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# pH-dependent ciprofloxacin sorption to soils: Interaction mechanisms and soil factors influencing sorption

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## ABSTRACT

A study of ciprofloxacin sorption to 30 soils from the eastern United States revealed a statistically significant effect of pH on the solid–water distribution coefficient ( $K_d$ ). Cation exchange capacity was the key soil factor influencing the extent of sorption at all pH values (3–8), with soil metal oxide content playing a smaller role at higher pH. Although, cation exchange, cation bridging and surface complexation mechanisms all appeared to contribute to the net extent of ciprofloxacin sorption to soils, the ciprofloxacin molecule appeared to be best suited for cation exchange. Notably, the ciprofloxacin cation (dominant at  $\text{pH} \leq 5$ ) exhibited a greater potential for cation exchange than the net neutral zwitterion (relevant at  $\text{pH} > 6$ ). In addition to ciprofloxacin speciation in aqueous solution, the availability of surface sites for cation exchange (cation exchange capacity) and surface complexation (metal oxide content) played a key role in determining the shape of the pH edge and the potential contributions from individual sorption mechanisms to the net extent of sorption. Soils not limited by the availability of cation exchange sites and possessing a high effective cation exchange capacity ( $\text{ECEC} > 20 \text{ cmol}_c/\text{kg}$ ), exhibited distinct pH edges (general decrease in sorption with pH) and the highest extent of sorption at all pH values. In these soils, cation exchange was found to be a dominant mechanism of sorption, with potential contributions from cation bridging and surface complexation being either unimportant or not discernable. In soils of lower cation exchange capacity ( $\text{ECEC} < 20 \text{ cmol}_c/\text{kg}$ ), limited with respect to the availability of cation exchange sites, sorption initially increased with increasing pH, peaked at pH 5.5 and decreased at pH 7–8. In these soils, a specific contribution from surface complexation to the net extent of sorption was surmised at high pH values in metal oxide-rich soils, possessing low cation exchange capacities.

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## 1. Introduction

Antibiotics are routinely administered to humans and animals for the treatment of infections and are subject to prophylactic use in bioterrorism threats, concentrated animal feeding operations and aquaculture (Rooklidge, 2004; Lee et al., 2007). Although antibiotics are metabolized within the body, as much as 90% of orally-administered doses may be excreted unmetabolized (Kumar et al., 2005). Therefore, it is not surprising that antibiotics are routinely detected at sub-inhibitory concentrations in surface water, ground water, treated municipal wastewater, municipal biosolids, soils and sediments (Kolpin et al., 2002; Boxall et al., 2003; Giger et al., 2003; Kummerer, 2004; Xia et al., 2005). Currently, these trace concentrations of antibiotics cannot be causally linked to the global proliferation of antibiotic resistant strains of bacteria and the diminished effectiveness of human therapeutic

drugs (Kummerer, 2004; Rooklidge, 2004; Lee et al., 2007). Nevertheless, the continued detection of antibiotics in the natural environment is cause for concern.

An understanding of antibiotic fate and transport in the natural environment, and specifically knowledge of sorption–desorption phenomena, provides key insights into potential microbial exposure to antibiotics and the associated human and ecosystem risks. For example, the intentional or unintentional release of antibiotic-rich manure and biosolids can lead to a reservoir of antibiotics in soils that is protected from biotic and abiotic degradation due to sorption to solids, but that is susceptible to release from soils into the water column (leaching into ground water) due to desorption processes (Rooklidge, 2004).

Our current understanding of fluoroquinolone antibiotic sorption in soil systems is lacking when compared to our knowledge of the sorption behavior of other high-use antibiotic classes (Pico and Andreu, 2007). Several studies focused on the sorption of tetracycline, sulfonamide, and macrolide antibiotics have advanced our understanding of the soil properties and the antibiotic structural criteria influencing sorption (Fontaine et al., 1991; Rabolle and Spliid,

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2000; Boxall et al., 2002; Thiele-Bruhn et al., 2004; Figueroa and MacKay, 2005; Jones et al., 2005; Sassman and Lee, 2005; ter Laak et al., 2006). In contrast, knowledge of key soil properties, pH effects, and structural criteria affecting fluoroquinolone antibiotic sorption in soil systems has been limited because only small sets of soils (1–5) have been examined (Nowara et al., 1997; Drillia et al., 2005; Hari et al., 2005). Therefore, a broader range of soil types and pH conditions are required for a more complete understanding of fluoroquinolone sorption. An understanding of the pH-dependent sorption is important because fluoroquinolone speciation in soil pore water changes as a function of pH. For example, ciprofloxacin, a high-use antibiotic and the subject of this study, exists as cation, zwitterion, and/or anion species under environmentally-relevant soil pH conditions (Fig. 1). In addition, the high stability of fluoroquinolones in soil systems, save in the presence of light (Knapp et al., 2005), manganese oxides (Zhang and Huang, 2005) and select soil microbes (Chen et al., 1997; Wetzstein et al., 1999) demands an improved understanding of the role of soil properties on sorption behavior.

The nature (mechanisms) of fluoroquinolone sorption in soil systems can be anticipated, to some extent, based on the previous studies of sorption in soil and pure phase systems. As postulated for antibiotics by Tolls (2001), hydrophobic partitioning did not appear to drive fluoroquinolone sorption to soils. Instead, fluoroquinolone sorption to soils was suggested to occur via columbic attraction of the cationic amine moiety on the fluoroquinolone molecule (Fig. 1) to negatively charged quartz sand (Hari et al., 2005), or cation bridging (interaction between the fluoroquinolone carboxyl group and exchangeable cations) (Nowara et al., 1997). Pure phase studies with aluminosilicates pointed to fluoroquinolone sorption via cation exchange (Castela-Papin et al., 1999) and provided spectroscopic

evidence for cation bridging (Nowara et al., 1997; Otker and Akmeahmet-Balciglu, 2005). Batch and spectroscopic studies with pure phase iron and aluminum oxides confirmed fluoroquinolone sorption via complexation to surface bound aluminum and iron ions (Goyne et al., 2005; Gu and Karthikeyan, 2005; Trivedi and Vasudevan, 2007; Zhang and Huang, 2007).

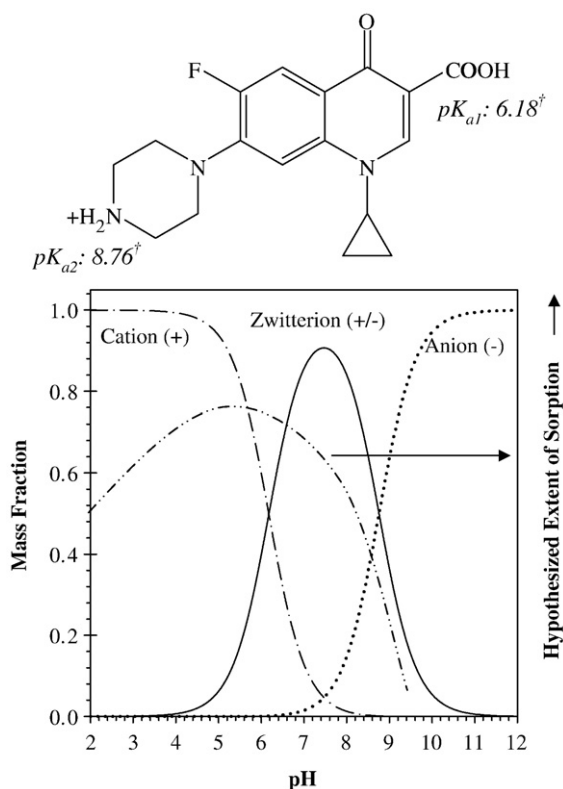
The above-mentioned mechanistic studies of fluoroquinolone sorption to pure phase minerals allow us to infer sorption via cation exchange, cation bridging, and surface complexation when mineral phases are mixed together as soil aggregates. Cation exchange in soil systems will involve the columbic attraction of the cationic amine group (Fig. 1) to negatively charged surface sites on soils and will occur via ion exchange with naturally-occurring cations associated with sites of permanent negative charge on aluminosilicate clays or pH-dependent negative charge arising from the deprotonation of surface hydroxyl (on soil metal oxide, aluminosilicate edge sites, and organic matter) and carboxylic acid groups (on soil organic matter) (Brady and Weil, 2002; Schwarzenbach et al., 2003). Cation bridging is expected to occur via columbic attraction or complexation of the fluoroquinolone carboxyl group (Fig. 1) with exchangeable cations associated with negatively charged sites, and surface complexation via the binding of the fluoroquinolone carboxyl group to surficial aluminum and iron ions on soil metal oxides and aluminosilicate edge sites.

We hypothesize an increase in the extent of ciprofloxacin sorption in soils with an increase in pH, for  $\text{pH} \leq 5$  (approximately), followed by a decrease in sorption with pH for  $\text{pH} \geq 5$  (Fig. 1) based on knowledge of ciprofloxacin  $\text{pK}_a$  and speciation (Fig. 1), mechanisms of organic compounds sorption to soils and soil minerals (Schwarzenbach et al., 2003), the pH-dependent charge of soil systems (Brady and Weil, 2002), and the established mechanisms of ciprofloxacin sorption in pure phase mineral systems (detailed above). This hypothesized pH-dependent sorption behavior (detailed description and rationale found in Supplemental information) assumed that all three mechanisms of interaction (cation exchange, cation bridging, and surface complexation) identified in pure phase studies are operative in soil systems and that sorption was not influenced by preferential capacity for sorption via a particular mechanism. The ciprofloxacin cation was expected to sorb primarily via cation exchange and the zwitterion by cation exchange, cation bridging and surface complexation. In addition, the anionic carboxylate moiety within the net neutral zwitterion was assumed to decrease the potential for cation exchange/columbic attraction via the cationic amine functionality on account of unfavorable columbic interactions between the anionic moiety and negatively charged sites.

Our consideration of soil aggregates as a simple combination of mineral and organic matter components (above) does not account for the unknown inter-associations between individual components. Hence, several characteristics of the nature of fluoroquinolone sorption within soil systems remain unclear: (i) the role of soil properties and surface site availability in determining the observed pH-dependent sorption; and (ii) the relative contributions from individual sorption mechanisms to the net extent of sorption. This study seeks to address these gaps in current understanding by investigating ciprofloxacin sorption onto a large set of soils as a function of pH. Our objectives were (1) to identify soil factors that may be used as predictors of the pH-dependent equilibrium sorption coefficient and (2) to understand the operative mechanisms of sorption.

## 2. Materials and methods

We measured the extent of ciprofloxacin sorption as a function of pH (3–8) onto 30 soils, quantified the extent of desorption, and performed a number of statistical analyses.



**Fig. 1.** Ciprofloxacin structure (top), speciation of the cation, zwitterion and anion as a function of pH (left y-axis, mass fraction) calculated based on  $\text{pK}_a$  values from Va'zquez et al. (2001)<sup>†</sup>, and our hypothesized pH-dependent sorption of ciprofloxacin in soil systems (right y-axis).

## 2.1. Soils

We obtained a set of 30 soils from the eastern United States collected at sites with no known history of animal husbandry or exposure to ciprofloxacin. Soils were selected to ensure that a wide range of soil properties was represented, thereby allowing for robust statistical analysis. In addition, this soil set represented the five dominant soil orders of the eastern United States, 28 distinct soil series, and, in every case, either a surface (0–15 cm) or subsurface (30–45 cm) soil. This same soil set was previously used to determine soil factors influencing oxytetracycline sorption at pH 5.5 (Jones et al., 2005). The 30 soils were previously characterized using conventional soil science techniques routinely applied in county and regional extension centers so that our findings could have direct application in regulatory decision-making. Soil characteristics measured included, cation exchange capacity (CEC) at soil pH (ECEC),  $pH_w$ , surface area (SA), texture (% sand, silt, and clay), total (TC) and organic carbon (OC) content, operationally-defined dithionite-citrate-bicarbonate extractable free or crystalline aluminum and iron oxide content (DCBAI, DCBFe), operationally-defined acid ammonium oxalate extractable poorly or non-crystalline (amorphous) aluminum and iron oxide content (AAOFe, AAOAl), and exchangeable Al (ExAl), Ca, K, Mg, Na and Na (Jones et al., 2005). Please see Supplemental information, for additional information on sampling, storage and characterization (Table S1).

For reasons stated above, the soil ECEC values reported and used in the analyses were measured at the soils' natural pH rather than at the buffered experimental pH values (3, 4, 5.5, 7, and 8). Nevertheless, knowledge of the pH dependence of CEC values in soils with significant domains of pH-dependent charge (organic matter, metal oxides and hydroxides, and kaolinite) (Brady and Weil, 2002), prompted us to evaluate if the use of ECEC instead of CEC biased the results of our statistical analyses. To this end, we have measured CEC as a function of pH for a limited number (seven) of soils possessing a range of %OC, ECEC, DCBAI and DCBFe values (see Supplemental information, Fig. S1, Table S1). We acknowledge that CEC measurements at the pH of the sorption experiments would have been ideal, but note that the measurement of CEC values for 30 soil under 5 pH conditions (close to 190 CEC experiments, assuming only 25% duplication) was outside the scope of this project.

## 2.2. Chemicals

Ciprofloxacin (>98%) was obtained from Bayer Corporation (West Haven, CT, USA); acetic acid, acetonitrile, 2-(N-Morpholino)ethanesulfonic acid (MES), sodium acetate and sodium azide from Fisher Scientific (Pittsburgh, PA, USA); 3-(N-Morpholinyl)-2-hydroxypropanesulfonic acid (MOPS) from Mallinckrodt (Phillipsburg, NJ, USA); 1,4-Piperazinediethanesulfonic acid (PIPES) from JT Baker (Phillipsburg, NJ, USA); and phosphoric acid from Wheaton Scientific (Millville, NJ, USA).

## 2.3. Sorption as a function of pH

This study used the soil–water distribution coefficient  $K_d$  (L/kg), defined as  $C_s / C_w$  (where  $C_s$  is the concentration of solute sorbed (mmol/kg) and  $C_w$  is the concentration of solute remaining in aqueous solution (mM)), to evaluate the pH-dependent sorption behavior of ciprofloxacin. The Freundlich constant or capacity factor  $K_F$  defined as  $C_s / C_w^n$  (where  $n$  is the Freundlich coefficient) was not selected because different soils typically exhibit sorption isotherms with distinct  $n$  values for the same solute (Sassman and Lee, 2005) and thereby limit the reliable comparisons of  $K_F$  values across soils. Furthermore, for large compounds such as ciprofloxacin, the low solubility precludes our ability to discern an adsorption maximum for all soils and calculate  $K_L$  (Langmuir constant) from the fit to the

Langmuir isotherm. Therefore, preliminary experiments were conducted to identify experimental conditions (equilibration time, soil loading and initial solute concentration) in which sorption falls within the linear range of the sorption isotherm such that  $K_d$  values could be calculated from a single solute concentration for comparing pH-dependent sorption across soils and pH conditions. Preliminary experiments were conducted with six soils representing the five soil orders and a wide range of soil properties to identify the above-mentioned experimental conditions (see Supplemental information – Figs S2–S4). Based on these studies an equilibration time of 72 h, a soil loading of 1 g/L and an initial ciprofloxacin concentration 0.05 mM were used in most experiments. For a small subset of soils (Iredell, Pledger and Sharkey) which exhibited close to 100% sorption at pH 5.5 under the above-mentioned experimental conditions, an initial concentration of 0.1 mM (also found to fall within the linear range of their respective sorption isotherms) was used. Environmentally-relevant ciprofloxacin concentrations are typically lower than the initial concentrations used in this study and, hence, are also expected to fall in the linear range of the sorption isotherm. Therefore, single point  $K_d$  values measured in this study will be applicable at environmentally-relevant ciprofloxacin concentrations.

Sorption was evaluated in reactors buffered at pH 3 (chloroacetate), pH 4 (acetate), pH 5.5 (MES), pH 7 (PIPES), and pH 8 (MOPS); tests (data not shown) revealed that the buffers used did not degrade ciprofloxacin or interfere with ciprofloxacin sorption or detection (Jones et al., 2005). A 10 mg subsample of soil, a fixed volume of aqueous solution containing 100 mM pH buffer set to the desired pH and 1.5 mM sodium azide (used to inhibit ciprofloxacin degradation by native soil microbes), and a known volume of ciprofloxacin stock solution also prepared in 100 mM pH buffer and 1.5 mM sodium azide were sequentially added to a 15 mL polypropylene centrifuge tube to achieve a final volume of 10 mL and the soil loading and initial ciprofloxacin concentrations listed above. Triplicate soil-containing and soil-free reactors (which served as a measure of initial ciprofloxacin concentration ( $C_0$ )) were prepared for each experimental condition and equilibrated end-over-end. At the end of the equilibration period, the reactors were centrifuged (3400 rpm), syringe filtered (0.45  $\mu$ m nylon membrane filters) and the supernatant analyzed for the concentration of ciprofloxacin ( $C_w$ ) by HPLC with diode array detection (DAD) (Agilent 1100 Series). The HPLC/DAD system was operated at 1 mL/min with an Agilent Zorbax Eclipse EDB-C18 column (5  $\mu$ m 4.6 mm  $\times$  250 mm) and a mobile phase containing 30% acetonitrile and 70% 0.05 M  $H_3PO_4$  (pH 2.74). The concentration sorbed ( $C_s$ ) was calculated by subtracting the concentration of ciprofloxacin in the soil-containing reactors ( $C_w$ ) from the concentration of ciprofloxacin in the corresponding soil-free reactors ( $C_0$ ) and then normalizing for the mass of the soil in the reactor. Subsequently, single point solid–water distribution coefficients ( $K_d$ ) (defined as  $C_s / C_w$ ) were calculated and used to compare the extent of sorption across both pH and the 30 soil samples. Mass balance and potential degradation were assessed via desorption studies detailed in Supplemental information (section on Mass Balance Studies). Notably, an average extent of desorption of  $92 \pm 9\%$  (Table 1) confirmed that the observed loss from bulk solution was due to sorption. In all cases, triplicate experiments assured representative soil samples and compensated for the low soil loading required to operate within our limit of ciprofloxacin quantitation (LOQ: 1.5  $\mu$ M).

In 10 of 150 sorption experiments (30 soils each at 5 pH values), the extent of sorption observed under the above-mentioned experimental conditions was greater than 97% and  $C_w$  values were below the LOQ. In these cases, calculations based on the LOQ yielded  $K_d$  values greater than or equal to 50,000 L/kg. We have set  $K_d = 50,000$  L/kg (instead of  $K_d \geq 50,000$ ) in these cases because our statistical analyses (below) required the input of a single numerical value for  $K_d$ .



**Table 1**  
Ciprofloxacin soil–water distribution coefficients ( $K_d$ ) and extent of desorption.

Soil order	Soil name <sup>a</sup>	$K_d^{pH4}$ ( $10^3$ L/kg) <sup>b</sup>	$K_d^{pH7}$ ( $10^3$ L/kg) <sup>c</sup>	% desorbed <sup>d</sup>
<i>Greater cation sorption: <math>K_d^{pH4}</math> (cation) &gt; <math>K_d^{pH7}</math> (zwitterion)<sup>e</sup></i>				
Alfisol	Iredell/SS	45 ± 1	7.9 ± 1.1	85 ± 17
Vertisol	Sharkey/S	36 ± 0.65	8.1 ± 0.032	94 ± 1
Vertisol	Sharkey/SS	36 ± 0.66	9.8 ± 0.26	83 ± 1
Vertisol	Pledger/S	35 ± 1.3	6.4 ± 0.18	98 ± 1
Vertisol	Heiden/SS	27 ± 1.1	2.2 ± 0.037	100 ± 13
Vertisol	Heiden/S	26 ± 0.82	2.3 ± 0.066	100 ± 1
Vertisol	Moreland/SS	26 ± 1.7	3.3 ± 0.14	100 ± 4
Ultisol	Appling/SS	0.30 ± 0.0025	0.26 ± 0.0082	100 ± 11
<i>Greater zwitterion sorption: <math>K_d^{pH4}</math> (cation) &lt; <math>K_d^{pH7}</math> (zwitterion)<sup>e</sup></i>				
Inceptisol	Burton/S	2.2 ± 0.33	7.6 ± 0.18	100 ± 1
Ultisol	Rains/S	1.1 ± 0.087	1.4 ± 0.18	100 ± 2
Inceptisol	Rosman/S	0.76 ± 0.037	1.3 ± 0.050	90 ± 6
Inceptisol	Ashe/SS	0.77 ± 0.048	1.2 ± 0.043	95 ± 2
Ultisol	Aycock/SS	0.72 ± 0.063	1.0 ± 0.050	100 ± 2
Alfisol	Enon/SS	0.74 ± 0.091	1.0 ± 0.10	92 ± 14
Inceptisol	Comus/S	0.48 ± 0.014	1.0 ± 0.098	95 ± 1
Spodosol	Adams/SS	0.29 ± 0.027	0.89 ± 0.070	59 ± 9
Ultisol	Georgeville/S	0.65 ± 0.085	0.82 ± 0.067	100 ± 2
Inceptisol	Codorus/SS	0.33 ± 0.020	0.46 ± 0.0093	86 ± 4
<i>Equal cation and zwitterion sorption: <math>K_d^{pH4}</math> (cation) ≈ <math>K_d^{pH7}</math> (zwitterion)<sup>e</sup></i>				
Alfisol	Hagerstown/S	1.7 ± 0.081	1.7 ± 0.10	98 ± 0
Ultisol	Orangeburg/SS	1.6 ± 0.56	0.75 ± 0.12	100 ± 3
Inceptisol	Chewacla/SS	1.4 ± 0.97	0.72 ± 0.12	92 ± 2
Alfisol	Kleinpeter/S	1.1 ± 0.14	1.0 ± 0.069	92 ± 3
Alfisol	Wilkes/S	1.1 ± 0.12	1.2 ± 0.031	95 ± 2
Spodosol	Peru/SS	0.99 ± 0.012	1.2 ± 0.19	79 ± 2
Alfisol	White Store/SS	0.86 ± 0.11	0.96 ± 0.064	88 ± 4
Spodosol	Colton/S	0.82 ± 0.15	0.90 ± 0.12	94 ± 2
Spodosol	Leon/S	0.46 ± 0.11	0.30 ± 0.022	74 ± 18
Ultisol	Goldsboro/S	0.43 ± 0.084	0.49 ± 0.073	100 ± 4
Spodosol	Tunbridge/S	0.20 ± 0.025	0.21 ± 0.042	81 ± 7
Spodosol	Berryland/SS	0.15 ± 0.034	0.26 ± 0.081	97 ± 4

Error: one standard deviation.

<sup>a</sup> S = surface, 0–15 cm; SS = subsurface, 30–45 cm.

<sup>b</sup> Cation ion dominant at pH 4.

<sup>c</sup> Zwitterion dominant at pH 7.

<sup>d</sup> Measured following sorption at pH 5.5.

<sup>e</sup> *t*-test:  $p < 0.05$  (test not conducted on Iredell).

## 2.4. Statistical analyses

Statistica® (Statsoft, Version 5.5, Tulsa, OK, USA) was used to examine distributions of the individual soil properties and the  $K_d$  values determined at the different pH values, and to calculate Pearson correlations among all combinations of soil properties. A two-way analysis of variance (ANOVA), conducted with a generalized linear model procedure in SAS for Windows Version 8.2 (SAS Institute, Cary, NC, USA), was used to determine if differences in pH (3, 4, 5.5, 7, 8) and soil order (Alfisols, Inceptisols, Spodosols, Ultisols, Vertisols) accounted for a significant proportion of the variance in the  $K_d$  data. Means were compared with a least-squared differences (LSD) procedure (SAS Institute, Cary, NC, USA) and an alpha level of 0.05 was utilized. To conform to the assumptions of the ANOVA, log transformations were performed on the  $K_d$  data prior to analysis.

Principal components analysis (PCA) was used to reduce the dimensionality in the dataset and further explore the relationships among the soil properties and  $K_d$  values. Individual PCAs were conducted at each pH to evaluate the relationship between the corresponding  $K_d$  values and 14 selected soil properties. Soil properties included in the PCA were % sand, SA, TC, OC, AAOAI, AAOFe, DCBAI, DCBFe, ECEC, ExCa, ExK, ExMg, ExNa, and ExAl. Percent (%) silt and % clay were excluded due to their lack of independence and collinearity with % sand. For all PCAs, we used 29 of the 30 soils, omitting the Burton soil in order to ensure normality of the data set (Jones et al., 2005). The PCAs were conducted using PC-ORD (MJM Software

Design, Gleneden Beach, OR, USA) and the significance of the principal component axes was tested with the broken-stick eigenvalue test (Legendre and Legendre, 1998). Biplots relating the individual soil samples with the measured soil properties and  $K_d$  values were created for visual interpretation of the PCA.

Multiple stepwise regression (MSR) (S+, Insightful Corporation, Seattle, WA, USA) was used to complement PCA and to explore the response of  $K_d$  at each pH (dependent variable) from a group of three soil properties (independent variables). Soil properties and the  $K_d$  values for 29 soils (Burton soil omitted as noted above) were log transformed so that the data would conform to the normality assumption required of the MSR analysis. Intercorrelated soil properties were not included in the MSRs due to the potential confounding effects of collinearity. Three soil properties, ECEC, DCBAI + Fe (sum of DCBAI and DCBFe) and OC, known to govern the extent of four primary mechanisms of sorption were selected: ECEC governs cation exchange and cation bridging, soil oxide content (DCBAI + Fe) influences surface complexation and %OC determines hydrophobic partitioning (Schwarzenbach et al., 2003). Pearson correlations confirmed that the selected variables were not correlated. Dithionate–citrate–bicarbonate Al + Fe was chosen instead of the individual values of DCBFe and DCBAI, in order to reflect the total number of surficial metal ions available for surface complexation.

Although %OC and DCBAI + Fe values primarily govern the extents of hydrophobic partitioning and surface complexation, respectively, these soil properties are also indirect measures of a small component of the soil's CEC because organic matter and aluminum/iron oxide contents also represent domains of pH-dependent negative charge. As such, MSRs based on ECEC/CEC, DCBAI + Fe, and %OC unavoidably double count the influence of a soil's cation exchange potential to varied extents. Given these considerations, MSR was only used to identify predictors for the sorption coefficients that were consistent with PCA and validation of the MSR results was not attempted.

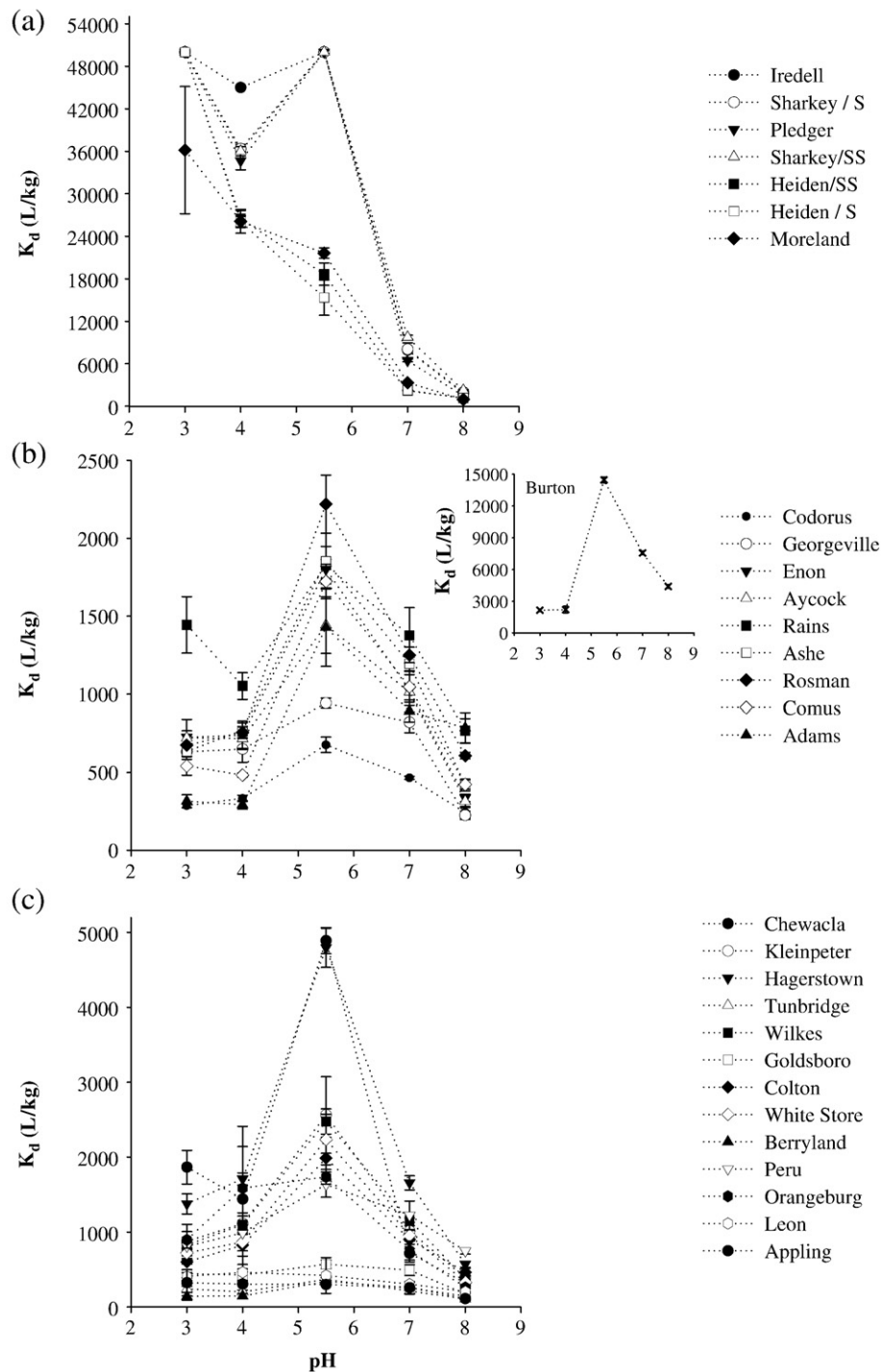
## 2.5. Approach to achieving research goals

Soil factors that may be used as predictors of the pH-dependent equilibrium sorption coefficient (objective 1, Introduction) were directly identified using the combination of statistical techniques mentioned above. An indirect approach was utilized to understand the operative mechanisms of sorption (objective 2, Introduction) because direct spectroscopic techniques were unable to discern the sorption mechanisms of organic solutes, such as ciprofloxacin, which sorb via multiple mechanisms (unpublished X-ray Absorption Spectroscopy data). This approach leveraged mechanistic information from the previous studies of fluoroquinolone interaction in pure phase systems and knowledge of ciprofloxacin speciation in aqueous solution (Fig. 1) to hypothesize pH-dependent sorption in the behavior in soil systems (Introduction and Supplemental information). Subsequently, possible mechanisms of sorption in soil systems were surmised by evaluating the observed pH-dependent sorption of ciprofloxacin in the 30 test soils (Fig. 2, Table 1) in relation to the hypothesized pH-dependent sorption behavior (Fig. 1), the soil factors found to influence pH-dependent sorption coefficient (objective 1), and measures of site abundance for sorption obtained from soil characterization.

## 3. Results

### 3.1. Effect of pH on the extent of ciprofloxacin sorption to soils

The extent of ciprofloxacin sorption as a function of pH followed two distinct profiles in the thirty soils examined (Fig. 2). The first profile (henceforth referred to as “pH edge 1”), exhibited by a group of seven soils was a general decrease in sorption with an increase in pH, with the greatest extent of sorption observed at low pH (pH 3–5.5) (Fig. 2a). Soils following “pH edge 1” exhibited a high extent of



**Fig. 2.** Sorption of ciprofloxacin as a function of pH onto 30 soils. Soil exhibiting “pH edge 1” (a) and “pH edge 2” (b, c). Inset (b): Burton soil, different y-axis. Dotted lines intended as visual guides. Error bars represent one standard deviation. (S—surface soil, 0–15 cm; SS—subsurface soil, 30–45 cm).

sorption over the entire pH range, with  $K_d$  values from 973 to  $\geq 50,000$  L/kg, and were comprised primarily (6 out of 7) of soils of the Vertisol order (Table 1, Fig. 2a). The second profile (“pH edge 2”), displayed by the remaining 23 soils, was an initial increase in the extent of sorption, a peak in sorption at pH 5.5 and a decrease sorption at pH 7–8 (Fig. 2b,c). Soils following “pH edge 2” exhibited a lower range of  $K_d$  values (106 to 14,464 L/kg) (Fig. 2b, c).

For each soil, the magnitudes of  $K_d^{pH4}$  and  $K_d^{pH7}$  were compared to examine the difference in the potential for ciprofloxacin cation and

zwitterion sorption (Table 1).  $K_d^{pH4}$  was assumed to approximate the sorption potential of the cation, as 99% cation was present in aqueous solution at pH 4 and  $K_d^{pH7}$  to estimate the sorption potential for the zwitterion, since 86% zwitterion was present at pH 7 (pH 7 was selected over pH 8 to avoid the presence of anions, Fig. 1). Surface protonation of the zwitterion (the conversion of the zwitterion to the cation in the more acidic layers of water adjacent to the surface) was not considered because this process was not clearly evident in soils, although noted in studies of amine sorption to pure phase

aluminosilicates (Theng, 1974). Comparison of  $K_d^{pH4}$  and  $K_d^{pH7}$  for each soil using a  $t$ -test (with unequal variances) revealed that soils grouped as follows: (i) cation sorption > zwitterion sorption ( $K_d^{pH4} > K_d^{pH7}$ ), (ii) cation sorption < zwitterion sorption ( $K_d^{pH4} < K_d^{pH7}$ ), and (iii) cation sorption  $\approx$  zwitterion sorption ( $K_d^{pH4} \approx K_d^{pH7}$ ) (Table 1, Fig. 2). Not surprisingly, most soils with greater cation sorption exhibited “pH edge 1”, whereas, soils with cation sorption  $\leq$  zwitterion sorption followed “pH edge 2” (Table 1). The anomalous presence of the Appling soil in the  $K_d^{pH4} > K_d^{pH7}$  category, instead of the  $K_d^{pH4} \approx K_d^{pH7}$  category, possibly resulted from the exceptionally low standard deviations of the Appling soil  $K_d$  values (Table 1).

### 3.2. Statistical analyses

A combination of statistical analyses was used to establish the effect of pH on the magnitude of  $K_d$  and to identify soil factors influencing the extent of sorption as a function of pH. A two-way ANOVA conducted on the entire dataset (30 soils) and a reduced data set of 24 soils (6 Vertisols exhibiting “pH edge 1” omitted) revealed that both pH and soil order accounted for a significant ( $p < 0.05$ ) amount of the variation in ciprofloxacin sorption ( $\log K_d$ ). The interaction between pH and soil order (pH\*soil order) was significant for the entire data set but not for the reduced dataset, indicating that the effect of pH on  $\log K_d$  was consistent across all soils except the Vertisols.

Although soil order accounted for a significant amount of variation in  $\log K_d$  values in the ANOVA, we have avoided suggesting that soil order had a significant effect on  $K_d$ . This study was restricted to 5 of the 12 soil orders, all of which were obtained from the eastern United States; hence, broad assertions with respect to soil order were not justified. Instead, ANOVA was used to confirm the statistical significance of the visually-observed effect of pH on  $K_d$  (Fig. 2) and to provide the required statistical support for the separation of the 30 soils into two groups based on their distinct pH edges (“pH edges 1” and “2”).

Principal component analysis involving a large suite of soil properties and  $K_d$  values at each pH provided information on the effect of pH on the primary soil factors influencing sorption. Overall, the PCA reduced the dimensionality of the dataset to three major axes, which were significant according to the broken-stick eigen value test. For example, the first three principal components (axes) accounted for 77.8% of the variation in the PCA of soil properties and  $K_d^{pH4}$  and 77.6% of the variation in the PCA of soils properties and  $K_d^{pH7}$  (Fig. 3). In both cases, axis 1 accounted for  $\sim 40\%$  for the variance, axis 2 for  $\sim 20\%$  of the variance and axis 3 for  $\sim 16\%$  of the variance. The biplots (Fig. 3) clearly showed the interrelationships among the 14 soil properties and the position of  $K_d$  in ordination space in relation to these properties. Consistent with our earlier study (Jones et al., 2005) descriptors of texture and exchange capacity loaded

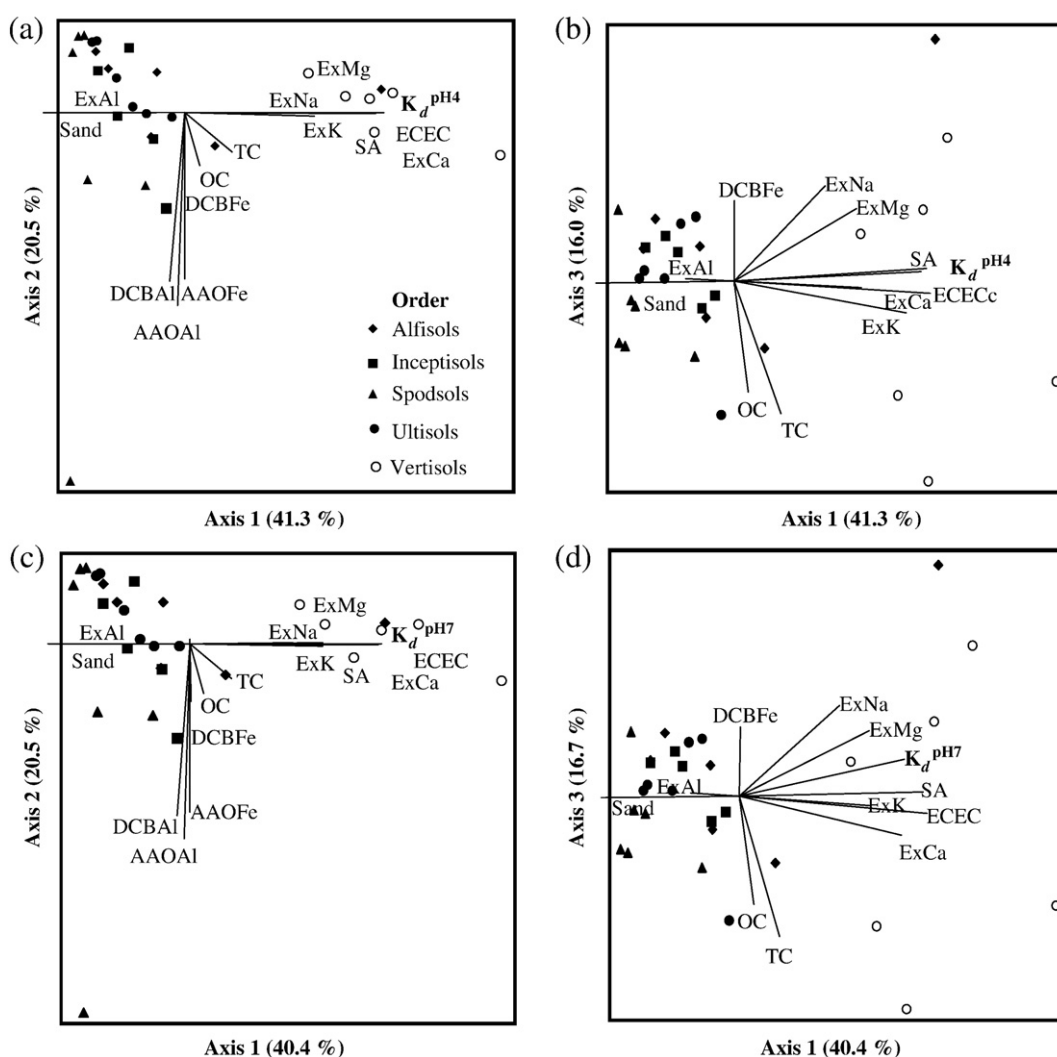


Fig. 3. Principal component analysis of soil properties and sorption ( $K_d$ ) (a) pH 4 – axis 1 vs. axis 2, (b) pH 4 – axis 1 vs. axis 3, (c) pH 7 – axis 1 vs. axis 2 and (d) pH 7 – axis 1 vs. axis 3.

strongly on axis 1 (positive loading: SA, ECEC, ExCa, ExMg, ExK, ExNa; negative loading: %sand), soil aluminum and iron oxide content on axis 2 (positive loading: AAOFe, AAOAl, DCBFe, DCBAI), and descriptors of organic carbon content, along with select descriptors of exchange capacity and iron oxide content on axis 3 (negative loading: DCBFe, Ex Mg, ExNa; positive loading: TC, OC) (Fig. 3). The position and loading of ciprofloxacin  $K_d$  in ordination space with respect to the texture/exchange capacity (axis 1) and aluminum and iron oxide gradient (axis 2) were almost identical at all pHs, with  $K_d$  loading along (strongly) axis 1 and orthogonal (weakly) to axis 2 (Fig. 3a, c). For example,  $K_d^{pH4}$  and  $K_d^{pH7}$  loaded strongly on the texture/exchange capacity axis (positive loadings of +0.38 and +0.35, respectively) and weakly on the aluminum and iron oxide gradient (−0.03 and +0.0006, respectively). Important differences were noted in  $K_d$  loadings on axis 3 (Fig. 3b, d) with change in pH.  $K_d^{pH4}$  showed a small negative loading (−0.14) on axis 3 corresponding to the position and loading of DCBFe (−0.37) on that axis whereas a higher negative loading (−0.25) was noted for  $K_d^{pH7}$ . Finally,  $K_d$  loaded negatively on axis 3, whereas %OC loaded positively, suggesting little influence of % OC on  $K_d$ . Together, these observations pointed to the strong correlation between  $K_d$  and texture/exchange capacity at all pH values and a moderate correlation between  $K_d$  and DCBFe at higher pH.

Relationships between log  $K_d$  and the three selected soil properties (log ECEC, log DCBAI + Fe, log OC), as determined by MSR, were highly significant for all five pH values ( $p < 0.05$ ) and explained between 77 and 90% of the variance in the data (Table 2). The best  $R^2$  and highest  $F$  values were obtained at lower pH, suggesting greater statistical robustness at these pH values. Consistent with the results of PCA, MSR analyses found that log ECEC was the most important independent variable (highest beta coefficient: 1.63–0.52) for the log  $K_d$  regression equation at all pH values (Table 2). In addition, the beta coefficient of the log ECEC variable decreased steadily with pH, consistent with a coincident decrease in the extent of ciprofloxacin sorption with pH (Fig. 2). Soil metal oxide content, represented by the variable log DCBAI + Fe, was significant in the log  $K_d$  regression equations at pH 5.5, 7, and 8. The beta value for this parameter was always positive and relatively constant (0.23–0.26) but lower than the beta value for log ECEC, suggesting that metal oxides provided a moderate and constant contribution to ciprofloxacin sorption between pH 5.5 and 8. Soil organic carbon content (log OC) was a significant parameter in the log  $K_d$  regression equations at pH 3, 4, and 8, with log OC possessing a negative beta coefficient at pH 3 and 4 (−0.26 and −0.25, respectively) and a positive beta coefficient at pH 8 (+0.11) (Table 2). Finally, the y-intercept in the regression was fairly constant (2.11–1.77) with change in pH and indicated  $K_d$  values between 59 and 129 L/kg for a “theoretical” soil with little to no ECEC, OC, or metal oxide content. Notably, similar  $K_d$  values (30–75 L/kg) were found for

norfloxacin sorption to aquifer material, comprised primarily of quartz sand (Hari et al., 2005).

## 4. Discussion and conclusions

### 4.1. Soil factors influencing ciprofloxacin sorption

Soil cation exchange capacity appeared to be the soil factor with the greatest influence on the magnitude of the sorption coefficient,  $K_d$ , at all pH values examined. The strong loading of  $K_d$  along the ECEC/texture axis in principal component ordination space at all pH values (Fig. 3), along with the highest beta coefficient for log ECEC in the MSRs (Table 2), emphasized soil ECEC as an important predictor of the pH-dependent  $K_d$ . In addition, the alignment of  $K_d$  values in relation to DCBFe in principal component ordination space and the significance of DCBAI + Fe as a predictor variable at pH ≥ 5.5 in the MSRs (Table 2) pointed to the smaller but notable influence of soil metal oxide content on  $K_d$  at higher pH values.

Our efforts to test a subset of our soils to examine whether or not the use of ECEC instead of CEC biased our statistical results (Supplemental information, Fig. S1) pointed to limited changes in CEC as a function of pH for soils with OC < 2% and DCBFe + Al < 454 mmol/kg. An increase in CEC with an increase in pH was only noted for soils with significant domains of pH-dependent charge — OC ≥ 3.9% and/or DCBAI + Fe between 850–899 mmol/kg. Extrapolations of these findings suggested that 7 of our 30 test soils were likely to possess significant domains of pH-dependent charge, and that, for these soils, the use of ECEC may have resulted in an underestimation of CEC in sorption experiments conducted at pH > pH<sub>w</sub> and an overestimation of CEC in experiments conducted at pH < pH<sub>w</sub>. All the same, we find that the use of ECEC (instead of CEC) did not bias interpretation of statistical results in over 80% of our experiments. Therefore, we find that ECEC and DCBAI + Fe are important predictors of the pH-dependent sorption coefficient of ciprofloxacin for soils without significant domains of pH-dependent charge, whereas CEC may be a more appropriate predictor in soils with high OC content (>4%) and/or high DCBAI + Fe values (>850 mmol/kg).

The influence of soil organic carbon content on ciprofloxacin sorption was not clearly evident from our statistical analyses. First, the position and loading of  $K_d$  and %OC in ordination space (Fig. 3) pointed to a lack of correlation between the two variables. Second, the presence of log OC in the MSR at pH 3, 4, and 8 and the absence at pH 5.5 and 7 could not be rationalized. As mentioned earlier, %OC and DCBAI + Fe are indirect measures of a small component of the CEC and contribute to the possible double counting of the influence soil's CEC on the extent of sorption. Hence, for compounds that sorb primarily via cation exchange, the simultaneous use of ECEC/CEC, DCBAI + Fe, and %OC as predictors of the pH-dependent sorption coefficient requires caution.

Mechanistic information may be surmised from the above-noted influence of cation exchange capacity and soil metal oxide content on the magnitude of  $K_d$ . The primary role of ECEC in defining the magnitude of the  $K_d$  at all pH values points to the likelihood that cation exchange and/or cation bridging, mechanisms dependent on the availability of cation exchange sites, were key interaction processes in soil systems. In addition, relationship between  $K_d$  and soil metal oxide context, indicated the possibility of a small contribution from surface complexation (a process dependent on the availability of surface bound aluminum and iron ions) to the net extent of sorption at higher pH (pH ≥ 5.5). The lack of a clear influence of organic carbon content on  $K_d$  is consistent with knowledge that hydrophobic partitioning is not likely to drive the sorption of charged antibiotic molecules (Tolls, 2001) and with the fact that the interaction with negatively charged sites on organic matter is accounted for by soil ECEC. Individual contributions from the cation exchange, cation bridging, and surface complexation to the observed extents of sorption are considered below.

**Table 2**  
Results from multiple stepwise regression.

pH	Equation	p value	Multiple $R^2$	F-statistic
3	$\log K_d^{pH3} = 2.01 + 1.63 * \log ECEC - 0.26 * \log OC$	$1.88 \times 10^{-13}$	0.89	110.8
4	$\log K_d^{pH4} = 2.11 + 1.48 * \log ECEC - 0.25 * \log OC$	$1.43 \times 10^{-13}$	0.90	113.5
5.5	$\log K_d^{pH5.5} = 1.97 + 1.18 * \log ECEC + 0.26 * \log (DCBAI + Fe)$	$3.95 \times 10^{-12}$	0.87	85.0
7	$\log K_d^{pH7} = 1.90 + 0.68 * \log ECEC + 0.29 * \log (DCBAI + Fe)$	$1.99 \times 10^{-9}$	0.79	48.0
8	$\log K_d^{pH8} = 1.77 + 0.52 * \log ECEC + 0.23 * \log (DCBAI + Fe) + 0.11 * \log OC$	$3.88 \times 10^{-8}$	0.77	27.9

Units:  $K_d$ : L/kg; ECEC: cmol<sub>c</sub>/kg; logDCBAI + Fe: mmol/kg; OC: %.



#### 4.2. Mechanisms of ciprofloxacin sorption in soil systems

As mentioned earlier, we used an indirect approach to obtain mechanistic insights and relied on the comparison of the observed pH-dependent sorption in 30 soils (Fig. 2) to a hypothesized pH-dependent sorption behavior in soil systems (Introduction, Fig. 1 and Supplemental information), and on the consideration of soil factors found to influence sorption. The small group of seven soils, exhibiting “pH edge 1”, did not conform to the hypothesized pH-dependent sorption behavior (Fig. 1 vs. Fig. 2a) and exhibited a greater potential for cation sorption (Table 1). This group of soils possessed a significantly higher ( $p < 0.05$ , two-tailed  $t$ -test assuming unequal variances) average ECEC value (mean: 34.6 cmol<sub>c</sub>/kg; standard error (SE): 4.6) than the other 23 soils (mean: 4.05 cmol<sub>c</sub>/kg, SE: 0.6). Furthermore, these soil systems were not limited by the availability of cation exchange sites but by the number of ciprofloxacin cations and zwitterions available to participate in the cation exchange process. For our experimental conditions, a reactor containing a soil with an ECEC of 20 cmol<sub>c</sub>/kg had  $2 \times 10^{-3}$  mmol of charge and  $5 \times 10^{-4}$  mmol of ciprofloxacin; as such, soil negative charge was typically an order of magnitude greater than the mass of ciprofloxacin cations and zwitterions. Therefore, even an increase in soil negative charge (CEC) with pH, expected to occur in soils with significant domains of pH-dependent charge, would not have appreciably enhanced the long range electrostatic attraction that facilitates the extent of cation exchange, as previously hypothesized. Instead, the general decrease in sorption with pH simply mirrored the decrease in aqueous cation concentrations (Fig. 1) and emphasized that the net neutral zwitterion (dominant at pH > 6) had a lower potential for cation exchange than the ciprofloxacin cation. Furthermore, the greater extent of cation sorption ( $K_d^{pH4} > K_d^{pH7}$ ) and the lack of maximum sorption at  $pH \approx pK_{a1}$  (when the zwitterion concentration is prominent) emphasized that contributions from cation bridging and surface complexation did not offset the lower cation exchange potential of the zwitterion or play a significant role in the observed extent of sorption, as previously hypothesized. Hence, in soils not limited by cation exchange sites, cation exchange appeared to be the dominant mechanism of interaction, with additional contributions from cation bridging and surface complexation being either unimportant or not discernable.

Sorption profiles of the remaining 23 soils, which exhibited the hypothesized pH-dependent sorption behavior (Fig. 1 vs. Fig. 2b,c), pointed to the importance of cation exchange, cation bridging and surface complexation as likely sorption mechanisms. These soils possessed lower cation exchange capacities (ECEC < 20 cmol<sub>c</sub>/kg), limited surface site availability for cation exchange (mmol charge ≤ mmol of ciprofloxacin), and exhibited cation sorption ≤ zwitterion sorption ( $K_d^{pH4} \leq K_d^{pH7}$ ) (Table 1). As hypothesized, the observed increase in sorption with an increase in pH, between pH 3 and 5.5, may be attributed to the increased attractive force and surface site availability for cation exchange and the increased favorability for sorption via surface complexation (Supplemental information). At higher pH (pH > 5.5), the lower cation exchange potential of the zwitterion (as compared to the cation) was likely offset by significant contributions from cation bridging and/or surface complexation to the observed extent of sorption.

A substantial contribution from surface complexation to the observed extent of sorption could be surmised from the group of 10 soils exhibiting greater zwitterion sorption ( $K_d^{pH4} < K_d^{pH7}$ ) (Table 1). This group of soils was distinguished from the remaining 20 soils by a significantly higher ( $p < 0.05$ , two-tailed  $t$ -test, unequal variances) average DCBAI + Fe value (mean: 450 mmol/kg; SE: 81) than the other soils (mean: 224 mmol/kg; SE: 34). Furthermore, the average ECEC of this group of soils (mean: 3.9 cmol<sub>c</sub>/kg; SE: 0.8) was significantly lower than the group of soils exhibiting greater cation sorption ( $K_d^{pH4} > K_d^{pH7}$ ). Therefore, it is likely that the higher aluminum and iron oxide content of these soils afforded greater surface site availability for surface complexation and, hence, an appreci-

able contribution from surface complexation to the net extent of zwitterion ion sorption.

Contributions from cation bridging could not be isolated in this study because there was no soil factor or pH window unique to the cation bridging process; soil ECEC determined the site availability for both cation exchange and cation bridging, while cation bridging and surface complexation were both dominant in a similar pH window. As such, the contribution of cation bridging to the extent of sorption could not be excluded, despite the lack of substantial evidence for this process within the soil systems examined.

This work has addressed the two gaps in mechanistic understanding of ciprofloxacin sorption in soil systems identified in the introductory section. First, we have found that the pH-dependent sorption or the distinct shape of the pH edge is governed by surface site availability for cation exchange (cation exchange capacity) and surface complexation (metal oxide content). Second, it appeared that cation exchange, cation bridging and surface complexation mechanisms all contribute to the net extent of ciprofloxacin sorption to soils. The contribution from an individual sorption mechanism could only be identified for soils with appreciably “high” ECEC or metal oxide contents. Cation exchange was found to be the dominant mechanism of sorption in soils not limited by the availability of cation exchange sites, whereas the importance of contributions from surface complexation to the net extent of sorption was discerned only at high pH values in metal oxide-rich soils, possessing low cation exchange capacities. Nevertheless, the fluoroquinolone molecule appeared to be better suited for cation exchange (via the cationic amine) than for cation bridging or surface complexation (via the carboxyl group on the zwitterion). The importance of sorption via cation exchange was particularly evident in soils such as the Iredell (Fig. 2a), which possessed “high” surface site availability for both cation exchange (ECEC: 21.4 cmol<sub>c</sub>/kg) and surface complexation (DCBAI + Fe: 453.5 mmol/kg, similar to the average value for the group with “high” metal oxide content) (Table S1, Supplemental information) but exhibited a decrease in sorption with an increase in pH (pH edge 1). If all three interaction mechanisms were equally favorable, the decreased cation exchange potential of the ciprofloxacin zwitterion would have been offset by an increased potential for cation bridging and/or surface complexation.

#### 4.3. Significance to solute transport in soil systems

Results from this study revealed that ciprofloxacin transport is likely to be retarded in most soil and groundwater systems over a wide pH range. Greatest retardation is expected in high CEC soils, such as Vertisols, particularly if the availability of cation exchange sites exceeds the availability of ciprofloxacin. In these soils, higher retardation is expected in acidic soils or soils subject to acid input, while lower retardation is expected in alkaline soils, particularly those impacted by liming. In soils with moderate cation exchange capacity, greatest retardation is expected between pH 5 and 6 and lower retardation at alkaline pH values. Notably, this study clearly illustrated that the pH-dependent speciation of amphoteric solutes, such as ciprofloxacin, influenced the nature (mechanism) and extent of sorption. The approaches used in this study provide methods for gaining mechanistic insight into the sorption behavior of other amphoteric veterinary antibiotics and emerging contaminants similar in structure to ciprofloxacin.

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## Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at [doi:10.1016/j.geoderma.2009.03.007](https://doi.org/10.1016/j.geoderma.2009.03.007).

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