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Research paper

Adsorption and characterization of palygorskite-isoniazid nanohybrids

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ABSTRACT

Studies of the equilibrium and thermodynamic aspects of the adsorption of isoniazid onto a pharmaceutical-grade palygorskite and features of the resultant clay drug nanohybrid systems were carried out. Equilibrium studies were performed in aqueous medium at different times and temperatures. The overall adsorption process was explained as the result of two simple processes: drug adsorption on the activated sites of palygorskite and a slight precipitation phase of drug molecules over the adsorbed monolayer. Formation of the nanohybrid was spontaneous, exothermic and exoentropic, obtaining an increase in the thermodynamic stability of the system ($\Delta H = -48{,}82$ kJ/mol; $\Delta S = -0.14$ kJ/mol K). A full and comprehensive study of the solid state characterization corroborated the effective interaction between the components. Total amount of INH loaded was about 20% w/w. FTIR spectra revealed the interaction via water bridges between the endocyclic N of the drug and surface OH groups of palygorskite. Surface charge studies confirmed the non-electrostatic nature of the interactions.

1. Introduction

Nanotechnology offers numerous possibilities in the treatment of global concern diseases as tuberculosis, the second cause of death from an infectious illness worldwide (WHO, 2015). Design of nanoparticulate drug delivery systems with the current tuberculostatic agents appears as an interesting strategy for improvement of therapy, as a result of the increase in patient compliance and decrease of drug adverse effects (Sharma et al., 2017). The use of clay minerals as nanocarriers for tuberculostatic drugs is a current matter of growing interest (Carazo et al., 2016). In particular, halloysite nanotubes (Carazo et al., 2017) and montmorillonite-polymer nanocomposites (Verma and Riaz, 2017) have been proposed as effective drug platforms in tuberculosis treatment.

Palygorskite is a fibrous clay mineral with several industrial applications (Galan, 1996) and considered a suitable candidate to vehicle bioactive molecules due to its large surface area (López-Galindo et al., 2011; Mura et al., 2016; Tenci et al., 2017). Palygorskite structure was described as a 2:1 clay mineral with tetrahedral silica sheets periodically inverted with respect to the tetrahedral bases leading to a periodically interruption in the octahedral sheets and cations occupying terminal positions must complete their coordination sphere with water molecules (Bradley, 1940). The most intense absorption sites of palygorskite with organic molecules are surface hydroxyls and Lewis acidic centers (Serratosa, 1979). Isoniazid ($C_6H_7N_3O$; 137.14 g/mol), also known as isonicotinyl hydrazine, is a first-line drug in the prevention and treatment of tuberculosis (WHO, 2015). Akyuz et al. (2010) reported changes in infrared spectrum of palygorskite after interaction with isoniazid. Nevertheless, it has not been suggested until now the potential use of this mineral in the design of modified drug delivery systems of isoniazid.

With these premises, aim of this work was the study of the thermodynamics and equilibrium features of the adsorption of the first-line tuberculostatic drug isoniazid onto palygorskite as a prior step in the development of a modified release system based on the drug-clay mineral interactions. Solid state characterization of the pure materials and the resulting hybrid system was carried out in order to confirm the effectively loading of the drug, to assess qualitative and quantitatively the different interactions involved.

2. Materials and methods

2.1. Materials

Isoniazid (INH) from Sigma Aldrich (Spain) and a pharmaceutical grade palygorskite (Pharmasorb® Colloidal) (Pal) from Basf (Germany)

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were used as received. PAL had been fully characterized and used in previous studies (Viseras and López-Galindo, 1999, 2000; Viseras et al., 2000, 2001; Cerezo et al., 2001; Mura et al., 2016; Tenci et al., 2017).

All the reagents used were of analytical grade.

2.2. Adsorption studies

Adsorption experiments were performed following Carazo et al. (2017) to obtain equilibrium isotherms at different times and temperatures. Briefly, known amounts of Pal were dispersed into INH aqueous solutions with initial concentration (C_0) ranging from 0.05 to 0.5 mol/L, for different times (24 h, 48 h and one week) and temperatures (20, 30, 40 ± 0.1 °C). The resulting dispersions were centrifuged and the equilibrium concentration (C_e) of the drug in the supernatant was determined by UV spectroscopy (UV–Vis spectrophotometer Lambda 25, Perkin Elmer, S) at 262 nm. The difference between C_0 and C_e was used to calculate the amount of drug retained per gram of clay (expressed as n^s: mol of INH/g of Pal). Non-linear fitting of the data was performed using the software packaging TableCurve 2D® (Systat Software Inc., UK) and kinetic and thermodynamic parameters were determined.

2.3. Solid State characterization

2.3.1. Preparation of the drug-clay nanohybrids

Hybrid systems corresponding to the monolayer adsorption capacity of the clay mineral (48 h, $C_{0\ =}$ 0,2 mol/L) were prepared following the same procedure described above and then characterized.

2.3.2. Fourier transform infrared spectroscopy

Fourier transform infrared (FTIR) spectra were recorded on a FTIR spectrophotometer (JASCO 6200, with software SPECTRA MANAGER v2 and with an attenuated total reflectance (ATR) accessory). Measurements were carried out from 400 to 4000 cm^{-1} at 0.25 cm^{-1} resolution.

2.3.3. Thermal analysis

Thermogravimetric analysis (TGA) and Differential scanning calorimetry (DSC) were carried out by using a METTLER TOLEDO mod. TGA/DSC1 with FRS5 sensor and a microbalance (precision 0.1 μg) (Mettler-Toledo GMBH). Samples were heated in air atmosphere at 10 °C/min in the ranges 30–950 °C (TGA) and 30–400 °C (DSC).

2.3.4. X-ray powder diffraction

X-ray powder diffraction (XRPD) was done by using a Philips® X-Pert diffractometer with Cu Kα radiation. The diffraction data were analyzed using the XPOWDER® software (Ramos, 2004).

2.3.5. Surface charge

Surface charge properties of clay and drug-clay nanohybrid were determined from their zeta potential (ζ) values in aqueous suspension (0.05% w/v) on a Malvern Zetasizer Nano instrument (Malvern Instruments, USA).

3. Results and discussion

3.1. Equilibrium studies

Experimental equilibrium isotherms are plotted in Fig. 1 as n^s (moles of INH retained per gram of Pal; mol/g) vs C_e (mol/L).

The effect of time was almost negligible in the range of temperatures studied. Only a better outline of the plateau after 48 h in comparison with 24 h was observed, with no further improvement after one week of contact time. Replicates of the 48 h experiments were performed and the experimental data were collected to be mathematically treated. The isotherms fit the following equation, previously proposed to describe the adsorption of drugs to inorganic solid sorbents (Carazo et al., 2017) (Eq. 1):

$$n^s = n_1^s + n_2^s = \sum_{i=1}^{i=2} \frac{K_i.\ n_{m(i)}^s.\ C}{K_i.\ C + 1} + k_f C^m \quad (1)$$

Where n^s = moles of adsorbate adsorbed per gram of sorbent, n_1^s = adsorption at the active surface sites of the sorbent, n_2^s = precipitation of drug molecules over the adsorbed monolayer, n_m^s = monolayer retention capacity, C = equilibrium concentration, k_i = kinetic equilibrium constant, k_f = kinetic precipitation constant, n = partial order of the process respect to the concentration (C) and m = constant.

Average experimental data and theoretical calculated curves (adsorption, precipitation and the sum of both processes) are shown in Fig. 2. The global adsorption process is composed by the sum of two simple processes (adsorption of INH on the activated sites of Pal (n_1^s) followed by a slight precipitation of INH over the adsorbed monolayer (n_2^s)). The calculated fitting parameters (Table I) described adequately the experimental results with correlation coefficient ≥ 0.998. Monolayer retention capacity (n_m^s) slightly increased with temperature, whereas kinetic equilibrium constant (k_i) significantly decreased. The increase in temperature makes easier the dehydration of the drug molecules previous to their adsorption but concomitantly increase their mobility. K_f values are very low, suggesting a slight precipitation over the adsorbed drug monolayer.

K_i values obtained from Eq. (1) were used to determine the differential adsorption enthalpy ΔH° (kJ/mol) and the differential adsorption entropy ΔS° (kJ/mol K) values using the linearization of the Eyring equation (Eq. 2) by plotting ln (k/T) vs (1/T):

$$ln\frac{k_i}{T} = ln\frac{R}{Nh} + \frac{\Delta S^\circ}{R} - \frac{\Delta H^\circ}{R} \times \frac{1}{T} \quad (2)$$

(k = kinetic equilibrium constant (ki), R = gas constant, N = Avogadro's number, h = Planck's constant, T = temp (K)).

The calculated values are given in Table II, which also includes the differential activation energy ΔG° (kJ/mol) calculated via the expression: $\Delta G^\circ = \Delta H^\circ - T\Delta S^\circ$. The previous mentioned decrease of k_i values with the increase of temperature suggested an exoenergetic process that was corroborated by negative values of enthalpy (ΔH°) and activation energy (ΔG°). Adsorption of isoniazid over palygorskite was therefore an exothermic process. The thermodynamic probability of adsorption (ΔG°) revealed that the reversible adsorption-desorption process moved towards the net adsorption. Negative values of ΔS° corresponded to the reduced degree of freedom of the INH adsorbed molecules with respect to those in dissolution.

3.2. Solid State characterization

3.2.1. Fourier transform infrared spectroscopy

FTIR spectra of INH, Pal and the clay–drug nanohybrid were carried out to determine the nature of the interactions involved in the adsorption process (Fig. 3). The stretching mode of the Si–OH bond in Pal spectrum was observed as a sharp band around 3700 cm^{-1}. Some intensity and frequency changes in the OH stretching band of surface hydroxyls (Si–OH) of the Pal-INH were observed, in line with previously reported results (Akyuz et al., 2010). The band at 3612 cm^{-1}, well documented in all bibliographic references on FTIR of palygorskite (Mendelovici, 1973; Frost et al., 2001; Chahi et al., 2002; Chang et al., 2009) was related with the OH-stretching mode of structural hydroxyl groups. In the drug-clay nanohybrid, that band was detected at 3615 cm^{-1} and was assigned to coordination of INH molecules on the surface silanol (Si–OH) groups, directly or indirectly through water bridges. Bands appearing at 3543, 3400 and 3370 cm^{-1} were assigned to water molecules at terminal positions of the octahedral sheets (coordinated water) and water inside palygorskite channels (zeolitic water). Band at 3543 cm^{-1} was also ascribed to OH-stretching in