

Mobility Characteristics of Azithromycin in Soil

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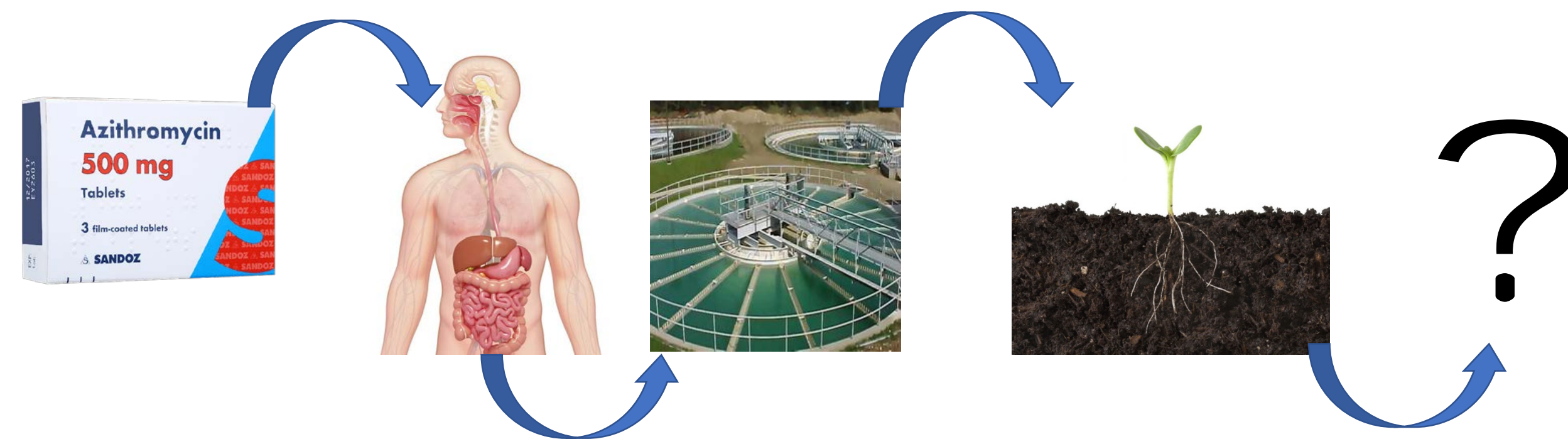
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Introduction

- Azithromycin is an ionizable macrolide antibiotic and the active ingredient in Zithromax or Zmax, prescribed heavily in human medicine.
- A significant portion of azithromycin is not broken down in the body or sewage treatment plant [1,2].
- Azithromycin can be introduced to agricultural soil through land-applied biosolids [3].
- Environmental contamination of antibiotics such as azithromycin is believed to have a detrimental effect on microorganisms [4] and humans [5].
- While data on river sediment and biosolid mobility exist, research into soil mobility must be conducted.

Fig. 1 Contamination Pathway



Method

- Contaminant mobility in soil is expressed with sorption coefficients: K_d or K_d^* (L/kg) or the nonlinear sorption parameters K_f , ($\mu\text{mol}^{(1-N)} \text{L}^N \text{kg}^{-1}$) and N (unitless).
- Cationic organic compounds, such as azithromycin, sorb to soil by forming ionic bonds to negatively-charged surfaces on soil clay and organic matter or through hydrophobic partitioning.

Fig. 2. Azithromycin ($\text{C}_{38}\text{H}_{72}\text{N}_2\text{O}_{12}$) 749 g/mol; pK_a values ≈ 8.6 & 9.5 (red-circled N); ionic sorption mechanism

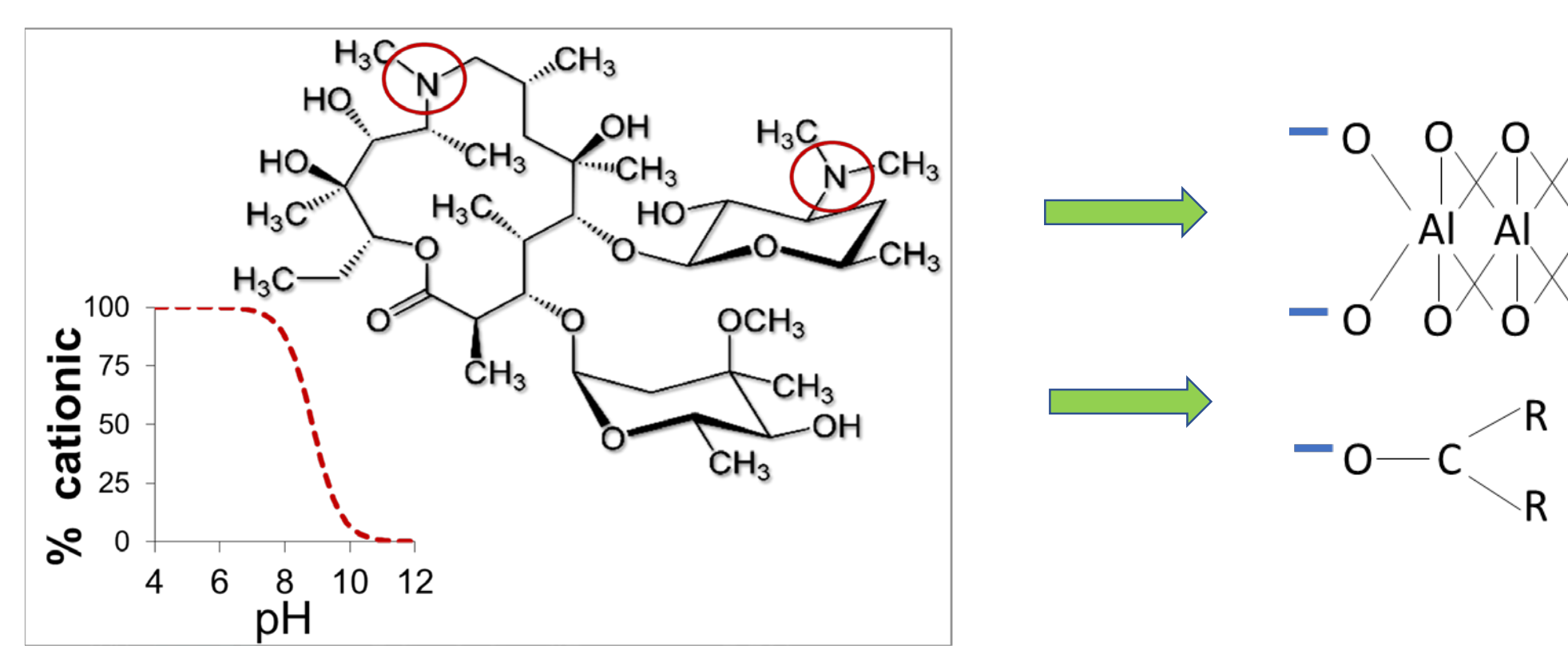


Fig. 3 Experimental Design

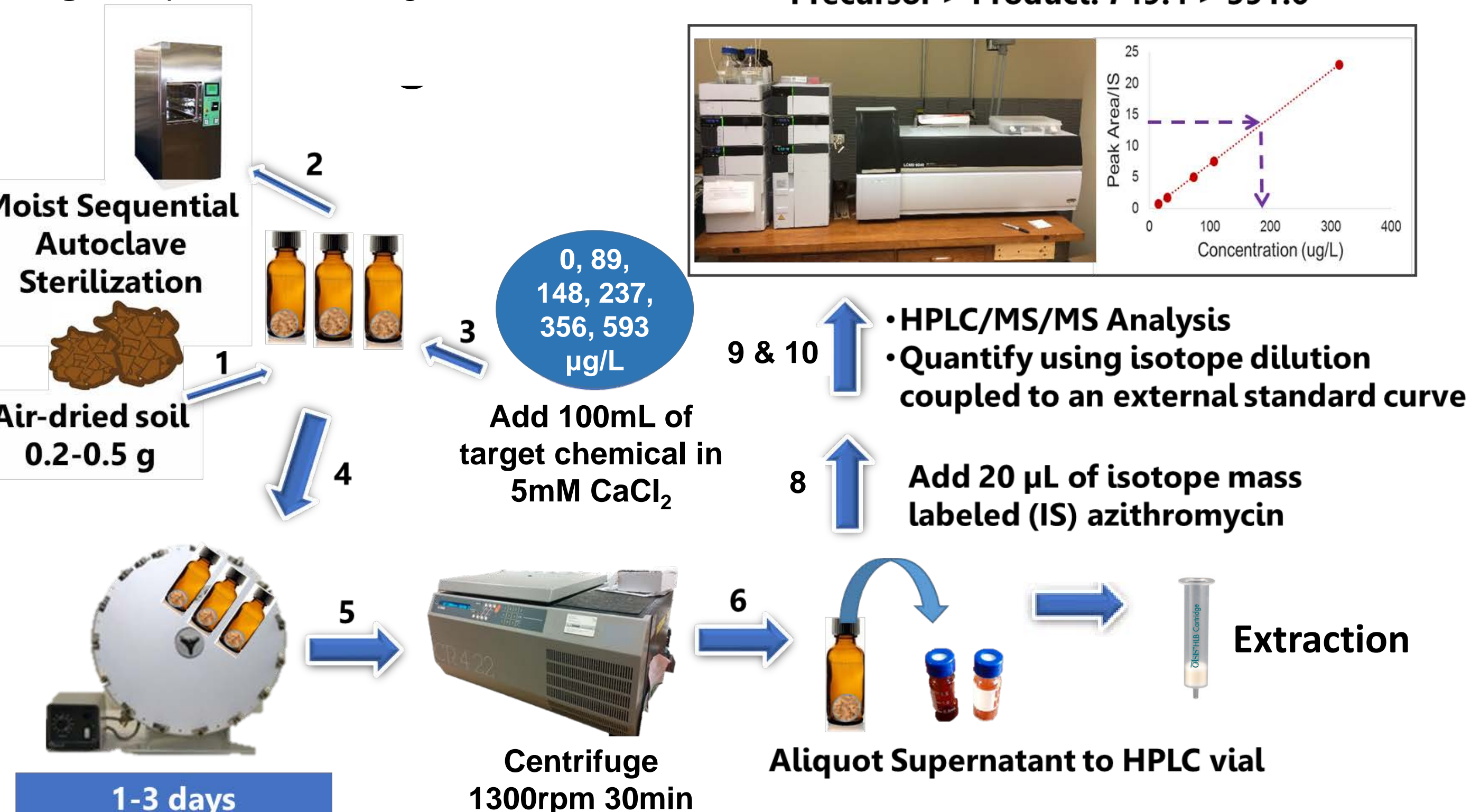


Table 1 Selected Soils

Soil	pH	Cation Exchange Capacity (CEC)	% Organic Carbon (OC)	% Clay
EPA-04	8.22	23.72	2.07	29.1
EPA-07	8.34	19.56	2.09	21.8
EPA-09	8.55	12.40	0.11	17.4
EPA-18	7.79	15.43	0.66	39.5
EPA-20	5.16	8.50	1.30	28.6
EPA-21	7.95	8.33	1.88	7.1
EPA-23	7.10	31.15	2.38	69.1
EPA-26	8.10	20.86	1.48	42.9

Results

Fig. 4 Example Linear Isotherm

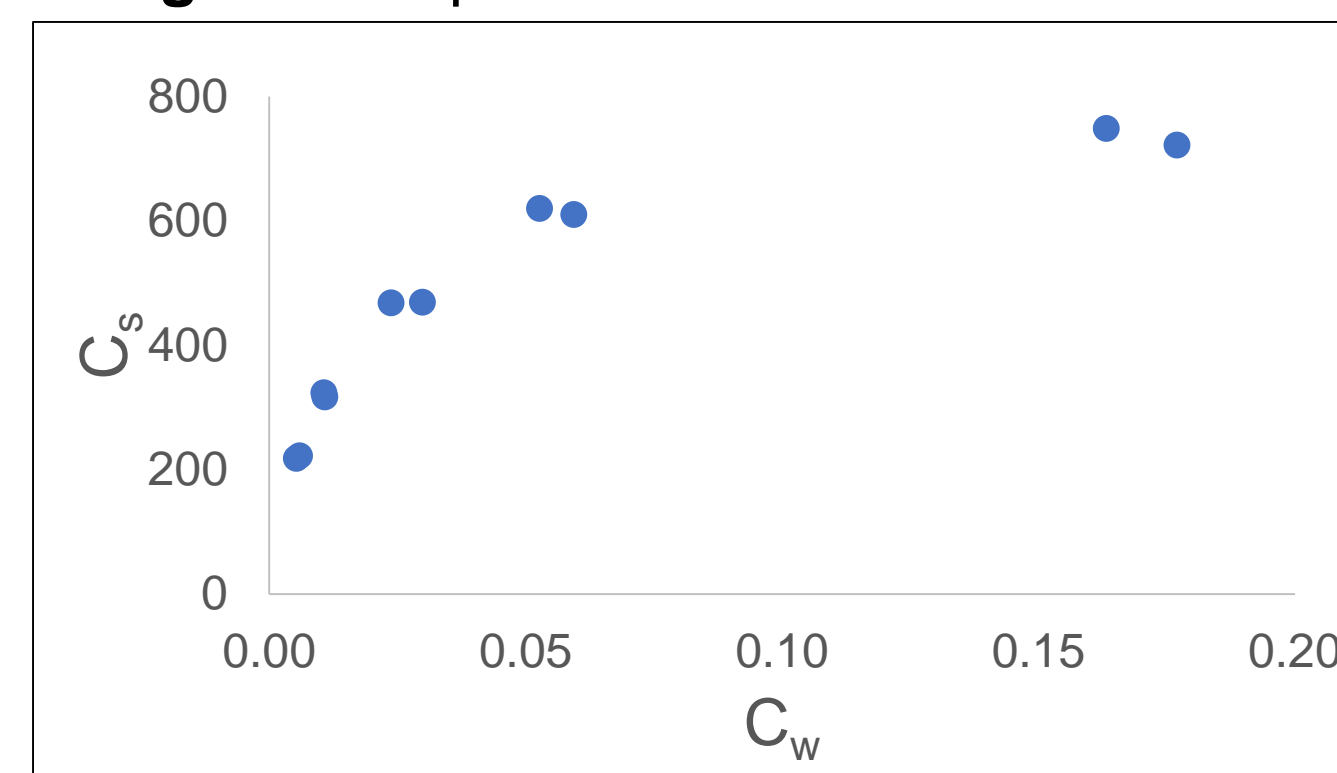
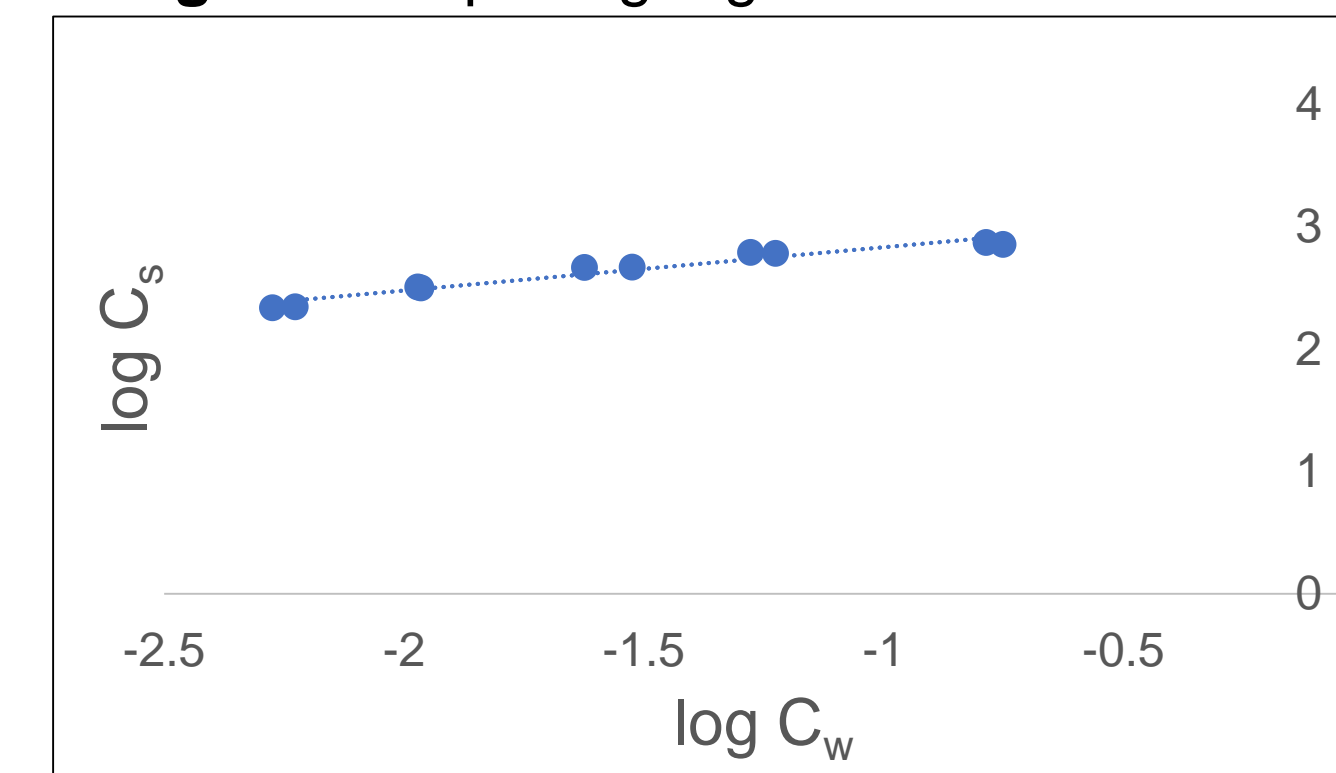


Fig. 5 Example log-log Freundlich Isotherm



- Freundlich isotherm accounts for isotherm nonlinearity by equating the trendline $y = mx + b$ to $\log(C_s) = N \log(C_w) + \log(K_f)$.
- Linear sorption values can be calculated at specific C_w values with $K_d^* = K_f * C_w^{N-1}$.

Table 2. Log K_f , N , and Log K_d^*

Soil	Log K_f	N	Log K_d^*	Soil	Log K_f	N	Log K_d^*
EPA04	3.58	0.42	4.74	EPA20	2.87	0.43	4.01
EPA07	4.83	1.04	4.75	EPA21	3.19	0.35	4.48
EPA09	4.20	0.67	4.86	EPA23	4.27	0.61	5.06
EPA18	6.86	2.14	4.58	EPA26	7.25	2.37	4.51

- K_d^* values were calculated at $C_w = 0.01 \mu\text{mol L}^{-1}$
- f_{BH^+} is the fraction of protonated base calculated by
$$f_{\text{BH}^+} = \frac{1}{1 + 10^{\text{pH} - \text{pKa}}}$$
- Soil sample information noted that EPA09 did not follow expected sorption trends in other studies for large organic molecules. ● = EPA09

Fig. 7 K_d^* vs % Clay Content

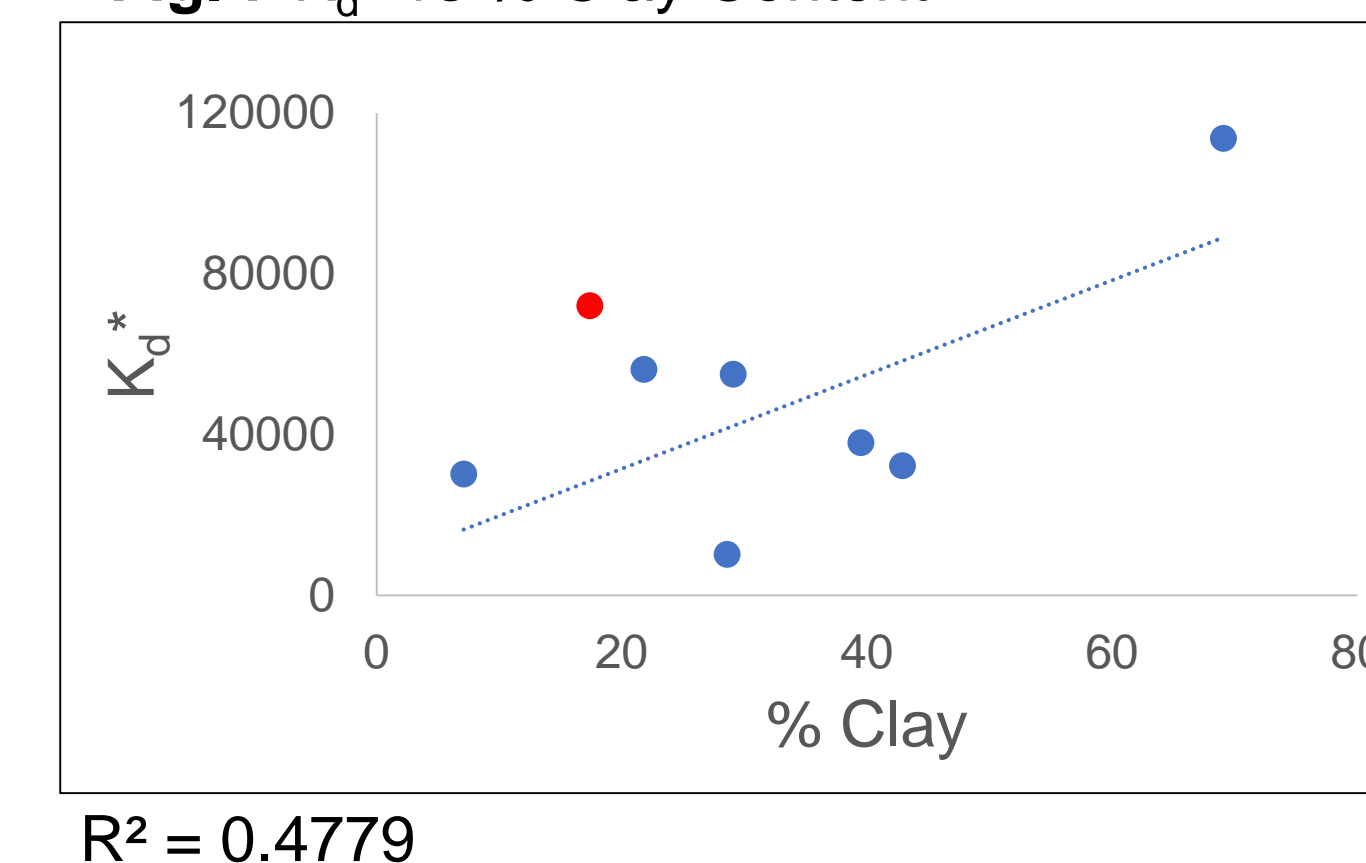


Figure 6 K_d^* vs Soil pH

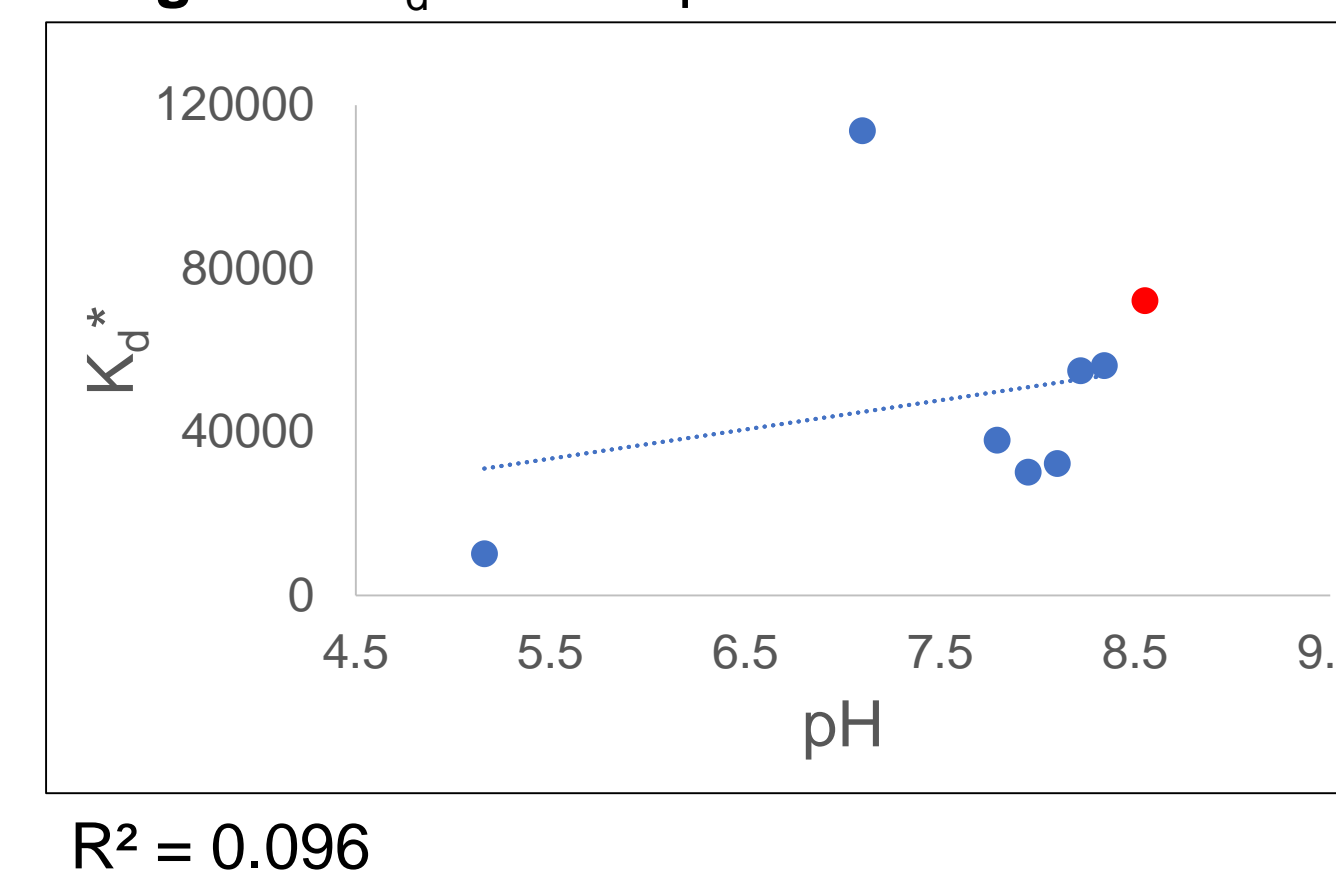


Figure 8 K_d^* vs OC Fraction (f_{oc})

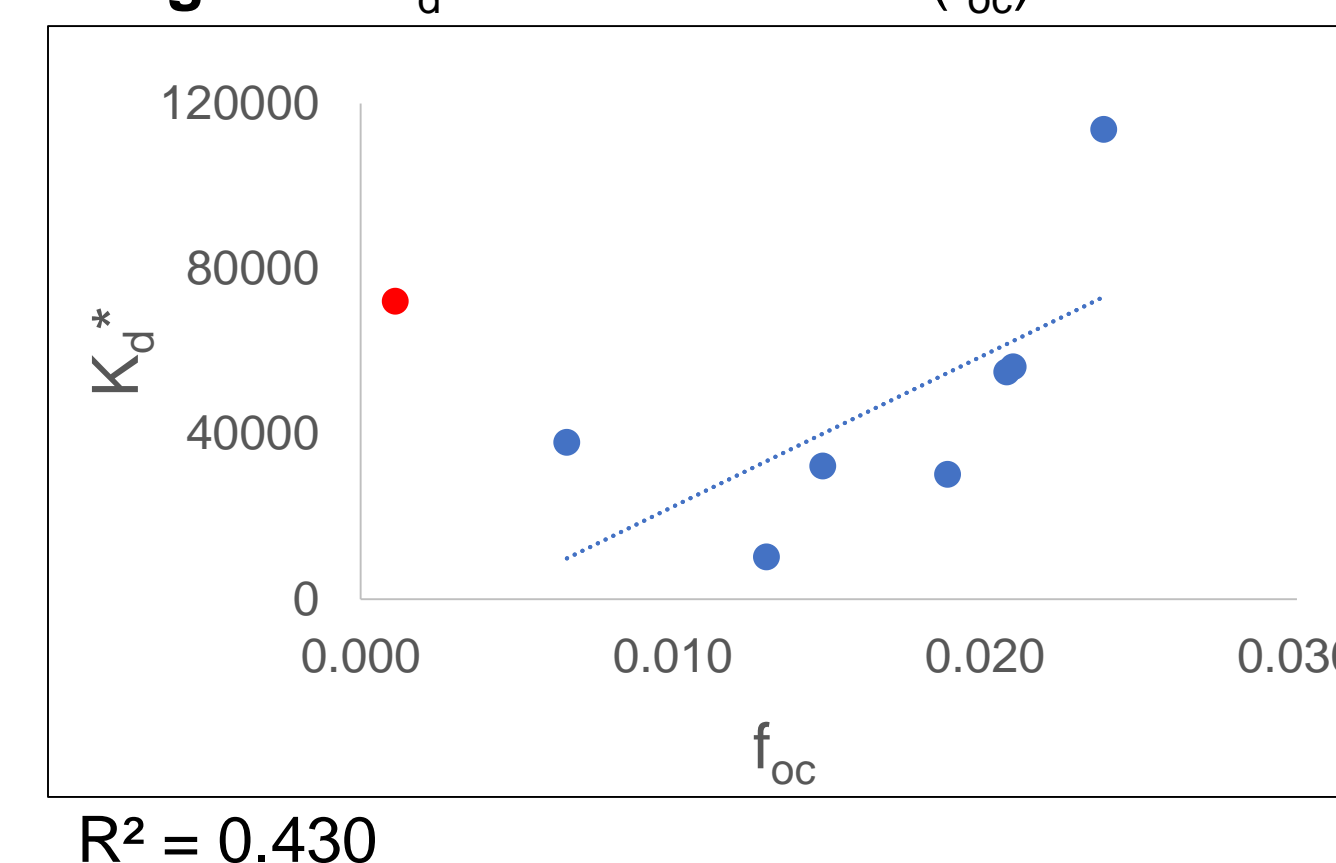


Fig. 8 K_d^* vs CEC

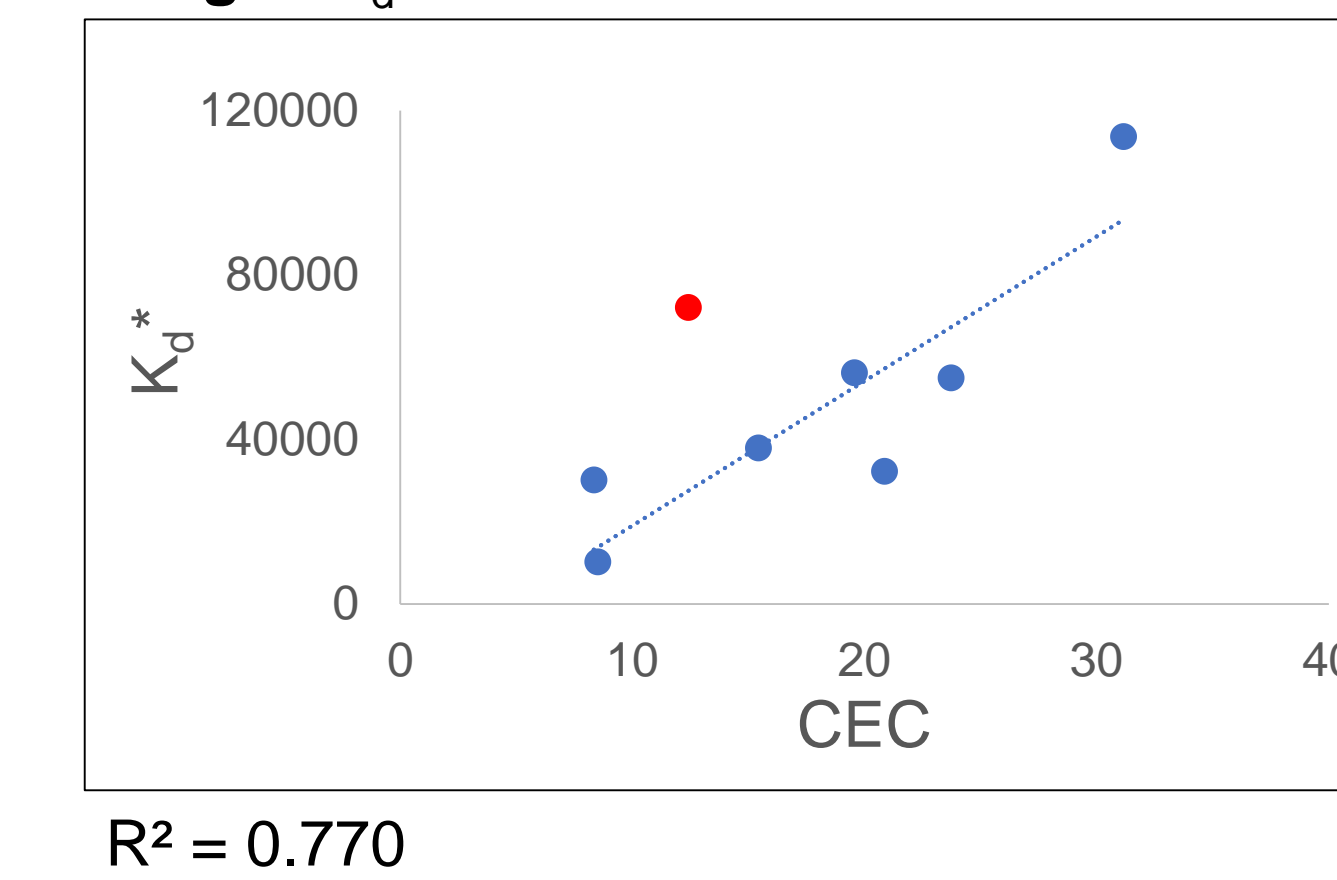
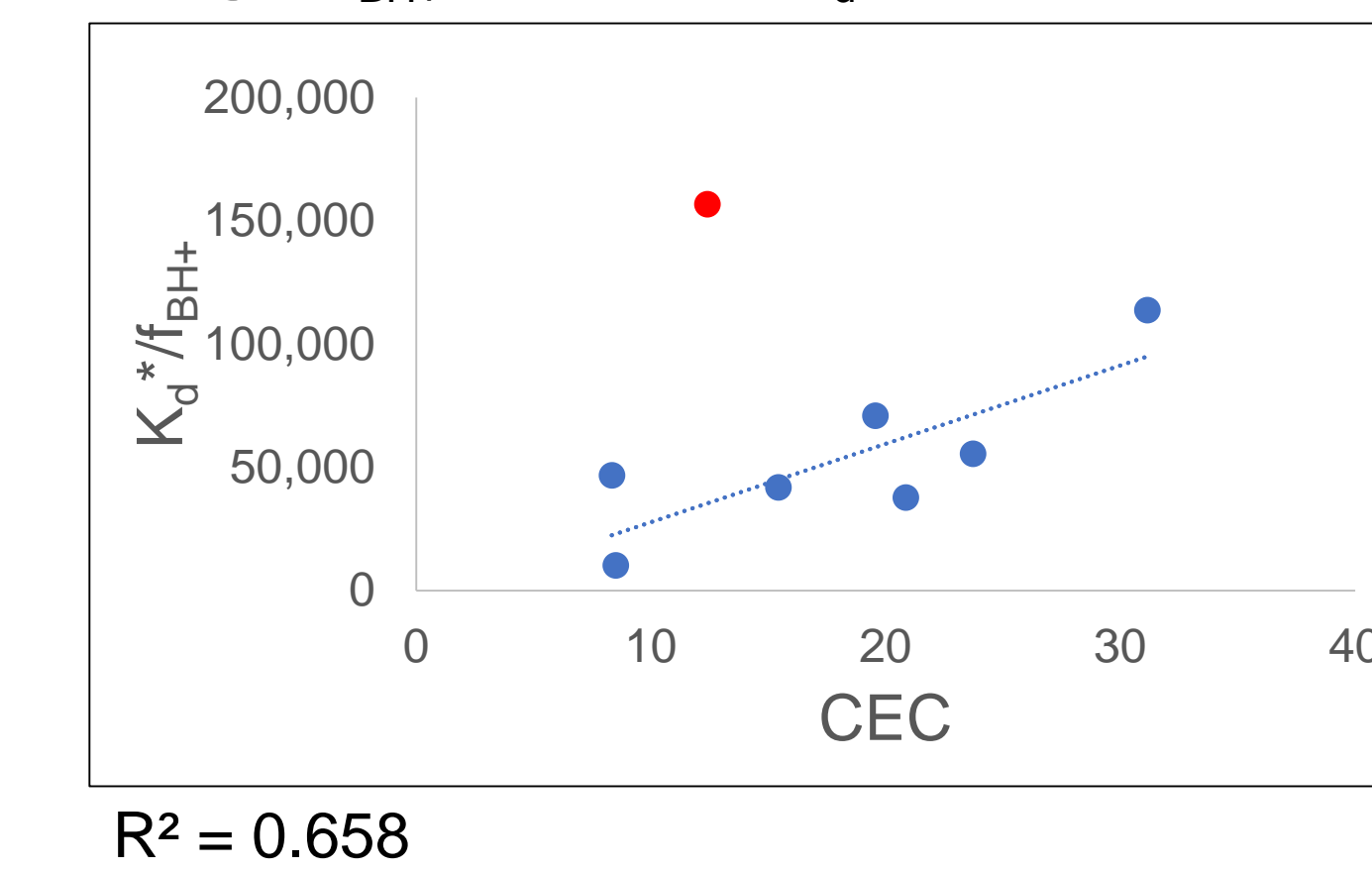


Fig. 9 f_{BH^+} -normalized K_d^* vs CEC



Discussion

- Stronger sorption than expected led to aqueous equilibrium concentrations being less than preferred (< 20% of the applied concentrations) for statistical purposes.
- Strongest observed correlation was K_d^* vs CEC, supporting hypothesis that sorption of the cation dominates.
- Single variable correlations of ionizables are weak because they do not account for both speciation and a soil property simultaneously.
- Provided CEC values were calculated at pH 7. Since CEC is pH-dependent, these values may have been an inaccurate representation of actual CEC at equilibrium isotherm pH.

Conclusion

- Strong sorption of azithromycin via cation exchange is due to its high pK_a values. The cationic fraction (f_{BH^+}) dominates at environmentally relevant pH values.
- Organic carbon and clay both contribute to cation exchange capacity, thus why K_d^* is positively correlated to these soil parameters.

Future Work

- Perform solvent extraction to validate the method of measuring sorption by mass balance and confirm azithromycin is not lost to degradation.
- For more accurate analysis, find an appropriate soil mass to aqueous volume ratio to produce C_w with 20 – 80% of the applied concentration.
- Using the same soils, assess sorption over a wide pH range.

References

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Acknowledgements

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