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ORGANIC COMPOUNDS IN THE ENVIRONMENT

Sorption/Desorption of Lincomycin from Three Arid-Region Soils

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The antibiotic lincomycin is commonly found in treated municipal waste water and in waste from swine and poultry production. Environmental disposal of these wastes has the potential to introduce a significant mass of lincomycin into the ecosystem. In the present study, a series of sorption and desorption experiments were conducted to determine the potential mobility of lincomycin in soils from arid environments. Sorption and desorption isotherms were obtained for lincomycin using three different soils. Isotherms were fit to the Freundlich equation. Adsorption of lincomycin was found to have a K_f of 11.98 for a biosolid-treated soil (1.58% OC) and a K_f of 210.15 for a similar unamended soil (1.42% OC). It was also found that for a low-organic-content soil the K_f was 5.09. The differences in adsorption can be related to the soil pH and the pKa of lincomycin (7.5–7.8). When the soil solution pH is below the pKa, the cationic species of lincomycin dominates, resulting in increased water solubility. Interaction with the cation exchange complex is minimal due to a high solution cation concentration (Ca^{2+} and Na^{+}). Desorption isotherms also indicate that when the solution pH is lower than the pKa, retention of lincomycin is reduced. Our results indicate that the mobility of lincomycin in these arid region soils is dependent on soil pH.

In the arid southwestern United States, the reuse of wastewater is often seen as a valuable water resource. Treated effluent can be reclaimed via recharge, irrigation, or release into surface waters for recapture and reuse downstream. Recently the presence of pharmaceutically active compounds at very low levels in treated effluent has gained the interest of regulators and municipal water providers. This increased scrutiny is due mainly to increased analytical capabilities to detect the compounds where they were previously not detected and the potentially unknown effects of these compounds on the environment and human health. The ability to detect and quantify these compounds at environmentally significant concentrations became widely available at the end of the last century (Jorgensen and Halling-Sorensen, 2000). Some of the earliest reports of finding pharmaceutically active compounds in the environment occurred in the early 1980s (Halling-Sørensen et al., 1998). More recently, the detection of numerous pharmaceutically active compounds in environmental samples has become commonplace (Kolpin et al., 2002; Ternes, 1998, 2001).

Antibiotics are a class of pharmaceutically active compounds that pose a threat to human health when found in the environment due to the potential development of antibiotic resistance (Chee-Sanford et al., 2009). Two main pathways by which antibiotics can enter the environment are land application of animal wastes and discharge of treated sewage effluent. Antibiotics are commonly added to animal feed as a prophylactic to prevent the spread of disease and to increase weight gain in livestock (Boxall et al., 2003). Administered antibiotics are only partially metabolized, resulting in relatively high concentrations in manure (Kumar et al., 2005). It is estimated that typical antibiotic concentration of manure ranges from 1 to 10 mg kg^{-1} (Kumar et al., 2005). In 2005 it was estimated that more than 200 t of manure was generated and applied to agricultural land (Aillery et al., 2005), resulting in an annual environmental loading rate of 130 to 1300 t. Karthikeyan and Meyer (2006) found that a number of antibiotics were present in the effluent from wastewater treatment plants. They found that typical effluent concentrations were 100 to 1000 ng L^{-1}. For perspective, the per capita sewage production in the United States is approximately

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Abbreviations: CEC, cation exchange capacity; SPE, solid phase extraction.

380 L d^{-1}; a population of 300 million people would result in annual environmental loading of between 4 and 40 t of each compound. In addition to treated wastewater, antibiotics can enter the environment from the application of animal manures. Combined, a conservative estimate for antibiotic release into the environment would be between 100 and 1000 t yr^{-1}.

Lincomycin [(2S-trans)-Methyl 6,8-dideoxy-6-[[(1-methyl-4-propyl-2-pyrrolidinyl)carbonyl]amino]-1-thio-D-erythro-α-D-galacto-octopyranoside] is an antibiotic commonly found in treated municipal waste water and in livestock manures (Boxall et al., 2003; Brown et al., 2006; Campagnolo et al., 2002; Karthikeyan and Meyer, 2006; Kuchta and Cessna, 2009a). Lincomycin was discovered in the 1950s from a screen of soil organisms originating from near Lincoln, Nebraska (Hornish et al., 1987). The structure was determined to be a derivative of an amino acid and a methylthio containing octose (Hoeksema et al., 1964). Lincomycin is very effective at controlling most anaerobes and most gram-positive organisms (Kaplan et al., 1965; Phillips, 1981) by blocking protein synthesis through inhibition of the peptidyltransferase reaction (Spížek and Řezanka, 2004). This is a common mode of antimicrobial action, and thus the development of cross resistance to other antibiotics is possible (Spížek and Řezanka, 2004).

Lincomycin has been found to enter the environment as a result of human and veterinary use. Brown et al. (2006) found that lincomycin was present in the sewage from two of five hospitals sampled in Albuquerque, New Mexico. Composited samples were taken from the sewage leaving the hospitals over a 26-d period. The concentration was 2000 ng L^{-1} from one hospital and 300 ng L^{-1} from the other. Lincomycin was not detected in the three other hospitals sampled. In Australia it was found that the concentration of lincomycin in the effluent from an activated sludge wastewater treatment plant averaged 50 ng L^{-1}, and lincomycin was detected in every sample (Watkinson et al., 2007). It was also found that only 11% of the lincomycin was removed through the treatment process. Treated effluent was then passed through a microfiltration/reverse osmosis treatment system, and lincomycin was detected in 66% of the product water samples with an average concentration of 1 ng L^{-1}.

Antimicrobials are commonly used in swine production for the control of dysentery in recently weaned piglets, which leads to increased weight gain (Dewey et al., 1999; Dunlop et al., 1998). Kuchta and Cessna (2009a) found that approximately 1.2% of administered lincomycin was excreted and present in manure. They also found that the swine manure had a lincomycin concentration between 25.1×10^6 and 38.5×10^6 ng L^{-1}. Lincomycin is registered for use in swine and poultry production throughout most of the world, including the United States, Canada, the European Union, Australia, Africa, and New Zealand (Sarmah et al., 2006). Manures are commonly collected and applied to adjacent crop lands as a fertilizer and soil amendment (Hoff et al., 1981; Liao et al., 1995), resulting in the addition of antimicrobials, including lincomycin, to the soil where there is the potential for leaching to groundwater or movement to surface waters through runoff.

A number of studies have confirmed that lincomycin is capable of leaching to groundwater as well as overland movement to surface waters associated with runoff (Campagnolo et al. 2002; Kuchta and Cessna, 2009b). The objective of this study was to determine distribution coefficients of lincomycin to arid region soils that receive reclaimed municipal wastewater. A series of batch equilibrium studies from three different arid-region soils used for the disposal of treated sewage effluent were used to determine the sorption coefficients of lincomycin.

Materials and Methods

The hydrochloride salt lincomycin [(2S,4R)-N-[(1R,2R)-2-hydroxy-1-[(2R,3R,4S,5R,6R)-3,4,5-trihydroxy-6-methylsulfanyloxan-2-yl]propyl]-1-methyl-4-propylpyrrolidine-2-carboxamide hydrate hydrochloride] (Fig. 1) was purchased from MP Biomedicals with a purity of 90%. Lincomycin is a white crystalline powder with a molecular weight of 443, a pKa of 7.6, a melting point of 156 to 158°C, and a water solubility of 50 mg mL^{-1}.

Soils were chosen for the experiment with different organic matter content and composition. The first soil was a low-organic-matter Casa Grande clay loam (Typic Natrargid) from Pinal County, Arizona (Casa Grande). The second soil was a higher-organic-matter Airport silt loam (Aquic Natrixeroll) from Davis County, Utah that had received biannual biosolid amendments (Airport-T) of 137 Mg (dry wt.) ha^{-1} for 8 yr. The third soil was also an Airport silt loam taken adjacent to the biosolid-amended field that had never had biosolids applied (Airport-UT). Soils were collected from the top 10 cm, air dried, and sieved to 2.0 mm, and some of their physical properties measured by standard techniques (Table 1).

Texture was determined using the hydrometer method (Gee and Bauder, 1986). Total organic carbon was determined using a Shimadzu TOC-V total organic carbon analyzer with a solid sample module. Organic matter was oxidized in an oxygen stream at 950°C, and CO_2 was analyzed using an infrared detector. Electrical conductivity and pH were measured using saturated paste extracts, and cation exchange capacity (CEC) was measured using standard sodium acetate methods (Polemio and Rhoades, 1977).

Sorption isotherms were determined on all three soils using batch equilibrium. Adsorption was determined by preparing lincomycin solutions of 50, 37.5, 25.0, 12.5, and 5.0 μg L^{-1} in a water solution made by adding NaCl (0.201 g L^{-1}) and $CaCl_2$ (0.355 g L^{-1}) to 18 MΩ water to create an electrical conductivity of 1 dS m^{-1} and a sodium adsorption ratio of 2. Unless otherwise

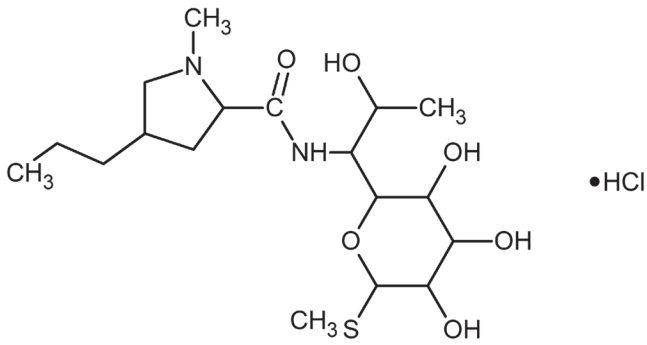

Fig. 1. Molecular structure of the hydrochloride salt of lincomycin [(2S,4R)-N-[(1R,2R)-2-hydroxy-1-[(2R,3R,4S,5R,6R)-3,4,5-trihydroxy-6-methylsulfanyloxan-2-yl]propyl]-1-methyl-4-propylpyrrolidine-2-carboxamide hydrate hydrochloride].

stated, this water was used in all studies reported herein. Lincomycin sorption was performed by placing 20 mL of each lincomycin solution in 50-mL Teflon centrifuge tubes containing 5 g soil. Each treatment was replicated three times. Centrifuge tubes were shaken for 24 h at 17°C and centrifuged for 15 min at 2000 × *g*, and 10 mL of supernatant was removed for analysis.

Desorption was determined by adding 10 mL of lincomycin-free water to the tubes containing the soil and the remaining solution from the adsorption experiments. Centrifuge tubes were shaken for 24 h at 17°C and centrifuged for 15 min at 2000 × *g*, and 10 mL of the supernatant was removed for analysis. The removed supernatant was again replaced with lincomycin-free water, and the equilibration processes were repeated for a total of two desorption events. Two desorption isotherms (DS1 and DS2) were determined from two sequential desorption events.

Solid phase extraction (SPE) was used for sample concentration and clean up before analysis. Oasis HLB (Waters Co.) SPE cartridges were preconditioned with two successive washes of 3 mL MeOH and two washes with 3 mL nano-pure water. Cartridges were loaded with 10 mL of supernatant followed by drying for 10 min. Lincomycin was eluted using two successive 2-mL aliquots of MeOH. Samples were evaporated to dryness and reconstituted in 0.1 mL of MeOH mixed, and an additional 0.9 mL of nano-pure water was added for a total volume of 1.0 mL.

Soils were analyzed using pressurized solvent extraction for background lincomycin and adsorbed lincomycin after the final desorption step for mass balance. Ten grams of soil was mixed thoroughly with 2 g diatomaceous earth in an extraction cell. Extraction was performed using accelerated solvent extraction (ASE 300, Dionex) with 25% MeOH and 75% nanopure water at 100°C. The cells were initially heated for 5 min, followed by three 5-min static cycles, a 60% volume flush, and a 100-s purge. Extract solutions were then diluted to 400 mL with nano-pure water to reduce the organic solvent fraction to less than 5% (v/v). The resulting solution underwent SPE using Strata-X (Phenomenex). Cartridges were preconditioned with two successive washes of 3 mL MeOH and two washes with 3 mL nano-pure water. Cartridges were loaded with 400 mL of diluted extract solution followed by drying for 10 min. Lincomycin was eluted using two successive 2-mL aliquots of MeOH. Samples were evaporated to dryness and reconstituted in 0.1 mL of MeOH and mixed, and an additional 0.9 mL of nano-pure water was added for a total volume of 1.0 mL.

Table 1. Physical properties of soils used to determine lincomycin sorption characteristics.

Soil characteristic	Airport-UT†	Airport-T‡	Casa Grande§
pH¶	7.8	7.3	7.3
EC,# dS m^{-1}¶	0.49	1.48	2.5
Sand, g 100 g^{-1}	43	39	63
Silt, g 100 g^{-1}	32.5	32	14.5
Clay, g 100 g^{-1}	24.5	29	22.5
Organic C, g 100 g^{-1}	1.42	1.58	0.29
CEC,†† cmol(+) 100 g^{-1}	12.3	13.1	11.4

† Airport silt loam.

‡ Airport silt loam with biosolids added at rate of 137 Mg ha^{-1} yr^{-1}.

§ Casa Grande clay loam.

¶ Determined from saturated paste extract.

Electrical conductivity.

†† Cation exchange capacity.

Lincomycin analysis was performed using LC-MS-MS. Separation was performed using a 2.1 × 30 mm XTerra MS C_{18} column with a 2.5-μm stationary phase (Waters Co.). Operating conditions were 0.25 mL min^{-1}, with a binary mobile phase of 0.1% formic acid in acetonitrile and 0.1% formic acid in water. Initial conditions were 10:90 acetonitrile:water followed by isocratic flow for 1.5 min. At 1.5 min, a linear gradient from 10:90 acetonitrile:water to 90:10 acetonitrile:water was applied over 3.5 min followed by 1.5 min isocratic flow at 90:10 acetonitrile:water. Lincomycin was quantified using electrospray/multiple reaction monitoring of the transition 407 → 126 (m/z).

Data analysis was performed using the Freundlich equation:

$$C_S = K_F C_L^N \quad [1]$$

where C_S is the amount of lincomycin sorbed per mass of soil, C_L is the solution phase concentration of lincomycin, K_f is the adsorption coefficient, and N accounts for the degree of nonlinearity in the sorption isotherm.

Results and Discussion

Initial soil concentrations of lincomycin were below method detection limits (0.01 μg kg^{-1}). Mass recovery of applied lincomycin ranged from 87.8 to 105%, with an average recovery of 98.5%. The high recovery indicates that all lincomycin can be accounted for and that isotherms calculated from the solution phase concentration are valid. All results presented are for equilibrium sorption, and care should be taken when extrapolating results to possibly nonequilibrium situations such as might be found in actual field situations.

Adsorption isotherms for all three soils are shown in Fig. 2. Sorption was nearly 20 times greater for the Airport-UT soil than for the Airport-T soil and 40 times greater than for the Casa Grande soil. Adsorption was also more linear for the Airport-T and Casa Grande soils than for the Airport-UT soil. Typically, sorption of organics to soil is a function of organic matter content. For the Airport-T and Casa Grande soils, it appears that this relationship holds. The Airport-UT soil has a lower organic matter content than the Airport-T soil, but the Airport-UT soil exhibits much higher sorption of lincomycin than the Airport-T soil. One explanation of the difference could be a result of biosolid-derived organic matter vs. non–biosolid-derived organic matter. It has been shown that biosolid-derived organic matter can increase or decrease organic sorption to soil (Nelson et al., 2000; Williams et al., 2002) but not to the extent exhibited by lincomycin in the current work.

In addition to organic matter content differences, the three soils have slightly different hydrogen ion activity with pH ranging from 7.3 to 7.8 (Table 1). Lincomycin (Fig. 3) contains two functional groups capable of acting as a weak base and accepting a proton. The first location for protonation is the amide group, which consists of an acyl group and an amine joined by a single bond between the carbon and nitrogen. The amide in lincomycin is a conjugated system (Abraham and Smith, 1988), resulting in potential protonation of the acyl oxygen and a net positive charge (Fig. 3) at the amine nitrogen (Purkina et al., 1971). The second location for protonation is the nitrogen in the pyrrolidine

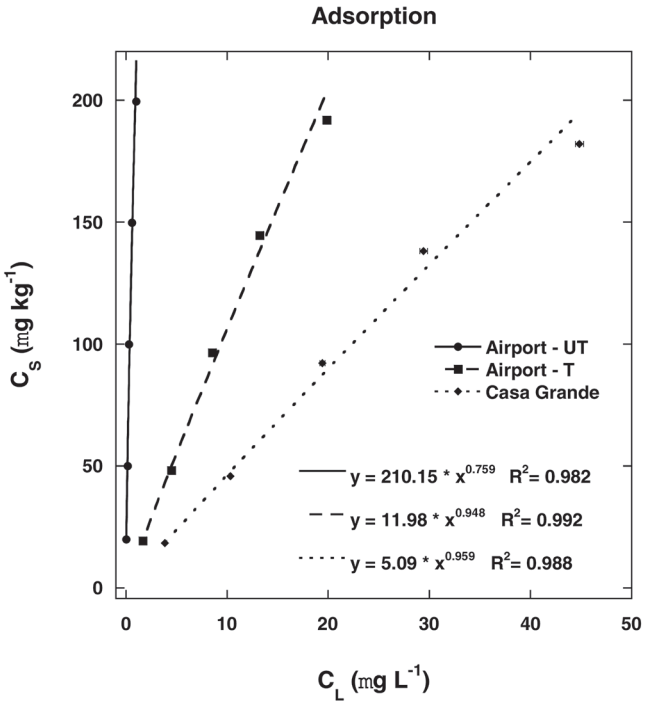

Fig. 2. Adsorption isotherm of lincomycin to an unamended Airport silt loam (Airport-UT), a biosolid-amended Airport silt loam (Airport-T), and a Casa Grande clay loam. Error bars are ±1 SEM, with some error bars smaller than the symbols. C_s is the amount of lincomycin sorbed per mass of soil, and C_L is the solution phase concentration of lincomycin.

ring (Khamidullina et al., 2005). The lone electron pair on the nitrogen can accept a proton resulting in a net positive charge (Fig. 3). Literature values for the pKa of lincomycin range from 7.5 to 7.8 (Qiang and Adams, 2004), indicating that the soils chosen had pH values near the pKa of lincomycin resulting in the presence of both the neutral and charged species. The fraction of cationic species depends on the pKa of lincomycin and the pH of the soil solution (Fig. 4). Based on initial conditions (adsorption event) of the Airport soil, the fraction of lincomycin in the cationic state ranges from 0.36 (Airport-UT with a pKa of 7.5 and a soil pH of 7.75) to 0.78 (Airport-T with a pKa of 7.8 and a soil pH of 7.25).

The cationic species of lincomycin is not expected to exhibit the same sorption phenomenon as the neutral species. The cationic species of lincomycin has a water solubility of 927 mg L^{-1} (Bhandari, 2009), whereas the solubility of the neutral form is reported as "very slightly" soluble. In soil clays, isomorphic substitution leads to a net negative surface charge capable of electrostatic interaction with solution cations. Wang et al. (2009) reported that lincomycin sorption to clays was dependent on the pH of the system. When the pH was lower than the pKa, sorption was increased due to the dominance of the cationic form of lincomycin being bound to negatively charged clay surfaces via electrostatic interactions. However, in the present study the sorption of licomycin was decreased when the pH was lower than the pKa (Fig. 2; Table 2).

The adsorption coefficient of the Airport-UT soil (pH 7.75) is 210, compared with 12 for the Airport-T soil (pH 7.25) and 5 for the Casa Grande soil (pH 7.20). At pH 7.75, the neutral species comprises between 47 and 64% (Fig. 4) of the total lincomycin in solution, whereas the fraction of neutral species for the other two soils is at most 36% of the total. This indicates a contradiction because the electrostatic interactions between negatively charged clays and the positively charged cationic species would be stronger than the non-electrostatic interactions that control the sorption of organics to soil organic matter. Two possible explanations for this are related to the ionic character of the solution from which the lincomycin was sorbed. First, Wang et al. (2009) found that the sorption of lincomycin to clays was greatly reduced by the presence of other cations in solution. They found that K_f was reduced approximately 14 times by the presence of Ca^{2+}. It was also found that the interlayer spacing of clays hydrated with Ca^{2+}

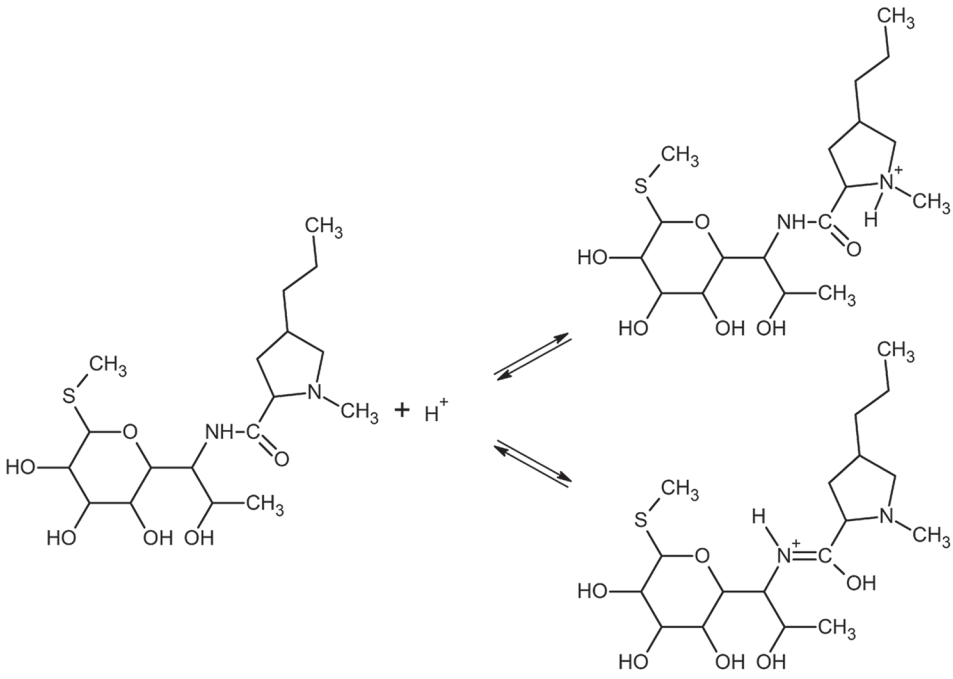

Fig. 3. Protonation of the lincomycin at the pyrrolidine ring (top) or amide group (bottom) resulting in a positive charge.

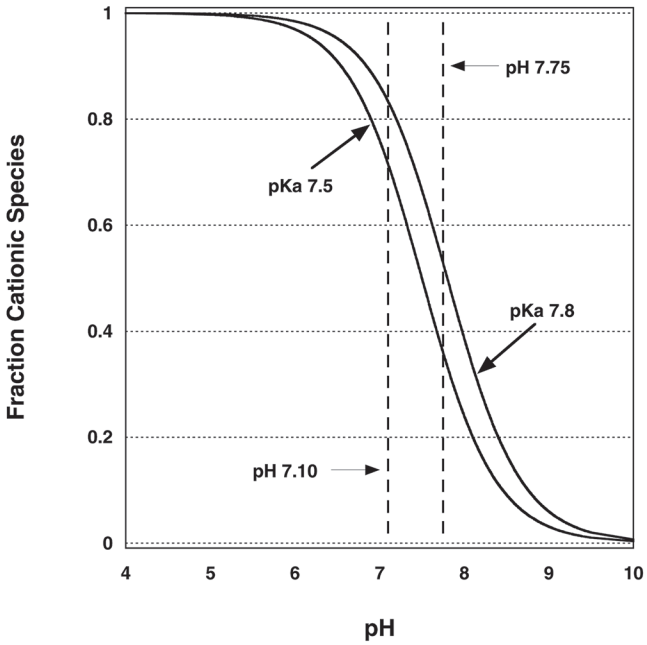

Fig. 4. Fraction of the cationic form of lincomycin from pH 4 to 10 over the range of pKa values reported in the literature. The vertical lines at pH 7.1 and 7.75 represent the highest and lowest pH observed in the adsorption or desorption solutions.

Table 2. Equilibrium solution pH of adsorption and desorption events.

	Airport-UT†	Airport-T‡	Casa Grande§
Adsorption	7.75 (0.36–0.53)¶	7.25 (0.64–0.78)	7.25 (0.64–0.78)
Desorption 1	7.50 (0.50–0.67)	7.23 (0.65–0.79)	7.21 (0.66–0.80)
Desorption 2	7.50 (0.50–0.67)	7.10 (0.72–0.83)	7.20 (0.67–0.80)

† Airport silt loam.

‡ Airport silt loam with biosolids added at rate of 137 Mg ha^{-1} yr^{-1}.

§ Casa Grande clay loam.

¶ Numbers in parentheses are the range of fractions of cationic species of lincomycin present at the specified pH and a pKa between 7.5 and 7.8.

resulted in partial dehydration of organics located within the interlayer space and a corresponding reduction in lincomycin sorption. The solutions used for sorption could lead to reduced sorption because the Ca^{2+} concentration was 3.2 mmol L^{-1} in addition to the Ca^{2+} already present in the soil.

The second possible explanation for the reduced sorption of the cationic form of lincomycin is related to the homeostasis of the reversible association of charged ions with the negatively charged CEC of the soil. The solutions used in the present study were made by adding lincomycin to water containing Ca and Na salts. The concentration of these salts on a charge basis is 100,000 times greater than the concentration of the cationic species of lincomycin. According to Le Châtelier's principle, the CEC would favor Ca^{2+} and Na^{+} in the reversible electrostatic interaction to clay surfaces, leading to the majority of the lincomycin in the Airport-T and Casa Grande soils residing in the more soluble ionic form but excluded from the cation exchange complex. Conversely, the Airport-UT soil has a pH above the pKa, and the majority of the lincomycin is in the neutral form and is subject to sorption to soil organic matter.

Sorption isotherms for the Airport-T and Casa Grande soils were generally linear, with exponent terms of 0.95 and 0.96, respectively. The Airport-UT soil had a nonlinear sorption

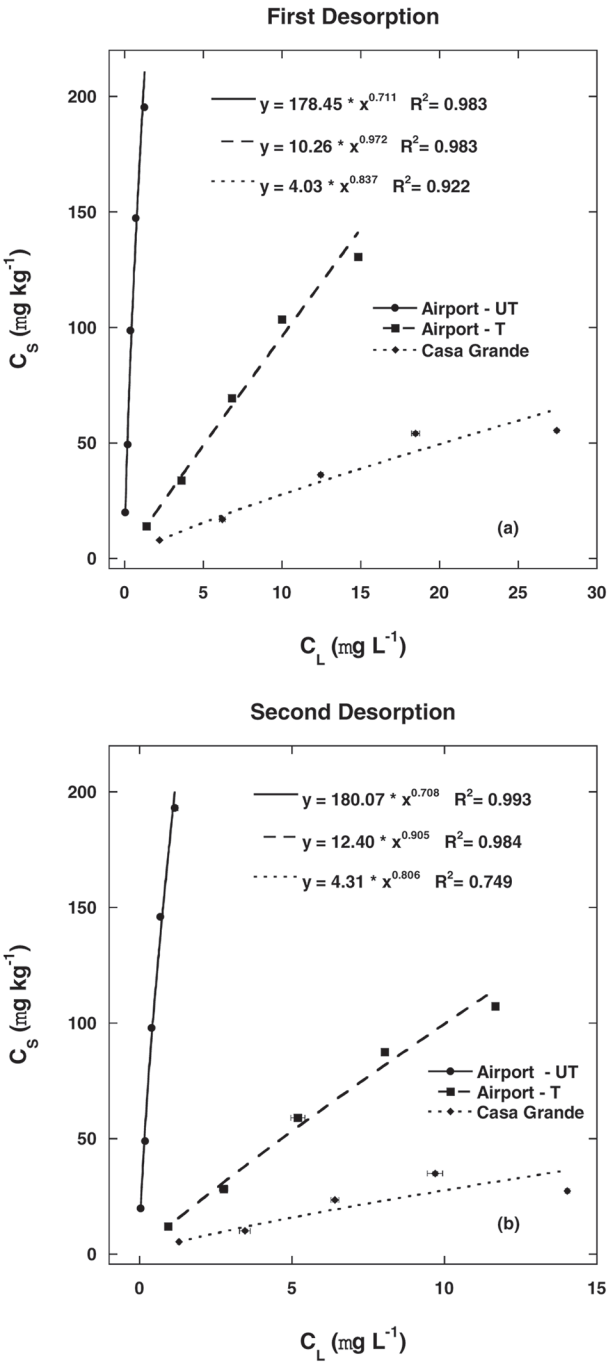

Fig. 5. (a) First and (b) second desorption isotherms of lincomycin from an unamended Airport silt loam (Airport-UT), a biosolid-amended Airport silt loam (Airport-T), and a Casa Grande clay loam. Error bars are ±1 SEM, with some error bars smaller than the symbols. C_S is the amount of lincomycin sorbed per mass of soil, and C_L is the solution phase concentration of lincomycin.

isotherm with an exponent term of 0.76. Exponent terms <1 often indicate the presence of specific binding sites (Schwartzenbach et al., 1993) such that as the sites fill, sorption capacity diminishes. This would be expected for sorption of the cationic species. However, the soils with pH below the pKa would have the greatest fraction of the cationic form of lincomycin and are the most linear, whereas the Airport-UT soil with a pH above the pKa has the lowest fraction of the cationic form and is the most nonlinear. This indicates that the sorption of the neutral lincomycin species to soil organic matter has some specificity.

Figure 5 presents the plots of the first (Fig. 5a) and second (Fig. 5b) desorption of lincomycin from the three soils. The Airport-T soil exhibited the least amount of hysteresis, whereas the Casa Grande soil had the most. Typically hysteresis leads to higher K_f for desorption than adsorption due to irreversible sorption. However, K_f for the first desorption (Fig. 5a) is lower for all three than the K_f for adsorption. The decrease in K_f can also be attributed to the presence of the cationic form of lincomycin. Solution pH from all three soils (Table 2) was lower in the first desorption event than in the corresponding adsorption event. The reduction in pH resulted in an increase in the fraction of the cationic form, which leads to increased solubility and lower sorption. By the second desorption (Fig. 5b), the solution pH did not change as much as it did from the adsorption event to the first desorption event (Table 2), and the sorption coefficients were greater for the second desorption than for the first desorption. This indicates that for situations where the fraction of the cationic form of lincomycin remains relatively constant, hysteresis resulted in the more typical increase in K_f.

Conclusions

The results of this study indicate that the sorption of lincomycin to the chosen soils was affected by the solution phase hydrogen ion concentration after equilibration. The pH of the Airport-UT system after adsorption was less than the pKa of lincomycin and resulted in ionic species that had a K_f that was reduced by a factor of 10. Conversely, when the pH was greater than the pKa of lincomycin, the K_f was much higher. This poses an elevated environmental risk in areas where treated wastewater is applied to soils with low pH. However, in many of the places where reclaimed wastewater is most needed, the soils are basic, resulting in increased sorption of lincomycin when compared with soils with lower pH.

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