Roles of functional groups of naproxen in its sorption to kaolinite

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HIGHLIGHTS
- The sorption of naproxen to kaolinite occurred on the surfaces of siloxane.
- Electron donor–acceptor and hydrogen bond can account for naproxen sorption.
- Diaromatic rings of naproxen are π-electron acceptors.
- Siloxane oxygens of kaolinite are n-donors.
- Conceptual model is built to assess naproxen sorption to kaolinite.

GRAPHICAL ABSTRACT

K_{d,NPX} = K_{d,EDA} + K_{d,HB} \cdot f_0

AABSTRACT

The sorption of acidic anti-inflammatory drugs to soils is important for evaluating their fate and transformations in the water–soil environment. However, roles of functional groups of ionisable drugs onto mineral surfaces have not been sufficiently studied. In this study, batch experiments of naproxen (NPX, anti-inflammatory drug) and two kinds of competitors to kaolinite were studied. The K_d of naproxen to kaolinite is 1.30–1.62 L kg^{-1}. The n–π electron donor–acceptor (n–π EDA) interaction between diaromatic ring of naproxen (π-electron acceptors) and the siloxane oxygens (n-donors) of kaolinite is the dominant sorption mechanism. The carboxyl group of naproxen can contribute to the overall sorption. A conception model was put forward to elucidate sorption mechanisms, in which the contribution of n–π EDA and hydrogen bond to overall sorption was quantified. These sorption mechanisms can be helpful for estimating the fate and mobility of acid pharmaceuticals in soil–water environment.

1. Introduction

The anti-inflammatory drugs, a sort of pharmaceuticals and personal care products (PPCPs), have been catching more and more attention worldwide since they were first detected in the environment in the late 1990s. The source of those newly identified micropollutants can be the effluents of sewage treatment plant (STP), industry, hospitals and even the raw sewage for epidemiological researches to evaluate illicit drug consumption in communities (Ort et al., 2010). The anti-inflammatory drugs are widespread in rivers (Vieno et al., 2007), lakes (Broziniski et al., 2013) and recycled water (Al-Rifai et al., 2011) due to the extensive use and their incomplete elimination in STP. The concern of their possible environmental risks to aquatic ecosystems has been raised.

Abbreviations: NPX, naproxen; PPCPs, pharmaceuticals and personal care products; STP, sewage treatment plant; CEC, cation exchange capacity; HPLC, high performance liquid chromatograph; DNT, 2,4-dinitrotoluene; PZC, point of zero charge; EDA, electron donor–acceptor; HB, hydrogen bond.
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because pharmaceuticals are designed to be biologically active (Brozinski et al., 2013).

Sorption is an important process which can affect the fate and transport of PPCPs in the water and soil environment. Pharmaceuticals with high hydrophobicity (e.g., logKow > 4) have shown to be strongly sorbed by organic soils (Kwon and Armbrust, 2008; Xu et al., 2009). The sorption of selected PPCPs has a direct correlation with the total organic carbon content (foc) of soils or sediments (Xu et al., 2009; Dobor et al., 2012). Besides, a certain amount of sorbate molecules can be sorbed to high affinity internal microporoids within natural organic matter matrix (Xing and Pignatelatto, 1997). Those evidences may account for the isotherm nonlinearity (Stein et al., 2008). However, there are situations in which adsorption to mineral surfaces can be important or even control the overall sorption process (Haderlein and Schwarzenbach, 1993). This is especially true for the cationic pharmaceuticals (Martinez-Hernandez et al., 2014). These processes involving cation exchange (Lv et al., 2013; Chang et al., 2014; Lv et al., 2014), cation bridging (Nowara et al., 1997; Wu et al., 2012), surface complexation (Chen et al., 2013a,b) and hydrogen bonding (Qi et al., 2014) are very important sorption mechanisms contributing to whole sorption. These processes are not accounted for by organic carbon normalization suggesting that the sorption behavior cannot be appropriately described without taking these processes into account (Tolls, 2001).

Recently, the degree of ionization of some functional groups of PPCPs has been recognized as an additional factor that can affect the sorption of these compounds onto natural sediments (Schaffer et al., 2012; Martinez-Hernandez et al., 2014). In this study, anti-inflammatory naproxen (NPX) was chosen as a representative ionizable pharmaceutical. Naproxen can be frequently detected in the environment (Tixier et al., 2003; Trenholm et al., 2006; Duan et al., 2013). Recent study suggests that naproxen is suggestive of increased cardiovascular and cerebrovascular risk, although not definitive (Martin et al., 2006). The sorption of naproxen to different soils and sediments was reported (Table 1). The sorption was significantly influenced by the physicochemical properties (organic carbon content, clay content, etc.) of soils and experimental conditions (such as solution pH). Previous studies showed that specific chemical sorption on external surfaces and on the interlayered surfaces of clay minerals can play a role in sorption of ionic compounds like naproxen (Teijon et al., 2013). However, how the interaction happened between different functional groups of naproxen and surfaces of clay mineral is not clear, yet. That is the focus of this paper.

Kaolinite (Al₂Si₃O₉(OH)₄) is known as a 1:1 layered structure clay mineral with one alumina octahedral basal plane surface, one silica tetrahedral basal plane surface and one edge surface (Liu et al., 2014). It has limited cation exchange capacity and a pH-dependent surface charge. It was chosen as a sorbent in experiments because it is a major type of clay mineral in the soils and sediments in warm climates (Xiao et al., 2011).

The aims of this study are: (1) to investigate the impact of functional groups of naproxen on the sorption to mineral surfaces; (2) to assess the contributions of different sorption mechanisms of naproxen to mineral surfaces; and (3) to characterize the specific sorption sites of kaolinite for naproxen. To this end, sorption isotherms and competition experiments were carried out to determine the sorption mechanisms.

### 2. Materials and methods

#### 2.1. Materials

Kaolinite (chemical reagent grade) used in the experiments was obtained from Tianjin Fuchen Chemical Reagents Factory, China. Naproxen ((S)-(+) -2-(6-Methoxy-2-naphthyl) propionic acid, >99%) and 2,4-dinitrotoluene (DNT, >99%) were purchased from Sigma–Aldrich. 2-Naphthaleneacetic acid (>98.0%) and catechol (>99.0%) were purchased from TCI (Shanghai) Development Co., Ltd. Stock solutions of all the chemicals were dissolved in methanol (99.9%) from Thermo Fisher Scientific. NaCl (analytical grade, Beijing Chemical Works) was used as background electrolyte and ultrapure water (MILLI-Q) was used in the experiments. The properties of sorbates involved in the experiments are shown in the Supporting Information (Table S1).

#### 2.2. Batch experiments

For kinetic experiments, 10 mL brown crimp-top headspace vials were used. A mass of 1.6 g of kaolinite was precisely weighed into vials, and then 8 mL of sorbate solution (0.01 mol L⁻¹ NaCl as background electrolyte, pH = 3 ± 0.1) at a certain concentration was added (1:5 solid/water ratio). The samples were mixed on a reciprocal shaker for prescribed time intervals (10, 20, 30, 60, 120, 240, 480, 720 min) at 175 rpm and 25 °C. Then samples were centrifuged at 1751g for 20 min at each interval. The supernatants were taken for being analyzed. For sorption experiments, six initial concentrations of compounds were set as 53, 200, 400, 600, 800, 1000 µg L⁻¹. For the pH sorption experiment, 0.1 mol L⁻¹ HCl or NaOH solution was used to adjust pH. The initial solution pH was adjusted from 3 ± 0.1 to 6 ± 0.1 with a 1.0 increment. Then the mixtures were shaken to reach the equilibrium. For competitive sorption experiments of NPX, the competitor concentrations of 2,4-dinitrotoluene were set as 0.90, 1.46, 1.84, 11.42 mg L⁻¹. For competitive sorption experiments of NPX, the competitor concentrations of 2,4-dinitrotoluene were set as 0.90, 1.84, 11.42 mg L⁻¹. For competitive sorption experiments of catechol, the concentrations of catechol were set as 53, 200, 400, 600, 800, 1000 µg L⁻¹. The competitors with catechol were naproxen (1.16 mg L⁻¹) or 2,4-dinitrotoluene (1.88 mg L⁻¹). All experiments were run in triplicate. Meanwhile, blank samples (containing only sorbate solution) accounted for the minor solute losses during the experiments were also carried out in triplicate. The final methanol volume in fractions from stock solution were kept at <0.1% (v/v) to avoid co-solvent effects.

<table>
<thead>
<tr>
<th>Soils/sediments</th>
<th>foc (%)</th>
<th>Clay (%)</th>
<th>Kow (L kg⁻¹)</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Agricultural soils</td>
<td>0.44–3.16</td>
<td>3.6–42.5</td>
<td>0.74–26.57</td>
<td>Xu et al. (2009)</td>
</tr>
<tr>
<td>Soil/sediment</td>
<td>0.08–8.6</td>
<td>1–59</td>
<td>0.20–17</td>
<td>Williams et al. (2009)</td>
</tr>
<tr>
<td>Agricultural soil</td>
<td>3.77</td>
<td>20</td>
<td>11.00</td>
<td>Barron et al. (2009)</td>
</tr>
<tr>
<td>Wastewater irrigated soil</td>
<td>0.0018–0.025</td>
<td>45–49</td>
<td>2.09–4.41</td>
<td>Duran-Alvarez et al. (2012)</td>
</tr>
<tr>
<td>Natural sediment</td>
<td>1.44</td>
<td>7.5</td>
<td>1.86</td>
<td>Martinez-Hernandez et al. (2014)</td>
</tr>
<tr>
<td>Sandy aquifer matrix</td>
<td>&lt;0.6</td>
<td>0.04</td>
<td>0.40</td>
<td>Teijon et al. (2013)</td>
</tr>
<tr>
<td>Kaolinite</td>
<td>0</td>
<td>100</td>
<td>1.30–1.62</td>
<td>This study</td>
</tr>
</tbody>
</table>

foc: fraction of organic carbon in soils or sediments.
The sorbates were analyzed directly by a high-performance liquid chromatography (HPLC) with a UV detector (HPLC, Shimadzu Corp, LC-20AT, Japan). The column (XDB-C18 column, 150 mm × 4.6 mm, Agilent) was kept at 30 °C and the injection volume was 10 μL. For the naproxen, 2-naphthaleneacetic acid and 2,4-dinitrotoluene analysis, the mobile phase was composed of 65% methanol and 35% KH2PO4 solution (0.01 mol L⁻¹, adjusting pH to 3 ± 0.05 by phosphoric acid). The flow rate was 1.0 mL min⁻¹ and wavelength was set at 254 nm. For catechol, the same mobile phase was used. The flow rate for catechol analysis was 0.8 mL min⁻¹ and wavelength was set at 280 nm.

3. Results and discussion

3.1. Effect of functional groups of naproxen on sorption

Naproxen and 2-naphthaleneacetic acid were chosen to investigate the sorption contribution of the functional groups of naproxen, since those two compounds are similar in structure and all belong to naphthalene derivatives. The sorption in this study was matched against the linear isotherm model which can be described as follows:

$$C_s = K_d \cdot C_r$$  (1)

where $C_s$ (μg kg⁻¹) is the sorbent mass fraction in the solid phase; $C_r$ (μg L⁻¹) is the equilibrium aqueous concentration; $K_d$ (L kg⁻¹) is the sorption distribution coefficient.

The $K_d$ values of naproxen and 2-naphthaleneacetic acid are 1.62 L kg⁻¹ and 1.15 L kg⁻¹ respectively (Fig. 1). The $K_d$ value of naphthalene to kaolinite is 0.3–0.9 L kg⁻¹ from literatures (Lee and Kim, 2002; Winkler et al., 2007). The sorption capacity for those chemicals on kaolinite was in the sequence: Naproxen > 2-Naphthaleneacetic acid > Naphthalene. It is obvious that carboxyl can contribute to the sorption of naphthalene derivatives to the surfaces of kaolinite. Therefore, hypothesis is put forward that both carboxyl and aromatic ring may play a role in sorption of naproxen to kaolinite. Hydrogen bond (HB, by carboxyl) and electron donor–acceptor (EDA, by aromatic ring) are two possible sorption mechanisms.

3.2. Effect of cosolute (π-acceptor) on sorption of naproxen

To test hydrogen bond and EDA, competitive sorption experiment was carried out by adding 2,4-dinitrotoluene (DNT) to naproxen solution system (Fig. 2). DNT is a strong π-acceptor because of the withdrawing capability of the nitro groups (Teixido et al., 2011). Results showed DNT (π-acceptor) could depress the sorption of naproxen by competitive sorption. This phenomenon indicated that both NPX⁻ and NPX⁶ could be sorbed to surfaces of kaolinite by EDA. In this case, aromatic ring of naproxen can be π-acceptor and siloxane oxygens of kaolinite provide n-donors.

The inhibitive effect was more distinct for NPX⁻ than that for NPX⁶. This is because hydrogen bond also contributed to sorption for NPX⁶. For the sorption of NPX⁻, hydrogen bond is absent because of the dissociation of carboxyl group. So, sorption for NPX⁻, compared to NPX⁶, was easier to be depressed by DNT.

It is worth noting that $K_d$ values (1.51, 1.59 and 1.56 L kg⁻¹) for NPX⁶ were shifted slightly in the presence of DNT (0.90, 1.46 and 1.84 mg L⁻¹). It was experimental error which was inevitable in the narrow competition concentration range of DNT. The important point is that the trend of inhibitive effect caused by competitive sorption is clear enough. Above all, n–π EDA is an important mechanism in the sorption process of naproxen to kaolinite.

3.3. Effect of chemical speciation of naproxen on sorption

To evaluate the contribution of carboxyl group of naproxen to the overall sorption, the effect of chemical speciation of naproxen on sorption was tested at different initial pH conditions.

The point of zero charge of kaolinite is reported to be 3.8–4.1 (Appel et al., 2003). When pH = 3 ± 0.1, the surface charge of kaolinite is positive. Meanwhile, the percentage of NPX⁻ is only 6.6%. Thus, there is almost no electrostatic repulsion between naproxen and kaolinite at pH = 3. So, the $K_d$ at this pH is the maximum in this experiment. When the initial pH of solution varied from 3 ± 0.1 to 4 ± 0.1, the surface charge characteristics of kaolinite changed from positive to negative while NPX⁻ increased from 6.6% to 41.5%. The electrostatic repulsion increased rapidly in this pH range, resulting with a sudden drop of $K_d$ value (Fig. 3).

It is interesting that the $K_d$ value is almost undiminished when the initial pH of solution varied from 4 ± 0.1 to 6 ± 0.1. The solution pH is an important factor affecting the sorption process since the sorption of acidic organic chemicals is pH-dependent (Tuelp et al., 2009). However, there is little effect of pH on sorption of naproxen to kaolinite. The results indicated that hydrogen bond caused by carboxyl group of naproxen was important but not predominant in whole sorption process.

When the carboxyl group of naproxen was completely dissociated and naproxen was negatively charged, the two fused benzene rings are similar to naphthalene and may facilitate n–π interactions with aromatic moieties (Lin and Gan, 2011). This evidence was similar with this research. So n–π EDA interaction between diaromatic ring of naproxen and siloxane surfaces of kaolinite may control the sorption of naproxen.
3.4. The conceptual model for naproxen sorption to kaolinite

The following model (Eq. (2)) was proposed to assess the contribution of different mechanisms for naproxen to the overall sorption.

\[ K_d;_{\text{NPX}} = K_d;_{\text{EDA}} + K_d;_{\text{BH}} \cdot f_0 \]

\[ f_0 = \frac{1}{1 + 10^{(\text{pH} - \text{pK}_{\text{a0}})}} \]

where \( K_d;_{\text{NPX}} \) is the \( K_d \) for naproxen; \( f_0 \) is the percentage of the NPX; \( K_d;_{\text{EDA}} \) is the contribution of \( n-\pi \) EDA between the diaromatic ring of naproxen and basal siloxane surfaces; \( K_d;_{\text{BH}} \) is the contribution of hydrogen bond between carboxyl group of naproxen and hydroxyl groups of kaolinite.

\( K_d;_{\text{EDA}} \) and \( K_d;_{\text{BH}} \) were calculated by using the mathematical programming solver in Excel (based on the data in Fig. 3). \( K_d;_{\text{EDA}} \) is 1.26 L kg\(^{-1}\) and \( K_d;_{\text{BH}} \) is 0.38 L kg\(^{-1}\). Therefore, \( n-\pi \) EDA is the major sorption mechanism for naproxen to kaolinite. Hydrogen bond can be an important sorption mechanism in addition to \( n-\pi \) EDA when the carboxyl group is not dissociative.

Based on the model (Eq. (2)), the predicted \( K_d \) values at different pH were calculated using the values of \( K_d;_{\text{EDA}} \) and \( K_d;_{\text{BH}} \). Predicted \( K_d \) values are very close to the \( K_d \) values obtained from experiments (Fig. 4). Only the \( K_d \) calculated under the condition of pH = 4 ± 0.1 is a little higher (12.5%) than that obtained from experiments. The surface charges of kaolinite varied from positive to negative when the solution pH changed from 3 ± 0.1 to 4 ± 0.1. This shift of surface charge properties may cause the prediction error. In general, the conceptual model (Eq. (2)) is precise to assess the contribution of each sorption mechanism to the whole sorption (Fig. 4).

3.5. The specific sorption sites of kaolinite

Competition experiments were conducted to probe the specific sorption sites of kaolinite (Fig. 5). It is known that catechol can form bidentate surface complexes with aluminol surface groups but adsorbs very weakly to silica surfaces (Haderlein and Schwarzenbach, 1993). As shown in Fig. 5, the sorption isotherm of catechol was basically unaffected by the presence of naproxen (1.16 mg L\(^{-1}\)) or DNT (1.88 mg L\(^{-1}\)). In addition, no obvious change of the sorption of naproxen (1.16 mg L\(^{-1}\) as initial concentration) or DNT (1.88 mg L\(^{-1}\) as initial concentration) was observed in their respective competition experiments with catechol. Therefore, it can be assumed that the sorption for naproxen and DNT took place primarily at the basal siloxane surfaces of kaolinite and they share the same sorption sites. The sorption kinetics of naproxen and DNT showed the same characteristics which were different from catechol (Fig. S1). This result also convinced that both naproxen and DNT occupied the same sorption sites which differed from catechol. To be specific, naproxen and DNT can be retained by siloxane surfaces of kaolinite and catechol can be sorbed to aluminol surface groups of kaolinite.

Literature data indicate that soils can retain hydrophobic organic chemicals even at low soil organic levels because certain siloxane surfaces can be hydrophobic (Moyo et al., 2014). So, siloxane surfaces can provide possible sites for sorption of aromatic hydrocarbons (Jaynes and Boyd, 1991). The organic compounds like benzene, naphthalene can be adsorbed to the siloxane surfaces in smectites (Jaynes and Boyd, 1991; Moyo et al., 2014). Considering all the evidences mentioned, it can come to a conclusion that the diaromatic ring of naproxen (\( \log K_{\text{ow}} = 3.18 \)) can be adsorbed to the siloxane surfaces of kaolinite by \( n-\pi \) EDA and hydrogen bond (Fig. 6).
4. Conclusion

According to the experimental results, the sorption of naproxen to kaolinite ($K_{\text{Kd, napx}} = 1.30–1.62 \text{ L kg}^{-1}$) is considerable compared with sorption to soils reported in previous studies. The primary sorption mechanism is $n$-$\pi$ EDA interaction ($K_{\text{EDA}} = 1.26 \text{ L kg}^{-1}$) between diatomic ring of naproxen ($\pi$-electron acceptors) and the siloxane oxygens ($n$-donors) of kaolinite. The carboxyl group sorbed onto the surface of kaolinite by hydrogen bond can contribute to the overall sorption. The proposed conceptual model can precisely assess the contribution of $n$-$\pi$ EDA and hydrogen bond to overall $K_d$. EDA is an important mechanism for naproxen anion sorption to kaolinite surfaces. Thus, EDA and hydrogen bond could be taken into account in estimating the fate and mobility of the similar ionizable pharmaceuticals in soil–water systems.

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Appendix A. Supplementary material

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.chemosphere.2015.06.023.

References


