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Research Paper

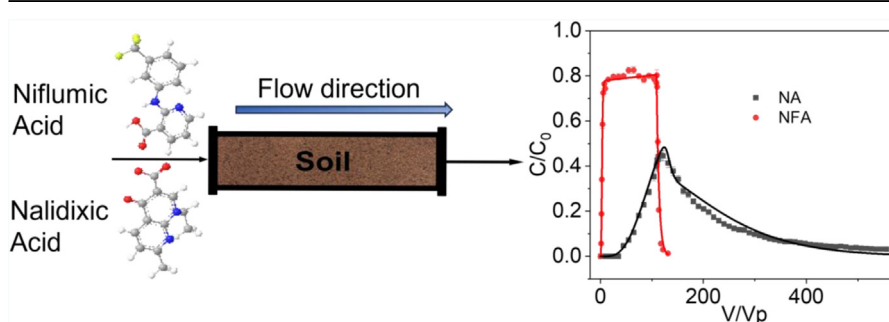
Mobility and transport of pharmaceuticals nalidixic acid and niflumic acid in saturated soil columns

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HIGHLIGHTS

- The co-mobility and co-adsorption of two pharmaceuticals depended on soil composition.
- NA and NFA sorption varied under equilibrium and non-equilibrium conditions.
- Ca^{2+} inhibited NA sorption but promoted NFA sorption under equilibrium conditions.
- Two-site transport model HYDRUS well described the pharmaceutical mobility.

GRAPHICAL ABSTRACT



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ABSTRACT

Pharmaceutical compounds often coexist in mixtures rather than as individual entities. However, little is known about their co-adsorption and co-mobility in soil and groundwater. In this study, we investigated the adsorption of a quinolone antibiotic (nalidixic acid, NA) and an anti-inflammatory agent (niflumic acid, NFA) onto two soils from France and Sweden in water-saturated soil columns. Despite its lower hydrophobicity, adsorption of NA is much greater than NFA, which can be ascribed to the presence of both carbonyl and carboxylic groups in NA molecule. The data suggest that adsorption to soil components can mainly take place through hydrogen bonding and surface complexation mechanisms, prevailing over hydrophobic interactions. Accordingly, more sorption of NA and NFA was observed in the Swedish soil because it contains more clay content, and much higher Al and Fe contents than the French soil. Injection of NA/NFA mixture in the column did not modify the breakthrough behavior compared to single systems, although cooperative adsorption was observed under static batch conditions. Ca^{2+} inhibited NA adsorption by forming a soluble NA-Ca^{2+} complex but promoted NFA adsorption both in single and binary systems. The mobility in soil columns was well predicted using a new transport model that accounts for both kinetics and binding reactions of NA and NFA to soil constituents. This work will help in accurately predicting the mobility of coexisting pharmaceutical compounds in soils.

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1. Introduction

Pharmaceutical residues can enter the environment during production, consumption, inappropriate disposal of medicines, and livestock farming (Borgman and Chefetz, 2013; Hill et al., 2019; Revitt et al., 2015; Schübl et al., 2021; Siemens et al., 2010). Nonpoint source pollution from agricultural runoff and the urban periphery also contributed to this process. Consequently, those compounds are detected in concentrations ranging from ng L^{-1} to $\mu\text{g L}^{-1}$ in aquatic systems worldwide (Chaturvedi et al., 2021; Fatta-Kassinos et al., 2011; Khan et al., 2020; Li, 2014; Wilkinson et al., 2022).

The transport and mobility of these pharmaceuticals in sediments/soils are strongly controlled by adsorption and potentially abiotic or biotic transformation (chemical-induced or bacteria/fungi-induced oxidation). For instance, soil minerals exhibit excellent sorption capacity via surface complexation and hydrogen bonding (Cheng et al., 2021; Hanna et al., 2012; Martínez-Mejía et al., 2017; Revitt et al., 2015). Compared to pure minerals, soils contain complex mixtures consisting of sand, clays, natural organic matter (NOM), metal oxides and/or amorphous materials. As a result, the magnitude and complexity of adsorption will be greater in soils, as compared to individual minerals. For example, the clays, metal oxides, and NOM can provide sorption sites with varying reactivities (Cheng et al., 2021; Maged et al., 2020; Sheng et al., 1996), while the aggregation of minerals with NOM can affect sorption ability (Huang and Zhang, 2020; Tadjale and Zhang, 2012). Most notably, by consuming sorption sites NOM can weaken the sorption ability of clays/metal oxides (Luo et al., 2022; Zhang et al., 2015). Soil reactivity can also be influenced by the porewater chemistry, such as pH and the presence of cations (Ca^{2+} and Mg^{2+}) and anions (silicates, phosphates) (Das Chagas et al., 2020; Sharma and Kappler, 2011; Zhou et al., 2004). Additionally, soil liming is a common practice employed in agriculture soil for adjusting the acidity of soil, resulting in high Ca^{2+} and Mg^{2+} concentration in the soil (Das Chagas et al., 2020; Goulding, 2016).

Many papers have reported the sorption behavior of emerging contaminants individually and onto pure minerals, but little is known about co-sorption or co-transport in multiple contaminants systems (Cheng et al., 2019; Evanko and Dzombak, 1999; Gu and Karthikeyan, 2005; Luo et al., 2022). For instance, considering competitive or synergistic adsorption at soil surfaces is crucial for determining the transport of mixed pollutants. In addition, much of the knowledge that currently exists concerns the adsorption of organic compounds in soil slurry systems, and under static batch conditions (Figueroa and Mackay, 2005; Kasteel et al., 2010). Little knowledge is available on the impact of water flow on competitive or cooperative sorption, and even less in flow-through systems where non-equilibrium prevails. Moreover, column experiments allow monitoring the effect of non-equilibrium sorption onto the transport of co-contaminants (Stanford et al., 2010; Zhao et al., 2018). Effects of hydrodynamic parameters on the solute breakthrough can also be evaluated in continuous flow-through conditions (Pokharel et al., 2020; Zhou et al., 2019). Estimation of field parameters could be more accurate in column tests which provide a suitable soil-aqueous phase ratio (Van Glubt et al., 2021). The emerging contaminants could migrate into groundwater during infiltration or leaching through soil, and thus the investigation of the adsorption mechanisms under dynamic conditions is in favor of better understanding of the mobility of those compounds under real-world conditions.

In this study, two representative European soils (in Sweden and France) sampled from agriculture fields, were collected due to their different properties in terms of clay/metal oxides content. The goal of this study was to investigate the co-mobility of nalidixic acid (NA) and niflumic acid (NFA), two common detectable pharmaceuticals in the environment, under both flow-through and equilibrium conditions, using a series of column and batch experiments. NA and NFA were chosen as the model pollutants because they are widely used in human and veterinary medicine. Divalent Ca^{2+} was also introduced to determine its effect on NA and NFA adsorption and transport in soil columns, as compared to

monovalent sodium (Na^+). This study broadens our knowledge of the importance of dynamic flow experiments in accurately determining and predicting the mobility of NA-NFA mixtures in complex soil media.

2. Materials and methods

2.1. Chemicals

Nalidixic acid (NA), niflumic acid (NFA), ciprofloxacin (CIP), sodium chloride (NaCl), calcium chloride (CaCl_2), sodium hydroxide (NaOH), and hydrochloric acid (HCl) were purchased by Sigma Aldrich, and were of analytical grade or better. Ultrapure water ($18.2 \text{ M}\Omega/\text{cm}$) was used in all experiments.

Two agricultural soils sampled from Sweden (S, $63^\circ 03' 32.9'' \text{N}$ $18^\circ 19' 46.1'' \text{E}$) and France (F, $48^\circ 01' 43.9'' \text{N}$ $1^\circ 28' 18.2'' \text{W}$) were used to conduct the batch and column sorption experiments. These samples were obtained from the 0–20 cm layer, air-dried, and then sieved using 0.4–0.8 mm screens. The soil was first characterized to determine the percentage of sand-, silt-, and clay-size fractions. Second, the key parameters including organic carbon (OC), pH, and cation exchange capacity (CEC) were determined as well as the amount of major and trace elements. Relevant physical and chemical properties of soils are reported in Table S1.

2.2. Batch experiments

Considering pH ranges of most soils and their buffering power, equilibrium adsorption experiments as a function of pH (pH 5–8) were conducted in single ($[\text{NA}]_{\text{tot}} = 20 \mu\text{M}$ or $[\text{NFA}]_{\text{tot}} = 20 \mu\text{M}$) and binary ($[\text{NA}]_{\text{tot}} = 20 \mu\text{M}$, $[\text{NFA}]_{\text{tot}} = 20 \mu\text{M}$) systems. Adsorption isotherms of NA and NFA were determined under 100 mM NaCl and pH 7 over the concentration range (1–30 μM) for both compounds. Typically, batch experiments were conducted in 15 mL polypropylene tubes, which contained 2 g/L soil, 100 mM NaCl, different concentration of NA and NFA. The pH was then adjusted to the desired value with diluted HCl or NaOH solutions. The tubes were sealed by caps and then shaken continuously on a platform shaker at 200 rpm and 25°C . Preliminary kinetics experiments showed that a reaction period of 24 h was enough to achieve the equilibrium of NA and NFA in solution and soil surface. Therefore, after equilibrating for 24 h, final pH was measured before filtration (0.2 μm), and then residual NA and NFA in the solution were analyzed by HPLC-UV to determine sorption amounts of NA and NFA. The same procedure was applied to test the effect of Ca^{2+} on NA and NFA sorption in the single and binary systems. All experiments were independently carried out two times at least.

NA and NFA concentrations in the aqueous solution were determined using a high performance liquid chromatography (HPLC) system. This set-up was equipped with an auto sampler (Waters 717 plus), using a C18 column ($250 \text{ mm} \times 4.6 \text{ mm i.d.}$, 5 μm) and a UV detector operating at 258 nm and 283 nm, respectively (Waters UV). The mobile phase was a mixture of water/acetonitrile (60:40 v/v) containing 0.1% of formic acid. The flow rate of the mobile phase was set at 1 mL/min in isocratic mode. The detection limit of NA or NFA in the HPLC system (50 μL injection volume) is 0.2 μM . To detect low concentration of NFA and NA, higher injection volume was employed.

2.3. Column experiments

Ten g of air-dried soil were packed into a glass chromatographic column (1.6 cm internal diameter). The porous bed had a length of 5.4 cm. After packing to a uniform bulk density (0.92 g/cm^3), the column was wetted upward using background electrolyte solution (NaCl, 100 mM) at a constant flow rate for at least 24 h. When parameters (pH, conductivity) were constant over time, the column was considered to be in a saturated condition and was ready for further reactive transport experiments. After water saturation, the mass difference of dry column and wet column was calculated to get the pore volume (PV). Then a 200

mM NaCl solution was injected in a pulse mode to determine the flow characteristics of the porous bed. NaCl concentration in the outlet solution was recorded by ionic chromatography. The breakthrough curves (BTC) were analyzed using the method of moments and inverse modeling with HYDRUS 1D software.

Five sets of column experiments were then conducted to measure NA and NFA transport process. 1) The first set was fed with 10 μM NA or NFA at pH 6.5 or 7.0 (depending on the soil pH) at 0.5 mL/min flow rate and in a pulse mode. 2) The second one was simultaneously fed with mixed 10 μM NA+NFA solution under same conditions. 3) After 110 V/Vp injection of mixed NA+NFA solution, 24 h interruption was taken and then continued to inject mix solution until initial level. 4) To test possible biotic transformation, 100 mg/L NaN_3 was added into the mixed NA+NFA solution. 5) To test the effect of cations, the CaCl_2 electrolyte was used instead of NaCl at same ionic strength in the mixed NA+NFA solution.

2.4. Modelling solute transport with HYDRUS

Displacement of solutes is generally described by the classical convection-dispersion equation (CDE) (Šimůnek et al., 2015) (Eq. (1)). For one-dimensional vertical transfer in a variably saturated medium where neither adsorption nor degradation occurs.

$$\frac{\partial C}{\partial t} = D \frac{\partial^2 C}{\partial x^2} - v \frac{\partial C}{\partial x} \quad (1)$$

According to the tracer experiment results, the breakthrough curve of Cl^- can be well fitted using CDE, indicating the absence of great dispersion/diffusion or physical nonequilibrium (immobile water zone) effect in the soil column. The Péclet number ($\text{Pe} = vL/D$) was ~ 21 in the column, suggesting the predominance of a convective regime, and the flow can be assumed as homogeneous.

The reactive transport can be described based on a two-site advective-dispersive transport model with Freundlich kinetic sorption because of the kinetically limited sorption process of NA and NFA on soil.

$$\frac{\partial C}{\partial t} + \frac{\rho \partial(S)}{\theta \partial t} = D \frac{\partial^2 C}{\partial x^2} - v \frac{\partial C}{\partial x} - \mu_1 C - \frac{\rho}{\theta} \mu_s S \quad (2)$$

In this equation, θ is the volumetric water content (L^3/L^3), C is the volume-averaged solution concentration (M/L^3), t is time (T), ρ is solid bulk density, S is the sorbed concentration (M/M), D is the dispersion coefficient in the liquid phase (L^2/T), v is the water velocity (L/T), μ_1 and μ_s are first-order degradation rate constants (T^{-1}) for the liquid and sorbed phases.

Two sites adsorption model consider that adsorption can occur instantaneously on equilibrium exchange sites (S^e) or kinetically on the

remaining exchange sites (S^k). The following provides the mass balance for this two-site sorption concept:

$$S = S_1 + S_2 \quad (3)$$

$$S_1 = fK \frac{C^\beta}{1 + \eta C^\beta} \quad (4)$$

$$\frac{\partial S_2}{\partial t} = \alpha \left[(1-f)K \frac{C^\beta}{1 + \eta C^\beta} - S_2 \right] - \mu_s S_2 \quad (5)$$

where α is a first-order kinetic rate coefficient (T^{-1}), f is the fraction of instantaneous adsorption sites (Type-1), and K , β and η are empirical coefficients.

The inverse algorithm of HYDRUS-1D uses a least-squares method that minimizes an objective function, and which provides a best-fit model solution to firstly calibrate the water flow parameters (e.g., dispersivity) using Eq. (1) without considering adsorption and degradation. We then used the same method to estimate fate and transport parameters of reactive solutes. In addition, because NA and NFA are only removed by sorption, μ_1 and μ_s were set to 0. This also allows the reduction of the number of estimated parameters, thus avoiding non-uniqueness issues (a sensitivity analysis has been done in previous works (Zhou et al., 2023, 2019)). Values for the sorption parameter K , fraction of equilibrium sites f , kinetics adsorption α are determined through fitting the breakthrough curves of NA and NFA, and are reported in Table S2.

3. Results and discussion

3.1. Adsorption of nalidixic acid and niflumic acid under flow conditions

Dynamic column experiments were carried out to investigate the sorption of nalidixic acid (NA) and niflumic acid (NFA) on soils using the pulse injection mode, i.e. injection of 110 V/Vp of solution. According to the breakthrough curves (BTC) (Fig. 1), NA was more strongly sorbed than NFA and the transportation of NA was retarded for both column soils. The breakthrough point of NFA in the S soil lied at 3 V/Vp, while it increased up to 95 V/Vp for NA. The total breakthrough of NFA can reach 0.8 as relative concentration, while only 0.1 was obtained in S soil column within 110 V/Vp of injection volume. When we further increased the injection volume to 1500 V/Vp, the total breakthrough values of NA also only reach 0.8 (Fig. S1). Desorption tests showed that mass balance was achieved, indicating that NA or NFA removal was only due to adsorption, and transformation induced by, for instance, minerals can be excluded. We further compared the compound transport in S soil with or without NaN_3 that can inhibit microbial activity (Chen et al., 2022;

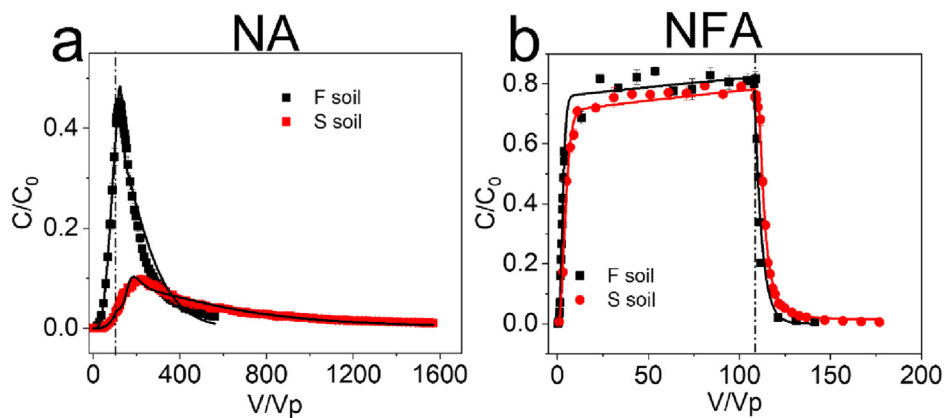


Fig. 1. Breakthrough curves of NA and NFA in the single system. Initial condition: 100 mM NaCl, 10 μM NA, 10 μM NFA, pH 6.5 ± 0.1 for S (Swedish) soil, pH 7 ± 0.2 for F (French) soil, room temperature. The vertical dash lines indicated the beginning of desorption process, i.e. injection of background electrolyte. The solid lines indicated the modeling results. V/Vp is the ratio of the injected volume to the pore volume.

Figueroa and Mackay, 2005). Our results (Fig. S2) showed similar breakthrough curve in the presence or absence of NaN_3 , thus confirming the absence of biotic transformation in soil. Meanwhile, we also noticed that the signal of NA continues to increase in the beginning stage of desorption process, especially for S soil. This is probably due to the desorption behavior from varying soil components.

NA and NFA sorption on soils can take place through various mechanisms including: hydrophobic interactions, electrostatic interactions, and/or surface complexation with minerals. Looking at octanol-water partition coefficient ($\log K_{\text{owNA}} = 1.4$, $\log K_{\text{owNFA}} = 3.7$), we expect that NFA would strongly bind with soil organic matter through hydrophobic interactions. Surprisingly, NFA adsorption into soils was found much lower than NA. Electrostatic interactions may also exist which depends on the acid-base speciation of compounds and surface charge of soil constituents. For instance, NFA exists as ionized form ($\text{pK}_{\text{a}1} = 2.28$ and $\text{pK}_{\text{a}2} = 5.10$), while NA ($\text{pK}_{\text{a}} = 6.19$) exists under both neutral and ionized forms at the working pH in column. However, the determination of surface charge of soil is difficult because of the heterogeneous and complex nature of soils, notably in terms of particle sizes and the extreme variety in types of charged particles.

NA possesses carbonyl and carboxylic groups, while NFA is a monocarboxylate compound. Previous reports (Boily et al., 2000; Paul et al., 2014) showed that the existence of two carboxyl groups or carbonyl and carboxylic groups is in favor of hydrogen bonding and inner-sphere complexation to mineral surfaces. More specifically, our previous studies (Xu et al., 2017b, 2017a) showed that NA binds to goethite surfaces through bidentate binuclear complexes involved carboxylic and ketone groups, while NFA sorption only involved carboxylic group to form outer-sphere complexes. Therefore, the greater adsorption of NA with respect to NFA to soil components or minerals can be likely ascribed to the presence of carboxylic and ketone groups, via hydrogen bonding and surface complexation mechanisms.

Although we cannot observe difference in NFA sorption onto F and S soils because of the weak sorption of NFA, more NA sorption can be clearly observed in the S soil (Fig. 1a). According to the soil characterization (Table S1), cation exchange capacity (CEC) as well as organic carbon (i.e. soil organic matter) were found close in both soils. However, greater clay, Al and Fe contents were detected in the S soil, which may explain its greater adsorption capacity.

In addition to the breakthrough point, we can also observe an obvious tailing in the BTC of NA (Fig. S1), whereas NFA quickly reached steady-state breakthrough ($C/C_0 = 0.8$) within 15 V/V_p (Fig. 1b). This difference is also pronounced in desorption front where NFA can be entirely desorbed within about 14 V/V_p , while it required hundreds of V/V_p for NA. The long tailing on both adsorption and desorption fronts may suggest chemical or physical kinetic limitations of NA under flow-through

conditions. However, the BTC of non-reactive tracer can be perfectly described by the CDE equation (Fig. S3), thereby ruling out physical non-equilibrium such as water regionalization into mobile/immobile zones and/or diffusion limitations between two water zones. Therefore, the mobility behavior under flow-through conditions can be mainly controlled by chemical kinetic limitations related to NA and NFA sorption mechanisms onto soil components.

To check whether chemical kinetic may affect the NA and NFA sorption to soils, static batch experiments under equilibrium conditions were performed after 24h reaction. Indeed, a preliminary kinetic study showed that NA and NFA sorption can reach equilibrium within 24h (Fig. S4). We found that, similar to the column experiments, S soil has higher sorption capacity for NA and NFA over the entire concentration range (1–30 μM). A Freundlich model fitted well with our experiment data (Fig. 2), indicating multiple site binding and heterogeneity in solute adsorption (Hanna et al., 2012). The adsorption parameters n and K_f are reported in Table S3. These parameters could be good reference in our transport model. More details see Table S2.

The pH edges of NA or NFA sorption were shown in Fig. S5. Organic acids binding to single mineral by surface complexation reactions often exhibit a bell-shape with a maximum adsorption amounts happened on a pH nearly the pK_{a} of solute (Cheng et al., 2021, 2018; Marsac et al., 2016; Xu et al., 2017b). In this study, because of the presence of natural organic matter and minerals with contrasting composition and surface charge properties, pH-edges of NA and NFA sorption may change. However, their adsorption still followed the typical pH-dependent behavior of carboxylic acids where great adsorption was achieved at low pH and then decreased along with the increase of pH.

More NA was adsorbed on both soils in the whole pH range (e.g. NA sorption on S and F soils at pH 5 are 5.88 and 4.7 $\mu\text{mol/g}$, while 2.69 and 2.7 $\mu\text{mol/g}$ for NFA). By comparing sorption amounts in equilibrium (batch) vs. non-equilibrium (column), and the characteristic time of reaction under batch vs. the residence time in column, we conclude that sorption kinetics may alter the transport of target compounds under flow-through conditions.

As the complex matrix of soil makes it difficult to directly access molecular-level information, we used macroscopic sorption model as a mean to describe the sorption mechanisms. Considering the sorption kinetics, a two-site sorption model that consider kinetically and equilibrium sorption of reactive species was used to fit the BTCs of NA in single system (cf. Table S2 for parameters). Because the possibility of NA/NFA transformation was excluded, the oxidation parameter (μ_s) was set as 0. The rate constant k and exponent n obtained by fitting the sorption isotherms of NA and NFA (Table S3) were set as the initial parameters (Fig. 1a). However, different values were required to better fit the BTC of NA after optimization, suggesting that NA sorption mechanism may be

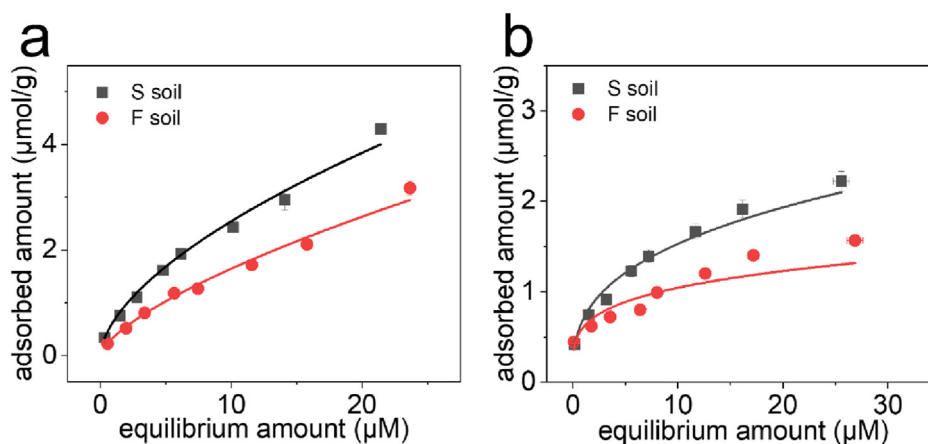


Fig. 2. Sorption isotherm of a) NA and b) NFA in S and F soil. Initial condition: 2 g/L soil, 1–30 μM NA, 1–30 μM NFA, pH 7, room temperature. The solid lines are indicative of fitting results.

altered under flow-through and non-equilibrium conditions. Although the BTC of NFA was much steeper and its breakthrough point occurred much earlier than NA, we needed to consider the contribution of kinetical sites to better fit the BTC of NFA. To this end, we used the same modeling strategy as in NFA. Accordingly, the model generated considerably lower sorption parameter values and fraction of equilibrium sites (k_d , and f) for NFA in the modeling results. Because NA/NFA sorption and desorption processes likely follow different kinetic behaviors, the two stages of the breakthrough behavior were modeled separately (cf. Table S3 for modeling parameters).

3.2. Co-mobility of nalidixic acid and niflumic acid in soil columns

NA and NFA co-transport under flow-through conditions was investigated at the same conditions as for the single systems. In the soil columns, BTCs of NA and NFA sorption in the binary system (Fig. 3) were close to the single system (Fig. 1). The peak of BTC of NA in S soil shifts to 221 V/Vp in binary system and the steady-state breakthrough of NFA still reach C/C_0 0.8. Then, the same parameters of the two-site model used in the single system were employed to fit the BTC of NA and NFA (Table S2). We also compared NFA sorption after 24 h of flow interruption in the single and binary system as an attempt to check the effect of residence time. The results (Fig. S6) showed that same BTC of NFA occurred, although a slight increase in NFA sorption was observed under stop-flow conditions.

NA and NFA sorption on soils were also checked in the mixed NA-NFA system under static batch (equilibrium) conditions. As shown in Fig. S7, NA and NFA sorption in the binary system both decreased with increasing pH, as in the single system. However, greater adsorption of NA and NFA was observed in mixed systems on both soils over the entire pH 5–8 range considered in this work (Fig. S7). This cooperative effect was more pronounced for NFA because of its weaker sorption in the isolated system. For instance, the NFA loading on the S soil in the single system was 2.7 $\mu\text{mol/g}$, yet it increased to 4.1 $\mu\text{mol/g}$ in the binary system. NA sorption on F soil at pH 5.3 reached 4.7 $\mu\text{mol/g}$, while this value increased up to 5.6 $\mu\text{mol/g}$ in the binary system.

Our previous work has highlighted the co-binding behavior at goethite surfaces which occurs in the form of a NFA-NA dimer stabilized by hydrogen bonding and van der Waals interactions (Luo et al., 2022; Xu et al., 2017b, 2017a). We also demonstrated that pre-sorbed NA effectively captured the otherwise weakly-binding NFA from solution. Because the pre-sorbed NA can serve as new sorption sites for NFA, the enhanced NFA sorption was strongly related to the amount of bound NA. The lack of cooperative adsorption under non-equilibrium flow conditions can consequently be the result of the smaller soil-bound NA. Indeed, NA loadings equilibrated at 24 h reached 2.1–3.0 $\mu\text{mol/g}$, while there was only 0.7–0.8 $\mu\text{mol/g}$ NA sorption in the column system.

3.3. Effect of Ca^{2+} on the co-mobility of nalidixic acid and niflumic acid

Divalent cations such as Ca^{2+} are known to affect organic adsorption through binary or ternary complexation reactions with soil minerals and/or Soil Organic Matter (SOM) (Singh et al., 2016; Weng et al., 2008). In the flow-through column system, the BTCs of NA and NFA sorption using Ca^{2+} as background electrolyte (Fig. 4) exhibited a similar behavior compared to Na^+ (Fig. 3). For example, the sorbed amount of NA by using Ca^{2+} as electrolyte within 110 V/Vp injection volume was 6.84 μmol , and almost same adsorbed amount was observed with Na^+ as electrolyte. Still, the final breakthrough of NFA was at 0.8 in both electrolytes, the BTC of NA was well predicted using the same parameters as in the Na^+ system.

Surprisingly, NA and NFA sorption were different under static conditions. Compared to Na^+ solution, Ca^{2+} in the NA solution inhibited NA sorption, but promoted NFA sorption in NFA solution (Figs. S8a and b). The Ca^{2+} effect could be explained by the formation of aqueous complex and/or competition effects toward surface sites. Firstly, because of the big difference in concentration between Ca^{2+} and NA/NFA (1750 times), most free Ca^{2+} was adsorbed onto the negatively charged soil particles. Unlike monovalent Na^+ , divalent Ca^{2+} in the solution can form solution-phase complexes with NA involving carboxyl and keto groups in the form of $\text{Ca}[(\text{NAH}/\text{NA}^-)]^{2+}$ complex, while NFA (as NFA^- at the working pH) with only one carboxyl group cannot complex with Ca^{2+} . Compared to positively charged $\text{Ca}[(\text{NAH}/\text{NA}^-)]^{2+}$ complex, NFA^- would interact more with soil- Ca^{2+} assembly. Similar results involving oxolinic acid (OA) adsorption on goethite in the presence of divalent Mg^{2+} were previously reported (Cheng et al., 2019). Inhibition of OA adsorption was attributed to the formation of soluble OAMg^+ complexes. This is also in agreement with a previous study (Hanna, 2007), where Ca^{2+} hindered 1-hydroxy-2-naphthoic acid sorption by forming soluble binary complexes. The same results were also observed here on ciprofloxacin (CIP) (Fig. S9), a quinolone drug with a similar structure as NA. Indeed, CIP sorption on soils was inhibited because of the presence of Ca^{2+} .

In the Ca^{2+} -binary system, NA sorption was slightly inhibited but NFA sorption was still enhanced compared to Na^+ . Additionally, NFA^- was not only adsorbed on soil-bonded NA but also on soil-bonded Ca^{2+} , and Ca^{2+} competitively weakened NA sorption (Figs. S8c and d). As a whole, the inhibitive role of Ca^{2+} on NA sorption under batch conditions was likely caused by aqueous complexation and competition adsorption processes, while the enhanced NFA sorption was driven by the changed surface charge resulting from Ca^{2+} binding. Still, the lack of a significant effect of Ca^{2+} under non-equilibrium flow conditions can be probably ascribed to smaller soil Ca^{2+} loadings in the column. Indeed, cation adsorption behavior onto soil components was strongly dependent on various factors, which include contact time, pH and soil mineralogical composition (Cherian et al., 2018; Eick et al., 1990). Taken together,

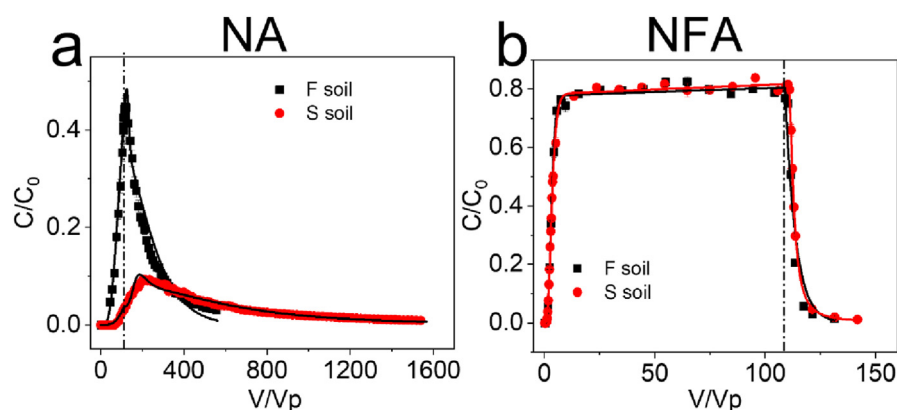


Fig. 3. Breakthrough curves of NA and NFA in the binary system. Initial condition: 100 mM NaCl, 10 μM NA, 10 μM NFA, pH 6.5 ± 0.1 for S (Swedish) soil, pH 7 ± 0.2 for F (French) soil, room temperature. The vertical dash lines indicated the beginning of desorption process, i.e. injection of background electrolyte. The solid lines are model predictions. V/Vp is the ratio of the injected volume to the pore volume.

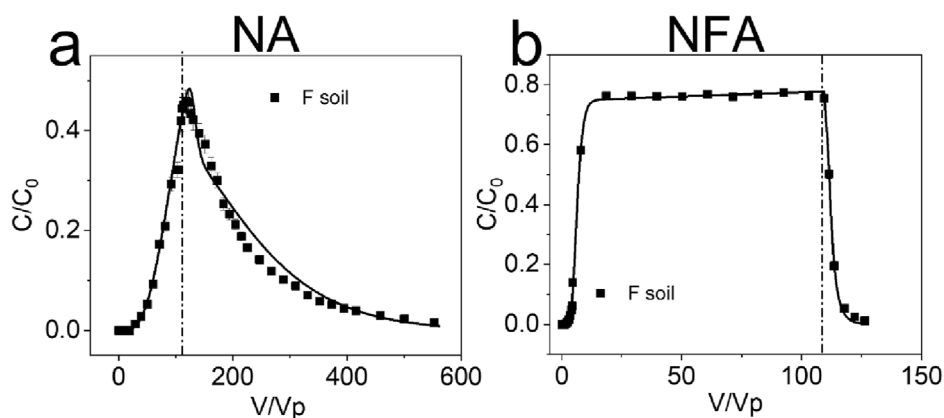


Fig. 4. Breakthrough curves of NA and NFA in binary systems. Initial condition: 35 mM CaCl_2 , 10 μM NA, 10 μM NFA, $\text{pH } 7 \pm 0.2$ for F (French) soil, room temperature. The vertical dash lines indicated the beginning of desorption process, i.e. injection of background electrolyte. The solid lines indicated the modeling results. V/V_p is the ratio of the injected volume to the pore volume.

these results show that soil interactions with co-existing contaminants and cations need to be considered depending on the relevant condition, i.e. equilibrium (static-batch) vs. non-equilibrium (flow-through column), to accurately predict the fate and transport of contaminants in complex environmental systems.

4. Conclusions

In this study, we demonstrated that adsorption of nalidixic acid (NA) and niflumic acid (NFA) differ in terms of adsorption amount and mechanisms under equilibrium (static-batch experiments) vs. non-equilibrium (flow column experiments) conditions. Under non-equilibrium conditions, we observed higher affinity of Sweden soil toward NA sorption, probably due to its higher contents in clay and metal oxides. No impact of mixture on the mobility of NA or NFA, since the same breakthrough behavior was observed in the single and binary systems. However, the enhanced adsorption of NFA was observed under equilibrium conditions, likely due to cooperative adsorption with the soil-bonded NA.

The type of electrolytes under equilibrium conditions also affects NA and NFA adsorption both in the single and binary systems. Indeed, Ca^{2+} promoted NFA adsorption but inhibited NA adsorption, as compared to Na^+ . This difference was ascribed to the formation of Ca^{2+} -NA complex and greater affinity of the anionic form of NFA⁻ towards soil- Ca^{2+} assembly. Surprisingly, no significant impact of cation type was observed under flow-through conditions, i.e. same breakthrough for Na^+ and Ca^{2+} . The lack of cooperative adsorption and/or surface ternary complexation with soil components under flow-through conditions may be correlated to the changes in contact time and/or resident pH in soil columns.

By taking kinetics into consideration, our proposed modelling satisfactorily simultaneously predicted the mobility of NA and NFA in single and binary systems. These results can help further understand the retention of contaminants and (co)-adsorption mechanisms in batch-static vs. flow-through conditions. This will also help in development of appropriate modeling framework to describe the mobility of pharmaceuticals through a soil column and then in the environment. However, more pharmaceutical compounds and different soil matrices should be investigated in order to form a general conclusion on the reactive transport of those compounds in nature. Further studies should also be conducted to assess the impact of varying physical and (bio)chemical parameters on the fate and mobility of pharmaceuticals in soils.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.seh.2024.100060>.

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