THE PRELIMINARY STUDY ON THE NATURAL ZEOLITE AS A POTENTIAL CARRIER OF TETRACYCLINE

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ABSTRACT

The purpose of this study is to investigate adsorption of the antibiotic tetracycline on the natural zeolite - clinoptilolite. The adsorption was followed at the different initial concentrations of the drug in buffer solution at pH 3.4. Characterization of adsorbent before and after adsorption of tetracycline was done by the determination of zeta potential and by FTIR spectroscopy. Results showed that adsorption of the drug increased with increasing of its initial concentration and maximum adsorbed amount of the tetracycline was 27.5 mg/g. Characterization results confirmed presence of tetracycline at the zeolitic surface.

Key words: Natural zeolite; Clinoptilolite; Tetracycline; Adsorption; Drug carrier

INTRODUCTION

The instinctive application of natural zeolites in treating wounds and gastrointestinal complaints is as old as humanity itself. Through the centuries, until today, these two main biomedical applications of zeolite have been perfected, creating space for modern therapeutic systems based on zeolite [1]. Bacterial resistance to antibiotics forces the application of broad-spectrum antibiotics, which are not so frequently used today, such as tetracycline. Topical application of antibiotics on carriers, such as zeolites, in addition to a prolonged therapeutic effect and a more compliant application for the patient, also reduces the concentrations used, which is an important factor nowadays, considering environmental pollution [2].

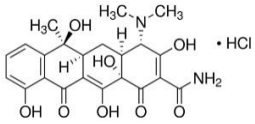
In this field important issue is to establish the balance between adsorption and release of the active ingredient kinetics at the required level, in this case, tetracycline from zeolite as a carrier. The carrier of choice is undoubtedly natural zeolite - clinoptilolite, because of its low cost, abundance and high availability. Recent studies published in the literature provided promising results on the antibiotic removal process using zeolites with the satisfactory removal rates [3]. The aim of this research is to investigate the potential of the natural zeolite – clinoptilolite as a carrier of the drug tetracycline. Characterization of the natural zeolite before and after adsorption of the drug was performed by the determination of zeta potential and by FTIR spectroscopy.

EXPERIMENTAL

A sample of natural zeolite-rich tuff from the Zlatokop deposit, Vranje (southern Serbia) (ZVB) was used as the starting material. The raw zeolitic tuff was sieved to obtain particles with a size of less than 43 μm. The complete chemical composition of the initial zeolitic tuff was as follows: 64.21% SiO_2, 0.25% TiO_2, 11.48% Al_2O_3, 0.88% Fe_2O_3, 1.45% MgO, 4.55% CaO, 1.71% Na_2O, 1.29% K_2O and 14.00% loss on ignition [4]. The cation exchange capacity (CEC) of the starting material was 146 meq/100 g measured by the ammonium chloride method, while the ECEC was 10 meq/100 g [5].

The adsorption of tetracycline hydrochloride (Sigma-Aldrich, USA) (TCl) on ZVB was carried out in batch experiments at room temperature. The physicochemical properties of TCl are listed in Table 1.

Table 1. Structural formula and physicochemical properties of the model drug [6].

Active pharmaceutical ingredient	Structural formula	MWt	pKa
Tetracycline hydrochloride *(4S,4aS,5aS,6S,12aS)-4-(Dimethylamino)-3,6,10,12,12apentahydroxy-6-methyl-1,11-dioxo-1,4,4a,5,5a,6,11,12aoctahydrotetracene-2-carboxamide hydrochloride*		480.9	pKa (strongest acidic) 3.26 pKa (strongest basic) 9.25

Aqueous stock solutions of the drug (pH 3.4) with different initial concentrations (0.05 – 0.5 mg/mL) were prepared in distilled water. Batch experiments were performed by shaking the mixture containing 40 mg of each composite and 10 mL of each drug solution on a laboratory shaker at 250 rpm for 1 h at room temperature and then separated after centrifugation at 3000 rpm for 30 min. The supernatants were used to determine the non-adsorbed drug concentrations. The initial and non-adsorbed drug concentrations were determined spectrophotometrically at λ=276 nm (Evolution 300 spectrophotometer, Thermo Fisher Scientific, UK). The amounts of adsorbed antibiotic were calculated from the difference between the initial concentrations of tetracycline and the amounts remaining in the aqueous medium after dynamic equilibrium.

Characterization of the natural zeolite and zeolite-drug composite was performed by zeta potential measurements of 0.1 mg/mL dispersions in deionized water using a Zetasizer NanoZS90 instrument (Malvern Instruments, UK) and by Fourier transform infrared (FTIR) spectroscopy using Nicolet iS50 spectrophotometer (Thermo Fisher Scientific, USA). FTIR spectra were recorded using Attenuated Total Reflection (ATR) with a diamond ATR smart accessory in the range of 4000-400 cm^{-1} at 64 scans per spectrum at 2 cm^{-1} resolution. A background scan was acquired before scanning the samples.

RESULTS AND DISCUSSION

The adsorption of TCl by the natural zeolite was studied by determining the adsorption isotherm. The isotherm was obtained by plotting amounts of the drug adsorbed per unit weight of adsorbent (mg/g) against the equilibrium concentrations of drug in solution (mg/L) (Figure 1.).

From Figure 1, it can be seen that adsorption of TCl by ZVB increased with increasing of the drug initial concentration. The drug adsorption followed a non-linear type of the isotherm, exhibiting the best fit of the experimental data to the Langmuir model (R^2 = 0.979), which indicates it was a saturable process with a monolayer formation. Good agreement of the experimental data with Langmuir model suggests that the surface of ZB may be homogeneous and only one single site (hydrated inorganic cations) could adsorb one molecule of TCl [7]. The calculated TCl maximum (Q_m) adsorbed amount was 27.5 mg/g, which corresponds to 57.2% of the ECEC value of the zeolite. These results suggested that adsorption of TCl at the surface of ZVB is occurred predominantly via ion exchange mechanism, through the replacement of the hydrated inorganic cations at the zeolitic surface with the positively charged TCl.

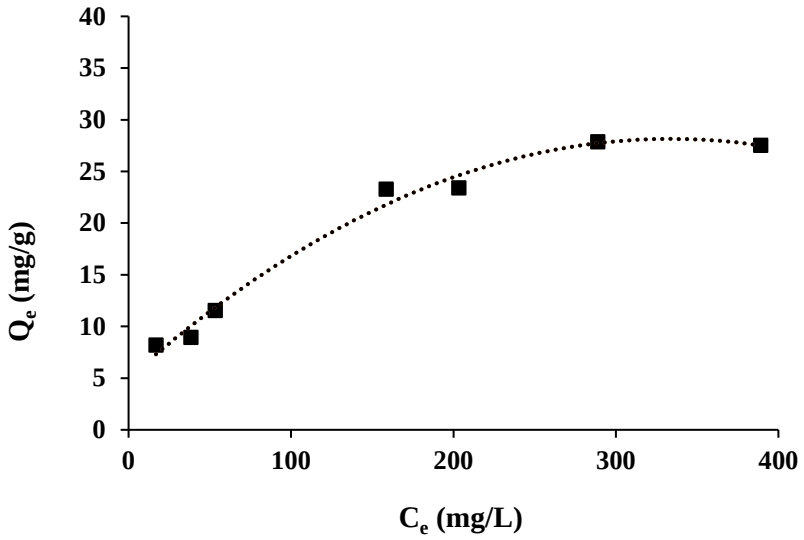


Figure 1. Adsorption of TCl by the natural zeolite (ZVB).

The interactions of TCl with the zeolite surface were determined by zeta potential measurement and FTIR analysis. The negative zeta potential value (–27.4 ± 0.8 mV) of the ZVB confirmed its negative surface charge. It was determined that after TCl adsorption, the zeta potential became even more negative (–36.3 ± 0.5 mV), indicating the interactions between the drug molecules and the zeolite surface occurred.

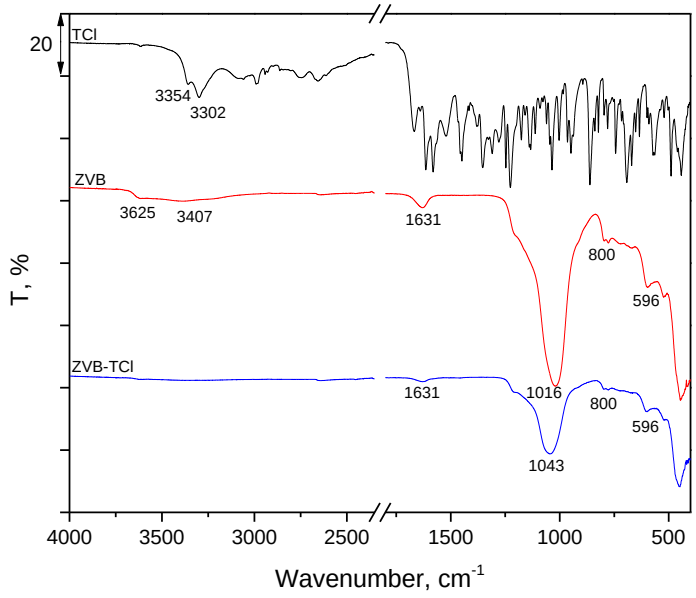


Figure 2. FTIR spectra of TCl, ZVB, and ZVB-TCl composite.

FTIR spectra of pure TCl and ZVB before and after adsorption of TCl are presented in Figure 2. The FTIR spectrum of the ZVB sample showed absorption bands characteristic for zeolites. These bands can be explained as follows: the broad bands at 3625 and 3407 cm^{-1} are attributed to the –OH stretching vibration of adsorbed water (water molecules coordinated Na^{+} and Ca^{2+} in the channels and at the zeolitic surface), intermolecular hydrogen bonding, and Si–OH–Al bridges; the band at 1631 cm^{-1} corresponds to the bending vibration of H_2O molecules; the strongest band at 1016 cm^{-1} is assigned to the asymmetric stretching vibrations of the internal

TO_4 tetrahedra; band at 800 cm^{-1} belongs to Si–O–Si bonds; and band at 596 cm^{-1} corresponds to bending vibrations between tetrahedra [8]. After adsorption of TCl, changes in FTIR spectrum of pure ZVB were noticed. The bands at 3625 and 3407 cm^{-1} disappeared while the intensity of band at 1631 cm^{-1} decreased suggesting that hydrated cations or hydroxyl groups at the surface of ZVB are involved in the adsorption TCl. Intensity of band at 1016 cm^{-1} significantly decreased after adsorption of TCl as well as peak was shifted toward higher wavenumbers (1043 cm^{-1}) indicating that these groups are involved in the adsorption process. The intensities of peaks at 800 and 596 cm^{-1} also decreased [3]. Results of FTIR analysis confirmed adsorption of TCl at the surface of ZVB.

CONCLUSION

The results of this study showed that the natural zeolite clinoptilolite is suitable for the adsorption of tetracycline. Adsorption of the drug was followed through the determination of the adsorption isotherm. Results showed the best fit of the experimental data with the Langmuir model suggesting that the surface of the clinoptilolite may be homogeneous and only one single site (hydrated inorganic cations) could adsorb one molecule of tetracycline. Further studies of the drug release and antibacterial activity of this composite will reveal its potential application as a drug carrier for skin formulations.

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