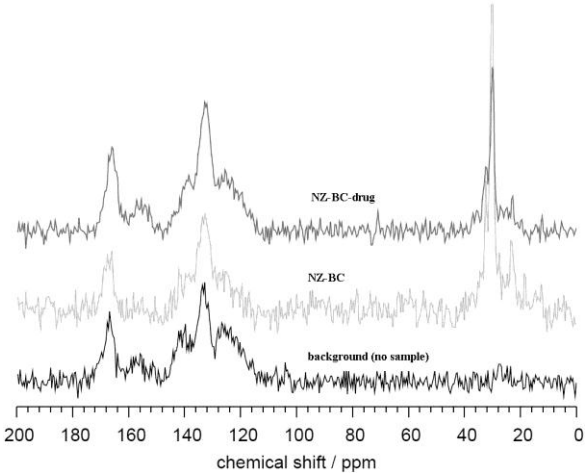

Figure 3. ^{1}H-^{13}C CPMAS NMR spectra of the NZ-BC and NZ-BC-drug composites.

The amount of aspirin adsorbed by the NZ-BC was determined by HPLC-UV method. It has been found that concentration of adsorbed drug increased with the initial concentration of the drug in solution. The results yield that NZ-BC with bilayer coverage exhibits the highest aspirin uptake.

Figure 4 shows the percentage of aspirin released from the NZ-BC-aspirin composite as a function of time. Aspirin delivery from the NZ-BC displays two stages. The first one occurs rather sharply within the first 15 minutes. Afterwards, the release proceeds more gradually. About 75% of the immobilized aspirin was delivered from the NZ-BC during 6 hours.

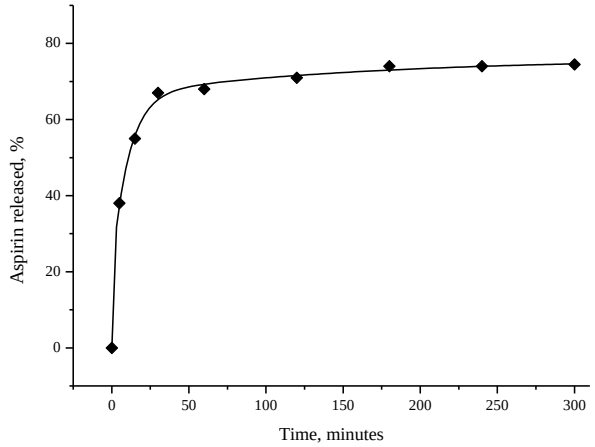

Figure 4. Percentage of aspirin released from the NZ-BC-aspirin composite.

CONCLUSION

We have studied the potential use of the surfactant modified natural clinoptilolite as a drug carrier. The natural zeolite shows a strong affinity for the cationic surfactant benzalkonium chloride which modified the zeolite surface without influence on the clinoptilolite crystallinity. The zeolite covered with the surfactant bilayer exhibits the highest aspirin uptake. Two stages are observed in the aspirin release. It could be supposed that in the first 15 minutes the delivery rate is controlled by a diffusion process whereas the electrostatic interaction between the carboxylic groups of aspirin and ammonium cations from the surfactant are predominant in the second stage.

REFERENCES

[1] A. Rivera and T. Farias, *Micropor. Mesopor. Mater.*, 2005, **80,** 337–346.

[2] T. Farias, L. C. de Menorval, J. Zajac and A. Rivera, *Colloid. Surface. B*, 2010, **76,** 421-426.

[3] T. Farias, L. C. de Menorval, J. Zajac and A. Rivera, *Colloid. Surface. A*, 2009, **345**, 51-57.

[4] D. Krajišnik, A. Dakovic, M. Milojevic, A. Malenovic, M. Kragovic, D. Bajuk-Bogdanovic, V. Dondur and J. Milic, *Colloid. Surface. B*, 2011, **83,** 165–172.

[5] H. Guan, E. Bestland, C. Zhu, H. Zhu, D. Albertsdottir, J. Hutson, C.T. Simmons, M. Ginic-Markovic, X. Tao and A.V. Ellis, *J. Hazard. Mat.*, 2010, **183,** 616–621.

[6] D. Krajišnik, M. Milojevic, A. Malenovic, A. Dakovic, S. Ibric, S. Savic, V. Dondur, S. Matijaševic, A. Radulovic, R. Daniels and J. Milic, *Drug Dev. Ind. Pharm.*, 2010, **36,** 1215–1224.

[7] A. Rivera, T. Farias, A. R. Ruiz-Salvador and L. C. de Menorval, *Micropor. Mesopor. Mater.*, 2003, **61,** 249–259.