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Affinity Studies between Drugs and Clays as Adsorbent Material

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Pharmaceuticals, with veterinary and human usage, have continuously been launched into the environment and their presence has been frequently detected in water bodies. The inefficacy of conventional water treatment processes for the removal of drugs, added to their potential adverse effects to human health and environment, suggest that new separation processes should be studied. Adsorption is highlighted as a promising method and the use of alternative adsorbents is encouraged due to the high costs of activated carbon. Different clay materials were evaluated in the present work for the removal of amoxicillin, caffeine, propranolol, and diclofenac sodium from aqueous solutions. The removal efficiency depended on the drug and adsorbent material used and varied between 23-98 % for amoxicillin, 21-89 % for caffeine, 29-100 % for propranolol, and 2-99 % for diclofenac sodium. The results showed that clays may be used successfully as alternative adsorbent material on the removal of selected emergent contaminants.

1. Introduction

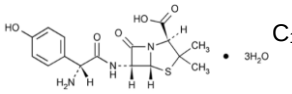
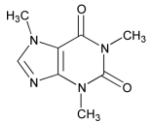
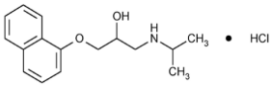
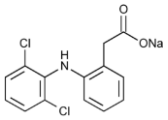
Pharmaceutical drugs are classified as emerging contaminants that have been frequently detected in effluents, superficial water and underwater. Even when present in trace concentrations, at the ng-µg/L level, these compounds possess chemical persistence, microbial resistance and unknown synergistic interactions, having the potential to induce adverse effects in aquatic life, such as endocrine disruption, reproductive inhibition or ecosystem-level responses (Kyzas et al., 2015; Ji et al., 2012). Human and animal pharmaceuticals are continuously released into the environment due to manufacturing process, excreta, and disposal of unused or expired products. While some drugs are released in their unaltered free form, others are metabolized to various extents or converted to more soluble forms, forming a great variety of transformation products that can have bioactivities higher than the parent compound (Daughton and Ternes, 1999). Recent studies report the presence of drugs in drinking water, such as antibiotics (amoxicillin), anti-inflammatory (diclofenac sodium), psycho stimulants (caffeine), and beta-blockers (propranolol), raising concerns about the effectiveness of conventional treatment methods on the removal of those contaminants, considering their potential toxicity and other detrimental effects (Yu et al., 2008).

Emerging contaminants have been found in surface water in different concentrations fluctuating according to the country, time of year, and even from one year to the next (Verlicchi et al., 2012). In countries like the United States, there are more than 3000 pharmaceuticals for prescription and hundreds sold as over-the-counter (OTC) drugs or used in the formulation of personal care products (Benotti et al., 2009).Studies show the presence of amoxicillin in Australian surface water at concentrations of 200 ng/L (Fatta-Kassinos et al., 2010). In Italy, caffeine and diclofenac sodium were detected in natural water with concentrations between 0.6 and 1,056 ng/L and 1.7 to 158 ng/L, respectively (Loos et al., 2007). In Germany, caffeine and diclofenac were detected with average concentrations of 80-265 and 1,030 ng/L, subsequently (Heberer and Reddersen, 2002). Propranolol was detected in Germany at concentrations that reached 590 ng/L (Daughton and Ternes, 1999) and in United Kingdom at concentrations between 10 and 215 ng/L (Ashton et al., 2004).

Adsorption is considered as a promising technology for pharmaceuticals uptake. Adsorption processes are widely applied for the removal of organic compounds, even in low concentrations, and are proven to be efficient and simple to design and operate (Ahmed et al., 2015). Activated carbon has been frequently

evaluated for pharmaceuticals adsorption (Zhang et al., 2016; Sotelo et al., 2012; Yu et al., 2008); nevertheless, the use of this material is prevented by its high commercial prices and difficult regeneration (Tahar et al., 2014). Therefore, there is an urge for alternative adsorbents with low cost and high availability.
Clays are potential drugs adsorbent materials due to high adsorption capacities, high surface areas, mechanical stability and various structural and surface properties (Bekçi et al., 2006). Taking into account that there are few studies about drugs adsorption onto clays, the present work aimed to evaluate the removal efficiency of four drugs (amoxicillin, caffeine, propranolol, and diclofenac sodium) from aqueous solutions by clay materials. The properties of these drugs are shown in Table 1.Four different modified bentonite clays were employed, namely commercial organoclay Spectrogel® (Type C), Fluidgel chemically modified with organophilic properties, and calcined Fluidgel and calcined Verde-lodo thermally modified.

Table 1: Pharmaceuticals and chemical proprieties.

Molecular Structure [a]	Molecular formula [a]	Molecular Weight (g/mol) [a]	Water Solubility at 298 K (mg/mL) [b]	pKa at 298 K [c,d]	λ_{max} (nm)*
Amoxicillin 	$C_{16}H_{19}N_3O_5S.3H_2O$	419.45	3.43	3.39, 6.71; 9.41	228
Caffeine 	$C_8H_{10}N_4O_2$	194.19	21.6	14.0	273
Propranolol 	$C_{16}H_{21}NO_2.HCl$	295.80	0.0617	9.47	215
Diclofenac Sodium 	$C_{14}H_{10}Cl_2NNaO_2$	318.13	0.00482	4.06	276

[a] U.S. Pharmacopeia, 2007; [b] Wishart et al., 2006; [c] Babić et al., 2007; [d] Ngeno et al., 2016
*Determined in the UV scanning spectroscopy equipment.

2. Materials and methods

The bentonite clay varieties Verde-lodo and Fluidgel were provided by Dolomil LTDA and the commercial bentonite organoclay Spectrogel® (Type C) by Spectrochem company from Brazil. The pharmaceuticals were donated by Geolab with purity content above 98.5 %.

2.1 Clay preparation

The Verde-lodo and Fluidgel clays were calcined in a muffle at 500 ºC and 750 ºC, respectively, for a 24-hour period. The organophilic bentonite was prepared with 10 grams of Fluidgel in 100 mL of water and 6,259 grams of HDTMA (hexadecyltrimethylammonium bromide) under constant stirring for 4-hour period. The solution was washed with DI, filtrated in vacuum pump, and dried in oven at 60 ºC. All clay varieties were sieved in Tyler sifters to achieve the medium particle size of 0.855 mm.

2.2 Affinity tests

Affinity tests were performed with 0.5 grams of different adsorbent materials in contact with 50 mL of pharmaceutical solution with known concentration in Erlenmeyers flasks of 125 mL, a blank solution was prepared similarly with each material less drug for control. The solutions were kept under constant 200 rpm agitation for a period of 24 hours at 25 ºC ± 2 ºC at an Incubated Shaker, SI 600R, Lab Companion Jeio Tech, Korea. The samples were collected, centrifuged at 4,000 rpm for 10 minutes, filtrated through a millex syringe 0.22 µm, and analysed in a UV-VIS spectrophotometer at the appropriate wavelength (Table 1). The adsorption capacity, q_e (µmol/g), and percentage removal, *%R* (%), were determined by Eq(1) and Eq(2), respectively.

$$q_e = \frac{(C_0 - C_e).V}{m} \quad (1)$$

$$\%R = \frac{(C_0 - C_e)}{C_0}.100 \quad (2)$$

In which C_0 is the initial concentration (approximately 90 µmol/L), C_e is the concentration (µmol/L) after 24 h of adsorption (equilibrium), V is the solution volume (50 mL), and m is the mass of adsorbent material (0.5 g).

2.3 Mercury porosimetry and Helium picnometry

In order to obtain the apparent density of the studied material, as well as information regarding porosity and pore's size distribution the mercury porosimetry technique was implemented, with Micromeritics Autopore IV equipment. The Helium picnometry analysis intent to measure the total volume of a solid, considering all the material's pores, based on the pressure variation of a gas (Webb and Orr, 1997). The equipment used, an Accupyc 1330 from Micromeritics (USA), was kept at a temperature of 30 ºC and equilibrium rate of 0.005 psig/min.

In possession of the obtained porosimetry and picnometry results, the material's porosity, ε_p (-), was determined by Eq(3):

$$\varepsilon_p = 1 - \frac{\rho_{apparent}}{\rho_{real}} \quad (3)$$

In which $\rho_{apparent}$ (g/cm^3) is the apparent density given by Mercury Porosimetry and ρ_{real} (g/cm^3) is the real density by Helium Picnometry.

2.4 Scanning electron microscopy (SEM)

The material's surface morphology was examined by scanning electron microscopy (SEM). Prior the analysis the samples were metallized with a thin layer of gold. The images were obtained in electron microscope (Electron Microscopy LEO, 440i model, England) with 10 kV voltage operating conditions (500X magnitude).

3. Results and discussion

3.1 Affinity tests

Affinity tests were performed in order to find the best adsorbent material for amoxicillin, caffeine, propranolol and diclofenac sodium. The percentage removal varied according the material and drug in question and the result is presented in Figure 1.

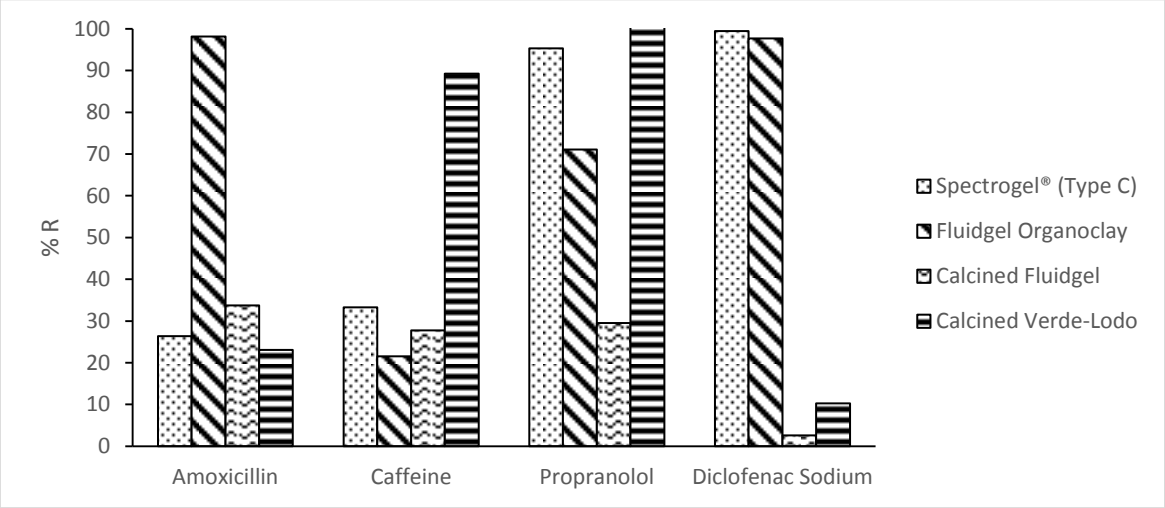


Figure 1: Percentage removal of amoxicillin, caffeine, propranolol, and diclofenac sodium by different clays.

The best amoxicillin *%R* was observed with Fluidgel organoclay, the laboratory prepared variety, with 98 % in a 24-hour period, suggesting that the high removal may be connected to the improved interactions between the drugs and the surfactant HDTMA present in the adsorbent material (Park et al., 2011). The commercial variety Spectrogel, also an organoclay, presented only 26 % removal for amoxicillin during the same period, the difference may be linked to the chemical reagent and method used during production of both clays. Similarly, Zha et al. (2013) obtained 97.9 % removal percentage of amoxicillin by Na-montmorillonite modified with HDTMA.

For caffeine, the best result was observed with calcined Verde-Iodo, around 90 %, almost three times higher than all other clay varieties. The same clay demonstrated a high affinity with propranolol with 100 % removal, Spectrogel and Fluidgel organoclay also exhibited satisfactory results, 95 % and 71 %, respectively. Verde-Iodo clay is more commonly used in metal ion removal from effluents (Cantuaria et al., 2014); nevertheless, it presented high potential as adsorbent of emergent contaminants as highlighted by the good adsorption capacities observed, 8.78 and 9.46 µmol/g for caffeine and propranolol, respectively.

Finally, diclofenac sodium depicted good interaction with both organophilic varieties, Spectrogel and Fluidgel organoclay, with 99 % and 97 % removal in the same period and good adsorption capacities, 9.85 and 9.68 µmol/g, respectively, for both clay varieties. The adsorption capacities values are shown in Table 2 bellow.

Table 2: Adsorption capacities, q_e (µmol/g), of amoxicillin, caffeine, propranolol, and diclofenac sodium by different clays.

Drug	Spectrogel	Fluidgel Organoclay	Calcined Fluidgel	Calcined Verde-Iodo
Amoxicillin	2.53	9.42	3.24	2.21
Caffeine	3.27	2.12	2.73	8.78
Propranolol	8.89	6.63	4.11	9.46
Diclofenac Sodium	9.85	9.68	0.26	1.02

Further analyses were performed onto Fluidgel organoclay contaminated with amoxicillin to determine some of the particle's characteristics. The pharmaceutical amoxicillin was selected due the high removal by this clay variety.

3.2 Mercury porosimetry and Helium picnometry

The material porosity was calculated by Eq(3). Table 3 depicts the adsorbent material (Fluidgel organoclay) apparent and real density as well as the porosity. It is noticeable that the material's porosity decreased after amoxicillin adsorption suggesting that the process happened, mainly, in the particle pores.

Table 3: Adsorbent material's porosity and density, prior and post amoxicillin adsorption.

Propriety	Prior adsorption	Post adsorption
$\rho_{apparent}$ (g/cm^3)	1.319	1.545
ρ_{real} (g/ cm^3)	1.629	1.642
ε_p	0.1904	0.059

3.3 Scanning electron microscopy (SEM)

The morphological characteristics of Fluidgel organoclay prior and post adsorption of amoxicillin were also investigated and the micrographs are shown in Figure 2. The main objective of the SEM was to determine if morphological changes were detectable after the adsorption process with amoxicillin. Fluidgel organoclay prior adsorption presented a rather irregular surface with some porosity (Figure 2-a). Zha et al. (2013) point out that surfactant modification of bentonites can cause the fragmentation of flakes and, consequently, the enhancement of contaminants adsorption.

After the adsorption process (Figure 2-b) the surface depicted a smother look with few amoxicillin crystals present, suggesting that the surfactant HDTMA was released to the solution where it may have been solubilized (Sarkar et al., 2011). It is possible to suggest that the change in the surface's appearance may be also linked to the pharmaceutical adsorption, a phenomenon that happens at the material's surface (Friedrich et al., 2006). Figure 2-c presents SEM micrograph of pure amoxicillin.

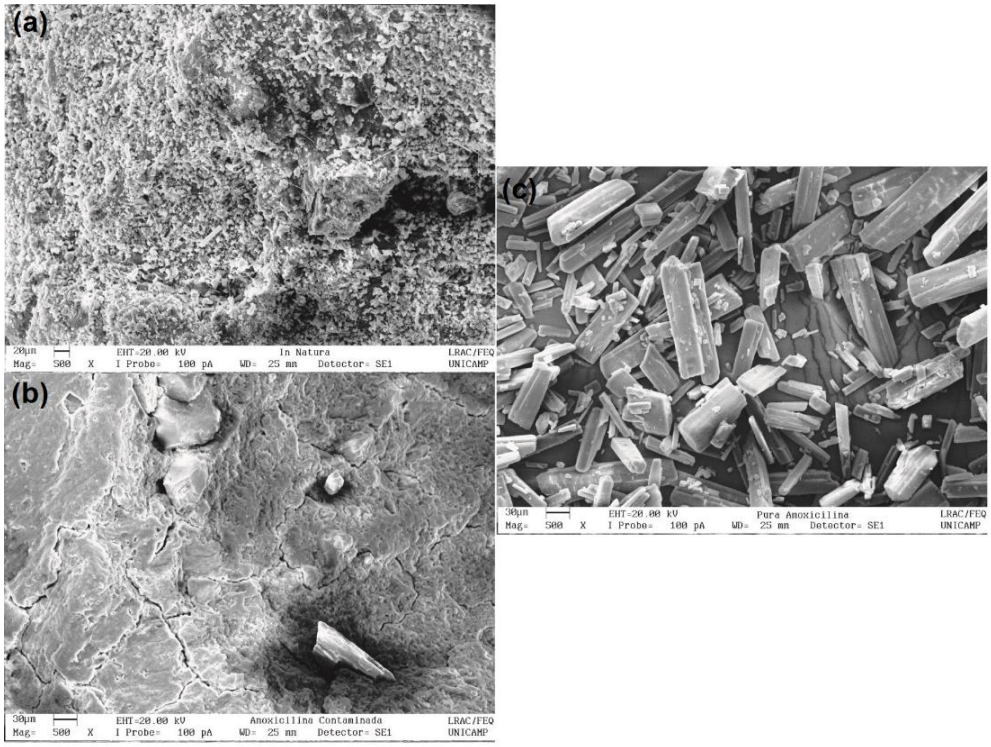


Figure 2: SEM micrographs (500x magnitude) of Fluidgel organoclay (a) prior adsorption, (b) after amoxicillin adsorption, (c) pure amoxicillin.

4. Conclusions

The affinity tests showed good percentage removal by the adsorbent materials, indicating the promising applicability of the studied clays. The best result for amoxicillin was achieved by the laboratory prepared Fluidgel organoclay, with 98 %. Caffeine and propranolol were best removed by calcined Verde-Iodo with 90 % and 100 %, subsequently, and diclofenac sodium was best removed by both organoclay varieties with 95 % and 97 %. The adsorption capacities indicated high potential for the studied materials with the exception of Fluidgel calcined that presented the worse capacities for all drugs. Fluidgel organoclay was characterized by mercury porosimetry and helium picnometry prior and post adsorption and the results suggested that amoxicillin was adsorbed in the particle's pores. The SEM micrographs depicted a change in the surface of the adsorbent material suggesting that the adsorption, a surface phenomenon, happened. Overall, this study showed that some clay varieties may be potentially employed as alternative adsorbent materials for the removal of emergent contaminants from effluents. Posteriorly, the continuous adsorption of drugs may be studied employing fixed bed systems. Bed regeneration may be investigated by adsorption-desorption cycles with suitable eluents. For instance, Vieira et al. (2014) used $CaCl_2$ solution as eluent of lead in fixed bed column packed with calcined Fluidgel clay.

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