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Calorimetric studies of removal of nonsteroidal anti-inflammatory drugs diclofenac and dipyrone from water

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Abstract Chitosan microspheres were applied to remove the pollutants diclofenac and dipyrone from water. Adsorption studies were adjusted to Langmuir equation. The maximum number of adsorbed moles gave 5.25×10^{-4} and 4.83×10^{-4} mol of diclofenac and dipyrone, respectively, per gram of chitosan microspheres. The interactions in solid/liquid interface were calorimetrically followed and gave endothermic values: $+22.1 \pm 1.3$ and $+48.7 \pm 1.5$ kJ mol^{-1}, respectively, for the same sequence. Both Gibbs energy values were negative. Adsorption processes were accompanied by an increase in entropy. These interactions were studied by FTIR spectroscopy which showed a strengthening of the CN stretching (dislocated shifts from 1,325 to 1,371 cm^{-1}) related to a weakening of the NH stretch caused by the interaction with drugs.

Keywords Chitosan microspheres · Calorimetry · Non-steroidal anti-inflammatories

Introduction

The drugs are continually being lost to the environment, as a result of manufacturing processes, disposal of unused product and/or losers as well as animal excretion [1, 2]. Thus, the drugs have been so-called "emerging contaminants" and have caused a great concern in recent years because they are liposoluble and resistant [3, 4]. Moreover, these compounds are produced to achieve a biological effect when administered at specific individuals. However, these drugs must also be applied to existing organisms in the environment [5].

The occurrence of drug residues in sewage and natural waters is an important international topic. Studies show that these drugs and their metabolites are present in aquatic environments in many parts of the world such as Brazil, Germany, Canada, Holland, Italy, Sweden, and the United States [6]. Latin America represents 4% of the total drugs market (16.5 billion dollars), of which 67% of this market is related to the Brazilian market that is the 10th consumer market of drugs in the world [7].

Among the classes of drugs that have been consumed and extensively discarded in the environment, there are the nonsteroidal anti-inflammatory ones (NSAIs), including diclofenac and dipyrone. These drugs should be highlighted due to their large consumption around the world.

The removal of these contaminants in the environment can be made by various physical and chemical processes such as photodegradation, biological treatment, adsorption, etc.

However, the industrial costs of photodegradation are very high and the demand for biological treatment requires large areas and long periods of time [8, 9]. In this way, the application of low cost materials such as chitosan, to remove these contaminants by adsorption process becomes an elegant and feasible [10, 11].

The high ability of chitosan in removing contaminants and its low cost make this material one of the main options of adsorbents. In this way, this study chitosan microspheres is applied to remove the emerging contaminants nonsteroidal anti-inflammatories diclofenac and dipyrone from water.

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Experimental

Chemicals

The chitosan was obtained from Genix Pharmaceutical Industry (Brazil) and sodium diclofenac and sodium dipyrone were obtained from Aldrich. The reagents as acetic acid, sodium hydroxide, and glutaraldehyde were obtained from Vetec.

Preparation of chitosan microspheres

The chitosan microspheres were prepared according to the method proposed by Rorrer and Hsien (split-coating), with some modifications from Prado et al. [12]. Chitosan 10% (w/v) was dissolved in 5% (v/v) acetic acid at room temperature. The solution was homogenized for 2 h and after dripped in a coagulant solution of sodium hydroxide 10% (w/v) kept under stirring. Then, the microspheres were washed with deionized water until reaching pH 7.0. Once neutralized, the gelled beads were crosslinked in a 25% glutaraldehyde solution, without stirring for 2 h. After that, microspheres were filtered, washed with deionized water and then with acetone and dried [12].

Characterization

The chitosan was characterized by FTIR spectroscopy in a spectrophotometer JASCOI 4100 with resolution of 4 cm^{-1} by accumulation 250 scans.

The sample surface images were morphologically observed in an Optical Video-microscope Bell Optics and in a Scanning Electron Microscope Zeis EVO 050. For SEM analysis, the samples were coated with gold plating for 100 s in a Baltec SCD 050 spray. The SEM was operated with an electron beam of 20 keV.

The chitosan and microspheres surface areas were determined through isotherm adsorption–desorption, employing a Quantachrome Nova 2200 analyzer. It was performed a preliminary drying at 100 °C under reduced pressure for 12 h.

Interaction between vitamins and microspheres of chitosan

The interactions of the microspheres with the vitamins were given by suspension of 100 mg of microspheres in a 2 g/L ethanolic solution of sodium dipyrone and sodium diclofenac. The reaction mixture was maintained for 30 min at room temperature and the amount of vitamins adsorbed microspheres was determined by a UV–Visible Spectrophotometer Cary-50.

For interaction infrared data, 100 mg of chitosan microspheres were suspended in a 2 g/L ethanolic solution of sodium dipyrone and sodium diclofenac. The reaction mixture was maintained for 24 h at room temperature, and the ethanol was removed by vacuum line at 50 °C during 3 h. Infrared spectra of the mixtures were analyzed in a spectrophotometer JASCO 4100, with resolution of 4 cm^{-1} and by accumulation 250 scans.

Calorimetric titrations

The titration consisted in suspending a sample of 500 mg in 100 mL of water in a dewar, which was vigorously stirred at 298.15 ± 0.02 K. After equilibrium, the ethanolic solution of sodium dipyrone or sodium diclofenac was incrementally added using a microsyringe, coupled to the calorimetry. For each increment, the thermal effect (ΔQ_{tit}) was recorded, as indicated by a constant thermal effect at the end of the operation. An ampoule of chitosan was opened into 100 mL of water to obtain ΔQ_{sol}. In order to determine ΔQ_{dil} solution of sodium dipyrone or sodium, diclofenac was incrementally added to 100 mL of water.

Results and discussion

Characterization

FTIR spectrum presents many peaks, which confirms the structure of chitosan (Fig. 1) such as: a large broad band between 3,600 and 3,000 cm^{-1}, which is assigned to O–H stretching of chitosan, one peak at 2,950 cm^{-1} and one peak at 2,830 cm^{-1}, which is related to C–H stretching of tetrahedron carbon; a peak at 1,655 cm^{-1} related to C=O stretching of amide groups; a peak at 1,590 cm^{-1} assigned to NH_2 deformation; peaks at 1,421 $-CH_2$ of angular deformation of glycosidic ring, and 1,350 cm^{-1} which is attributed to C–H stretching and deformation of glycosidic ring; one peak at 1,320 cm^{-1} related to C–N stretching of amine groups, and one peak at 1,000 cm^{-1} attributed to C–O bonds [13]. All peaks confirm the nature of chitosan structure.

The degree of deacetylation of natural chitosan can be followed by infrared spectroscopy. Thus, the degree of deacetylation (DD) was determined by infrared spectroscopy. The method is based on the relationship between the absorbance value at 1,655 cm^{-1}, attributed to amide groups, and the corresponding value of the hydroxyl band at 3,450 cm^{-1} by applying the following Eq. 1. [13, 14]:

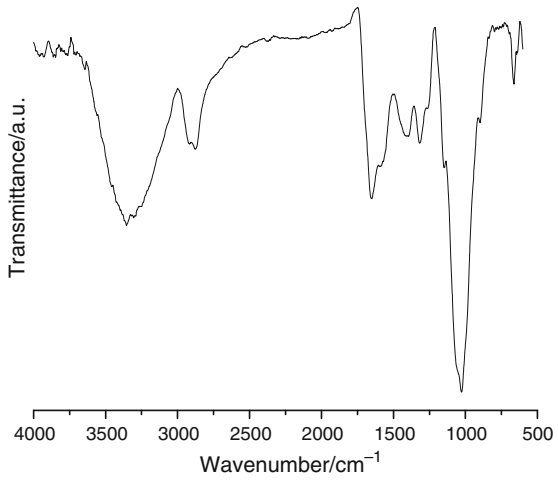

Fig. 1 Infrared spectrum of chitosan

$$\overline{\mathrm{DD}} = 100 - \left(\frac{\frac{A_{1655}}{A_{3450}}}{1,33}.100\right) \quad (1)$$

From application of these equations, the DD was 83.50%, confirming the presence of free amine groups of chitosan, which is capable to remove these emerging pollutants from water.

Once confirmed the DD of chitosan, the microspheres were prepared and reticulation of chitosan microspheres were carried out in order to obtain a more resistant polymer, as represented in Fig. 2.

The surface area values of materials were calculated by applying the BET equation in N_2 isotherms, which gave 4.2, 14.1, and 9.6 $m^2\ g^{-1}$ for start chitosan, chitosan microspheres, and reticulated chitosan microspheres, respectively. This fact evidences that the formation of microspheres from start chitosan causes a significant increase on the surface area of the material due to a morphological organization of the material, which is one of the new adsorbent qualities of this material when compared with the start material. On the other hand, the reticulation causes the decrease of the surface area because of the introduction of glutaraldehyde frameworks between linear polymeric chains of chitosan, which reduces the surface area after incorporation of organic groups, as shown in Fig. 2. This fact can be easily explained due to the fact that these groups block partially the adsorption of nitrogen molecules on the surface, resulting in a decrease of the surface area [15].

Optical microscopy showed that the chitosan microspheres presented spherical structure homogeneously dispersed (Fig. 3a). Scanning electron microscopy corroborated with this morphology and SEM image showed that the chitosan microspheres particles presented diameter lower than 100 μm (Fig. 3b).

NSAIs–chitosan microspheres interaction

The interaction between chitosan and NSAIs was followed by FTIR analysis, as presented in Fig. 4. These spectra show typical spectra of sodium dipyrone, sodium diclofenac, chitosan, and spectra of the interaction between NSAIs and chitosan (Fig. 4a). In order to understand the effect of interaction on chitosan structure, the region between 1,500 and 1,250 cm^{-1} was expanded (Fig. 4b). This figure shows the peak related C–N bond of chitosan, which was presented at 1,325 cm^{-1} and dislocated to 1,371 cm^{-1} during interaction with sodium dipyrone or sodium diclofenac. This fact is explained by the increase of energy of C–N bond due to the decrease of N–H bond of chitosan which was caused by interaction between amine groups of chitosan and carboxylate of diclofenac or between amine groups of chitosan and sulfoxide groups of dipyrone, as presented in Fig. 5.

Thermodynamics studies

The chitosan microspheres were used to remove nonsteroidal anti-inflammatories (NSAIs) diclofenac and dipyrone, which are emerging pollutants, from water. The adsorption ability of chitosan microspheres was determined by measuring the sorption isotherms.

The number of moles of the NSAIs adsorbed per gram of chitosan (N_f; mol g^{-1}) was obtained from Eq. 2 [16, 17]:

$$N_f = \frac{n_i - n_s}{m} \quad (2)$$

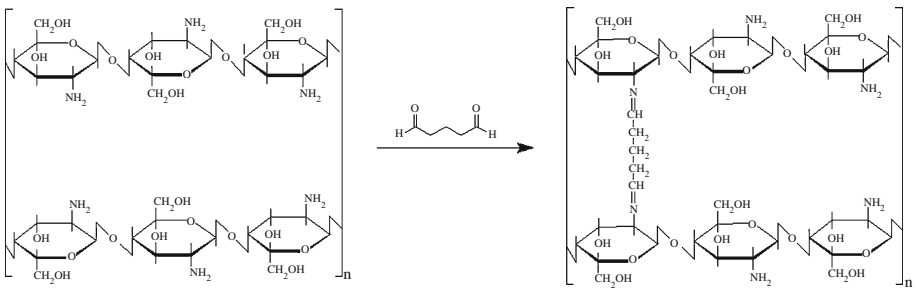

Fig. 2 Reaction of reticulation of chitosan with glutaraldehyde

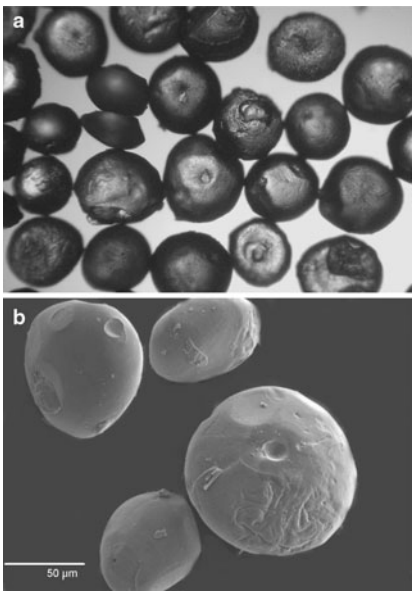

Fig. 3 Optical micrograph (**a**) and scanning electron micrograph (**b**) of chitosan microspheres

where n_i is the initial number of moles of NSAIs added to the system, n_s is the number of moles at equilibrium after adsorption, and m is the mass (g) of NSAIs [1, 9]. The adsorptive behavior represented by the number of moles adsorbed (N_f) versus the number of moles at equilibrium per volume of solution (C_s) is presented in Fig. 6a.

The experimental data were applied into the general equation of the modified Langmuir model presented in Eq. 3 [16, 17]:

$$\frac{C_s}{N_f} = \frac{C_s}{N_s} + \frac{1}{N_s \cdot K} \tag{3}$$

where C_s is the concentration (mol dm^{-3}) of the solution at equilibrium, N_s is the maximum amount of NSAIs adsorbed per gram of chitosan microspheres (mol g^{-1}), which depends on the number of adsorption sites, and K is a equilibrium constant (mol L^{-1}) [1, 9]. The linear form of the adsorption isotherm, i.e., from plots of C_s/N_f vs. C_s, in which N_s and K are represented by the slope and intercept, respectively, as showed in Fig. 6b. The values of the maximum amount of NSAIs adsorbed per gram of chitosan microspheres were 5.25 ± 0.35; 4.83 ± 0.21 × 10^{-4} mol for diclofenac and dipyrone, respectively.

The Gibbs energy changes may be calculated from Eq. 4, which corresponds to a ΔG value of −25.2 ± 2.0; −24.9 ± 1.7 kJ mol^{-1} for diclofenac and dipyrone, respectively.

$$\Delta G = -RT \ln K \tag{4}$$

All adsorption data were listed in Table 1, and these results show that the chitosan microspheres adsorbed better sodium diclofenac than sodium dipyrone.

The thermal effects of the interaction of NSAIs with chitosan microspheres were determined from a series of calorimetric experiments. The complete thermodynamic cycle can be summarized as follows in Eq. 5 [18].

$$\begin{aligned}
\mathrm{NSAIs_{(soIA)}} + \mathrm{Chitosan_{(soIB)}} &= [\mathrm{NSAIs\ldots Chitosan}]_{(soI)}\,(a)\,Q_{tit} \\
\mathrm{H_2O} + \mathrm{Chitosan_{(solid)}} &= \mathrm{Chitosan_{(soIB)}}\,(b)\,Q_{sol} \\
\mathrm{H_2O} + \mathrm{NSAIs_{(soIA)}} &= \mathrm{NSAIs_{(sol)}}\,(c)\,Q_{dil} \\
\mathrm{NSAIs_{(sol)}} + \mathrm{Chitosan_{(solid)}} &= [\mathrm{NSAIs\ldots Chitosan}]_{(sol)}\,(d)\,Q_{tot}
\end{aligned} \tag{5}$$

Three separated titration experiments were carried out in order to determine the component parts, namely: (a) the heat evolved by the Chitosan/NSAIs interaction (Q_{tit}), (b) the heat of solvation of the chitosan microspheres (Q_{sol}), and (c) the heat of dilution of NSAIs solution (Q_{dil}). The net interaction heat change Q_{int} (d) was given by Eq. 6 [18, 19].

$$\Sigma Q_{int} = \Sigma Q_{tit} + \Delta Q_{sol} - \Delta Q_{dil} \tag{6}$$

Since the heat of solvation of the aqueous suspended modified material was zero, the expression was reduced to Eq. 7 [1, 9]. The heat related to the Chitosan/NSAIs

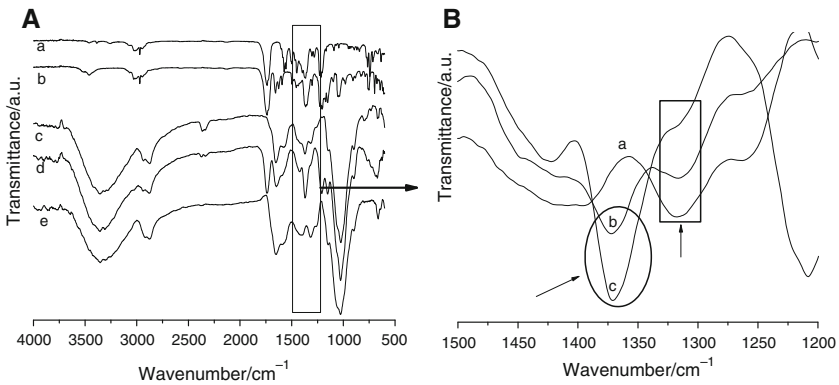

Fig. 4 FTIR of nonsteroidal anti-imflammatories dipyrone (*a*), diclofenac (*b*), of the interactions of chitosan-dipyrone (*c*), and chitosan-diclofenac (*d*), and of biopolymer chitosan (*e*) in (**A**); and the zoom of FTIR region of chitosan (*a*), and which presents the structure effects caused by interaction between chitosan-dipyrone (*b*) and chitosan-diclofenac (*c*) in (**B**)

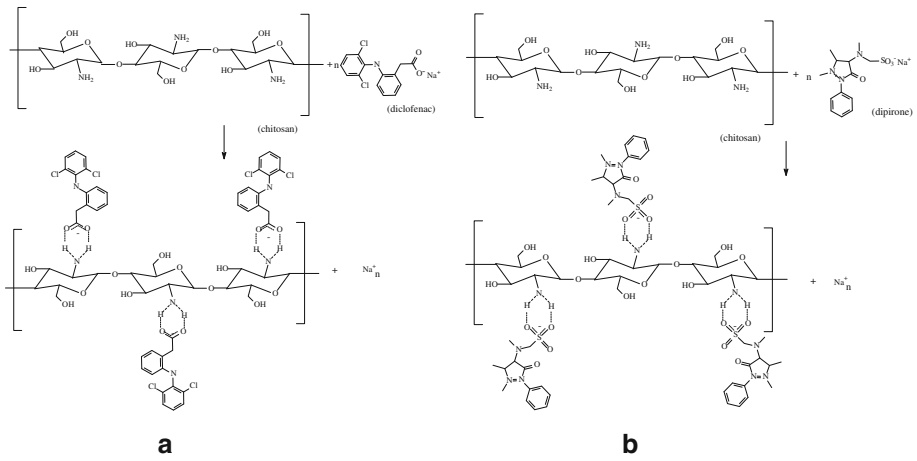

Fig. 5 Proposed scheme for the interaction of diclofenac (**a**) and dipyrone (**b**) with chitosan

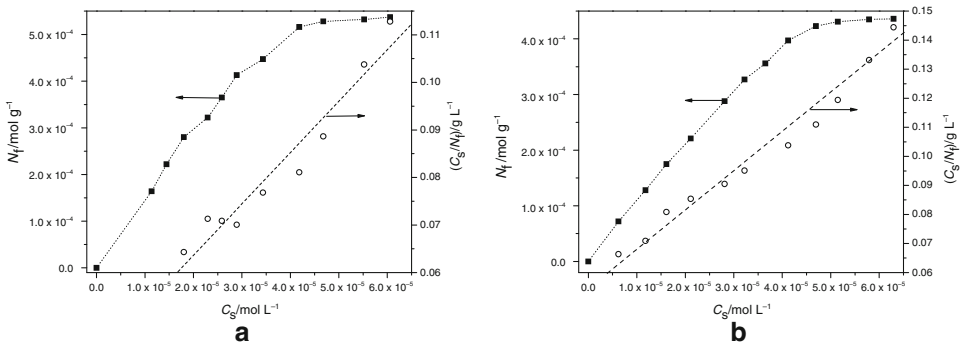

Fig. 6 Adsorption isotherms of diclofenac (*filled square*) (**a**) and dipyrone (*filled square*) (**b**) in chitosan microspheres and their respective linearizations by applying the Langmuir equation for diclofenac (*open circle*) (**a**) and dipyrone (*open circle*) (**b**)

Table 1 Maximum number of moles adsorbed, N_s, equilibrium constant, K, and thermodynamic data, ΔH, ΔG, and ΔS, the interaction of dipyrone and diclofenac adsorbed on chitosan microspheres

	Diclofenac	Dipyrone
N_s/mg/g	$5.25 \times 10^{-4} \pm 0.35 \times 10^{-4}$	$4.83 \times 10^{-4} \pm 0.4 \times 10^{-4}$
ΔH/kJ/mol	$+22.1 \pm 1.3$	$+48.7 \pm 1.5$
ΔG/kJ/mol	-25.2 ± 2.0	-24.9 ± 1.7
ΔS/J/mol K	$+16 \pm 2$	$+25 \pm 1$
K	$25{,}738 \pm 1{,}458$	$22{,}804 \pm 1{,}512$

interaction (Q_{tit}), the heat of dilution of NSAIs solution and the net resultant heat output for this interaction in the solid/liquid interface were obtained [18, 19].

$$\Sigma Q_{int} = \Sigma Q_{tit} - \Delta Q_{dil} \quad (7)$$

Using the net resultant heat output from the reaction, adjusted to a modified Langmuir equation, the integral enthalpies involved in the formation of a monolayer per unit mass of chitosan microspheres, $\Delta_{mono}H$ (Fig. 7), were calculated through Eq. 8 [18, 19]:

$$\frac{\Sigma X}{\Sigma \Delta_R H} = \frac{1}{(K_{ap} - 1)\Delta_{mono} H} + \frac{\Sigma X}{\Delta_{mono} H} \quad (8)$$

where $\sum X$ is the sum of the molar fractions of the herbicide remaining in solution after adsorption and X values are obtained for each addition of titrant, using the modified Langmuir equation, whose behavior was shown to be a good adjustable model for such heterogeneous systems, K_{ap} is a proportionality constant that also includes the equilibrium constant and $\sum \Delta_R H$ is the integral enthalpy of adsorption (J g^{-1}) obtained from the net thermal effect of adsorption and the number of moles of the adsorbate. Based on the Langmuir equation, it is possible to calculate the reaction enthalpy of the monolayer formed, $\Delta_{mono}H$, from plots of $\sum X/\sum \Delta_R H$ vs. $\sum X$ [18–21].

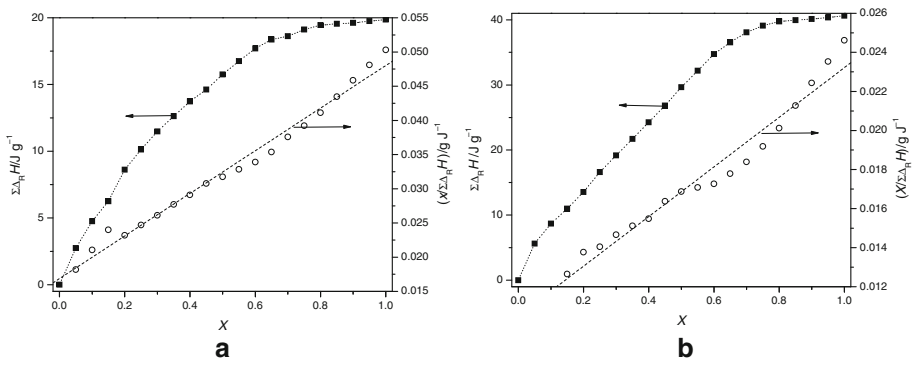

Fig. 7 Integral enthalpy of adsorption of diclofenac (*filled square*) (**a**) and dipyrone (*filled square*) (**b**) their respective linearizations diclofenac (*open circle*) (**a**) and dipyrone (*open circle*) (**b**)

The molar enthalpy, ΔH, of the interaction process was calculated from $\Delta_{\text{mono}}H$ and the maximum number of moles inserted, N_s, using Eq. 9.

$$\Delta H = \frac{\Delta_{\text{mono}}H}{N_s} \tag{9}$$

The Gibbs energy changes may be calculated from Eq. 10.

$$\Delta G = -RT \ln K \tag{10}$$

where R is universal gas constant and T is the temperature in Kelvin [1, 9].

The entropy values, ΔS, were determined from Eq. 11. All thermodynamic data are listed in Table 1.

$$\Delta G = \Delta H - T\Delta S \tag{11}$$

Thermodynamic results (Table 1), show that both adsorption processes are spontaneous ($\Delta G < 0$), being endothermic enthalpically disfavored ($\Delta H > 0$) and entropically favored ($\Delta S > 0$). Once both adsorption processes occurred due to the entropic favoring and enthalpic disfavoring, it can be suggested that these interactions must be occurred because of the dissociation of sodium ions of these NSAIs in aqueous solution followed by re-organization of water molecules around sodium ions and anionic formed polymers. This re-organization contributes to the increase in entropy and spontaneability of interaction contaminant/chitosan interaction at solid/liquid interface, as represented in Fig. 5. This proposed mechanism is supported by FTIR spectra of Fig. 4, which shows the strengthening of C–N bond caused by the impairment in N–H bond as a result of the interaction between amine groups of chitosan with carboxylate groups of diclofenac or with sulfoxide groups of dipyrone.

Conclusions

All results showed that the chitosan microspheres presented an excellent ability to remove these emerging contaminants from water. Data showed that the chitosan microspheres adsorbed better sodium diclofenac than sodium dipyrone. Both reactions occurred through a mechanism which favored entropic and disfavored enthalpy. This fact may suggest that the interactions of these drugs should occur due to the release of sodium ions once the increase in entropy can be interpreted by the decoupling of sodium ions of the drugs, followed by the re-organization of water molecules that must be organized around the sodium ions and anions of the polymer. Also, this re-organization of the species in solution contributed to the increase in entropic interaction and spontaneity of contaminant/chitosan in the solid/liquid interface.

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References

1. Kümmerer K. The presence of pharmaceuticals in the environment due to human use—present knowledge and future challenges. J Environ Manag. 2009;90:2354–2366.
2. Mompelat S, Le Bot B, Thomas O. Occurrence and fate of pharmaceutical products and by-products, from resource to drinking water. Environ Int. 2009;35:803–14.
3. Sodre FF, Locatelli MAF, Jardim WF. Occurrence of emerging contaminants in Brazilian drinking waters: a sewage-to-tap issue. Water Soil Pollut. 2010;206:57–67.
4. Khetan SK, Collins TJ. Human pharmaceuticals in the aquatic environment: a challenge to green chemistry. Chem Rev. 2007;107:2319–64.
5. Petrovic M, Gros M, Barcelo D. Multi-residue analysis of pharmaceuticals in wastewater by ultra-performance liquid chromatography–quadrupole–time-of-flight mass spectrometry. J Chromatogr A. 2006;1124:68–81.
6. Bila DM, Dezotti M. Pharmaceuticals in the environment. Quim Nova. 2003;26:523–30.
7. http://www.imshealth.com/imshealth/Global/Content/Static%20File/AMJ2007.pdf. Accessed May 2010.
8. Carballa M, Omil F, Lema. Removal of cosmetic ingredients and pharmaceuticals in sewage primary treatment. Water Res. 2005;39:4790–6.
9. Torres JD, Faria EA, SouzaDe JR, Prado AGS. Preparation of photoactive chitosan–niobium (V) oxide composites for dye degradation. J Photochem Photobiol A. 2006;182:202–6.
10. Prado AGS, Torres JD, Faria EA, Silva CLD. Comparative adsorption studies of indigo carmine dye on chitin and chitosan. J Colloid Interface Sci. 2004;277:43–7.

11. Silva CFS, Martins F, Santana MHA. Adsorption isotherms of mucin on granules containing chitosan microspheres. Adsorp Sci Technol. 2007;25:781–9.
12. Prado AGS, Pescara IC, Albuquerque RDA, Honorato FN, Almeida CM. Low-cost system to produce chitosan microspheres. Analytica. 2010;44:62–7.
13. Prado AGS, Macedo JL, Silvia CLD, Dias JA. Calorimetric studies of the association of chitin and chitosan with sodium dodecyl sulfate. Colloids Surfaces B. 2004;35:23–7.
14. Prado AGS, Faria EA. Kinetic studies of the thermal degradation of cellulose acetate/niobium and chitosan/niobium composites. React Funct Polym. 2007;67:655–61.
15. Prado AGS, Oliveira E. The interaction at the solid/liquid interface of 2, 4-dichlorophenoxyacetic acid with silica modified by reaction with ammonia gas. J Colloid Interface Sci. 2005;291:53–8.
16. Arakaki LNH, da Fonseca MG, da Silva EC, Alves APD, de Sousa KS, Silva ALP. Extraction of Pb(II), Cd(II), Hg(II) from aqueous solution by nitrogen and thiol functionality grafted to silica gel measured by calorimetry. Thermochim Acta. 2006;450:12–5.
17. Cestari AR, Vieira EFS, Mota JA. The removal of an anionic red dye from aqueous solutions using chitosan beads—the role of experimental factors on adsorption using a full factorial design. J Hazard Mater. 2008;160:337–43.
18. Prado AGS, Airoldi C. Humic acid–divalent cations interactions. Thermochim Acta. 2003;405(2):287–92.
19. Petrucelli GC, Meirinho MA, Macedo TR, Airoldi C. Crystalline polysilicate magadiite with intercalated *n*-alkylmonoamine and some correlations involving thermochemical data. Thermochim Acta. 2006;450:16–21.
20. Fonseca MG, Wanderley AF, Ferreira UVS, Arakaki LNH, Simoni JA, Airoldi C. Vermiculite-aliphatic amine interactions at the solid/liquid interface: thermodynamic approach. J Therm Anal Calorim. 2009;97:453–7.
21. Prado AGS, Moura AO, Andrade RDA, Pescara IC, Ferreira VS, Faria EA, Oliveira AHA, Okino EYA, Zara LF. Application of Brazilian sawdust samples for chromium removal from tannery wastewater. J Therm Anal Calorim. 2010;99:681–7.