Supporting information

Co-binding of pharmaceutical compounds at mineral surfaces: mechanistic modeling of binding and co-binding of nalidixic acid and niflumic acid at goethite surfaces

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7 pages, 6 Figures

1. NA and NFA speciation in solution

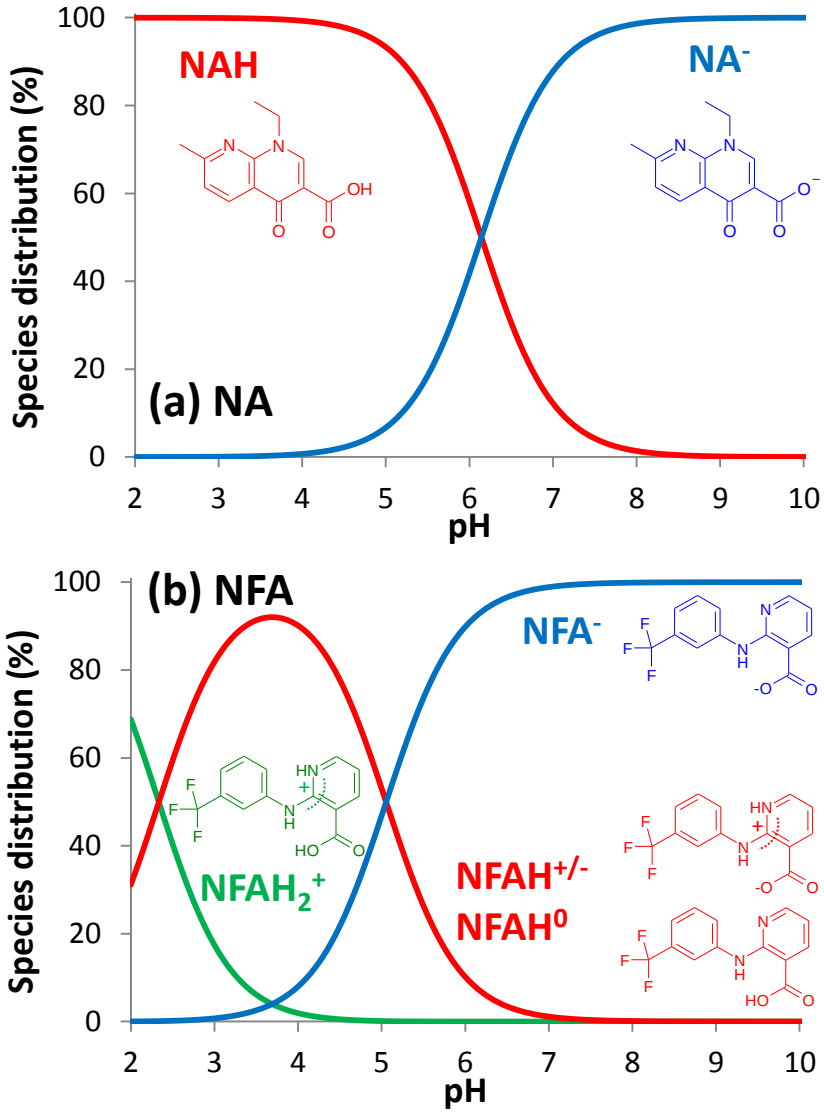

Figure S1. Distribution of (a) NA and (b) NFA at various pH values with molecular structures of different NA and NFA species. Ionic strength: 10 mM NaCl. pK_as of NA (pK_a=6.19) and NFA ($pK_{a,1}$=2.28 and $pK_{a,2}$=5.10) at infinite dilution were obtained from conditional pK_a values and the Davies equation.

2. Preliminary modeling results of NA adsorption to goethite

Figure S2 shows experimental NA adsorption to goethite data versus pH, [NaCl] and [NA] together with preliminary modeling results. In this model, NA is able to form only monomeric MB, HB and OS complexes. It allows a reasonable fit to the data at relatively low [NA] (Fig. 2a,b,c) at various pH and [NaCl] but strongly underestimates NA adsorption at low loadings (Fig. 2d). The introduction of NA-dimer formation (see main text) allows predicting accurately the whole NA adsorption dataset.

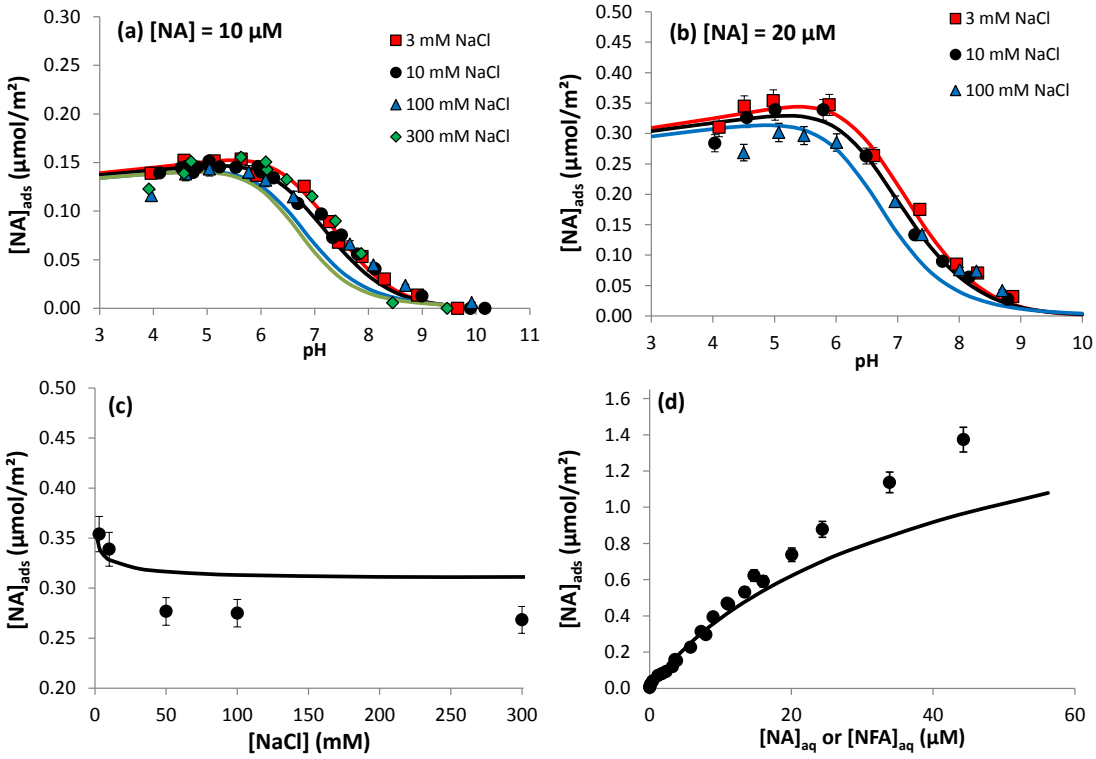

Figure S2. Modeling of single NA system, without considering NA dimer formation at goethite surface (preliminary model). (a) Adsorption of 10 µM NA to goethite (0.5 g/L) versus pH and [NaCl] (3-300 mM) (b) Adsorption of 20 µM NA to goethite (0.5 g/L) versus pH and [NaCl] (3-100 mM). (c) Adsorption of 20 µM NA to goethite (0.5 g/L) versus [NaCl] at pH 5. (d) NA-goethite adsorption isotherm at pH 6 in 10 mM NaCl. Solid lines are modeling results (the same color as the corresponding symbol).

3. Additional data for NA single system (final model in the main text)

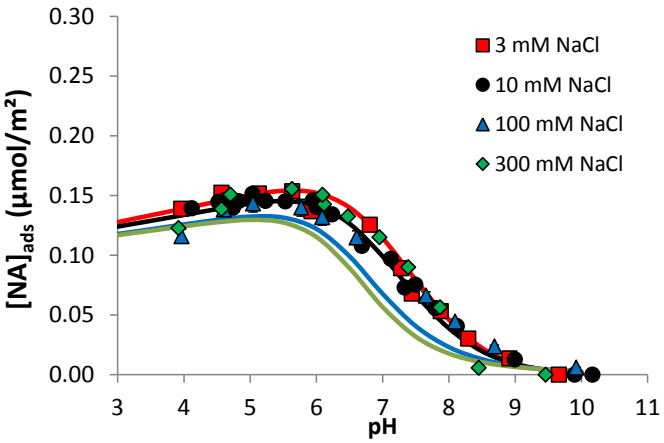

Figure S3. Modeling of single NA system, considering NA dimer formation at goethite surfaces (final model, see the main text for more details). Adsorption of 10 µM NA to goethite (0.5 g/L) versus pH and [NaCl] (3-300 mM). Solid lines are modeling results (the same color as the corresponding symbol).

4. Preliminary modeling results of NFA adsorption to goethite

Figure S4 shows experimental NFA adsorption to goethite data versus pH and [NaCl] together with preliminary modeling results. In this model, NFA zwitterion is able to form a HB complex and the anion is able to form an OS complex. While the effect of pH is well predicted in 10 mM NaCl solution, data at lower and higher [NaCl] are over- and under-estimated, respectively. A more accurate prediction of NFA adsorption to goethite as a function of [NaCl] can be obtained by including the formation of a sodium-NFA ion pair (see main text).

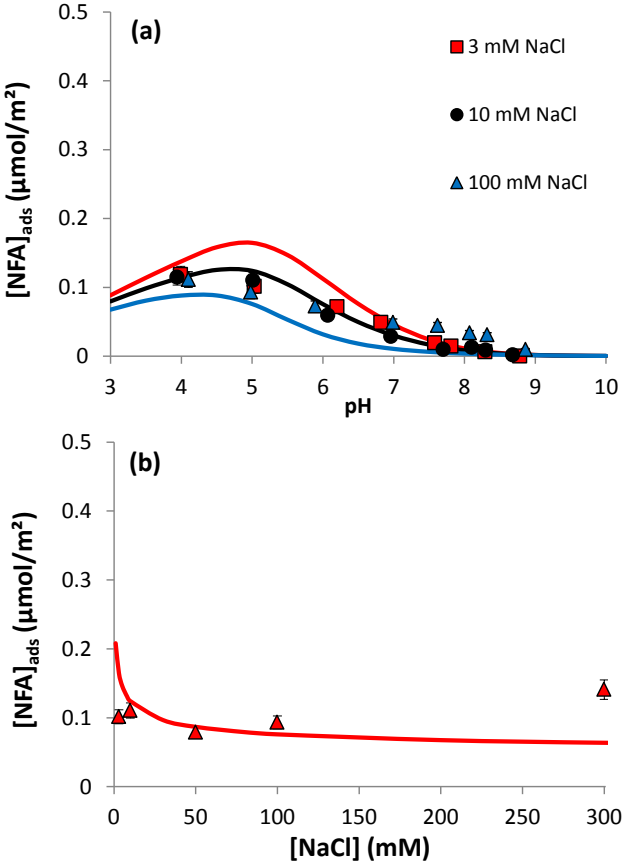

Figure S4. Modeling of single NFA system, without considering the formation of a sodium-NFA ion pair (preliminary model). (a) Adsorption of 20 µM NFA to goethite (0.5 g/L) versus pH and [NaCl] (3-100 mM). (b) Adsorption of 20 µM NFA to goethite (0.5 g/L) versus [NaCl] at pH 5. Solid lines are modeling results (the same color as the corresponding symbol.

5. Preliminary modeling results of NA-NFA: only competition

Figure S5 shows experimental and predicted adsorption of NA and NFA in binary NA-NFA systems in various conditions. The model does not include the formation of NA-NFA dimer (i.e. only eqs. 1-6 are used), hence predicts only competition between both molecules. This "competitive" model rather predicts decrease in adsorption of each molecule instead of enhancement.

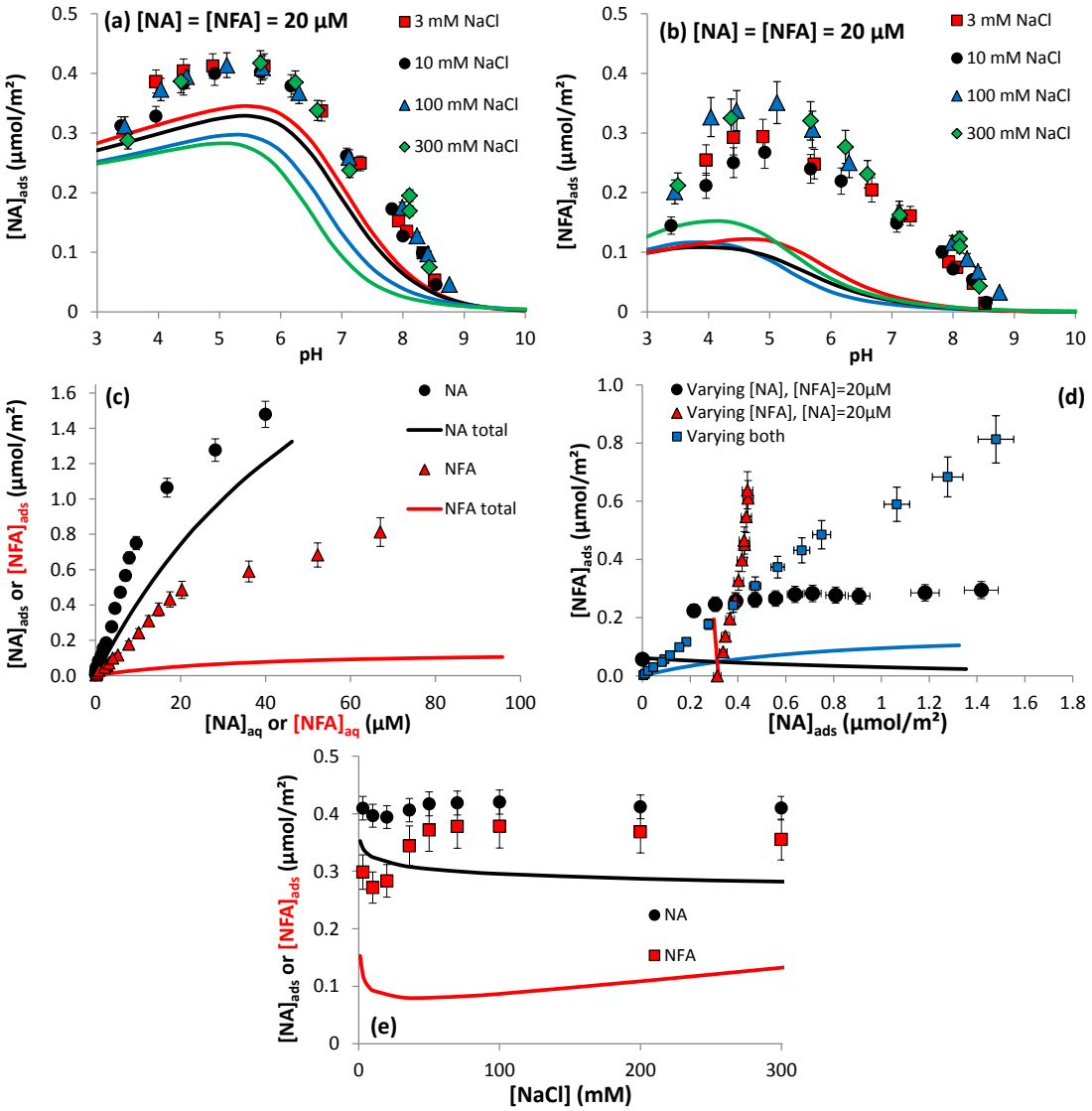

Figure S5. Experimental results and modeling data of binary NA-NFA system without NA-NFA dimer formation. Adsorption of (a) NA and (b) NFA to goethite (0.5 g/L) versus pH and [NaCl] (3-300 mM) for $[NA]_{tot} = [NFA]_{tot} = 20$ µM. (c) NA and NFA adsorption isotherms at pH 6 in 10 mM NaCl for $[NA]_{tot} = [NFA]_{tot}$. (d) $[NFA]_{ads}$ vs $[NA]_{ads}$ for three experimental conditions: (i) ($[NFA]_{tot} = 20$ µM, varying $[NA]_{tot}$, black), (ii) ($[NA]_{tot} = 20$ µM, varying $[NFA]_{tot}$, red), and (iii) varying both compounds with $[NA]_{tot} = [NFA]_{tot}$ (blue). (e) Adsorption of NA and NFA ($[NA]_{tot} = [NFA]_{tot} = 20$ µM) on goethite (0.5 g/L) versus [NaCl] at pH 5. In all graphs, solid lines correspond to overall adsorption predicted by surface complexation modeling (using the same color as the corresponding symbol).

Figure S6 shows preliminary modeling results considering NA-NFA dimer formation but without accounting for ion pair formation with sodium (i.e. only eqs. 1-9 are used). The effect of [NaCl] is not well predicted.

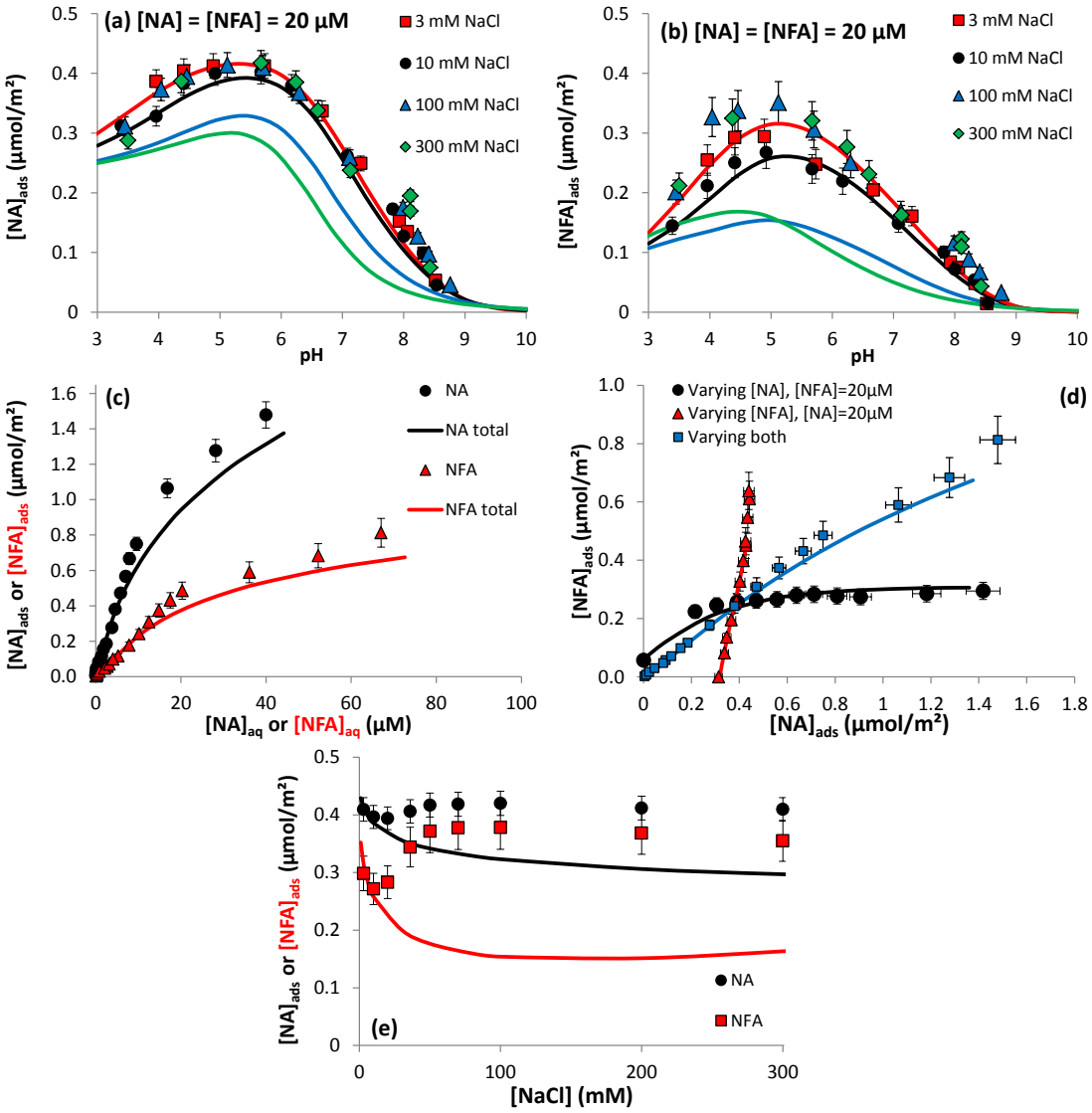

Figure S6. Experimental results and modeling data of binary NA-NFA system with NA-NFA dimer formation but without ion pair formation with sodium. Adsorption of (a) NA and (b) NFA to goethite (0.5 g/L) versus pH and [NaCl] (3-300 mM) for $[NA]_{tot}$ = $[NFA]_{tot}$ = 20 µM. (c) NA and NFA adsorption isotherms at pH 6 in 10 mM NaCl for $[NA]_{tot}$ = $[NFA]_{tot}$. (d) $[NFA]_{ads}$ vs $[NA]_{ads}$ for three experimental conditions: (i) ($[NFA]_{tot}$ = 20 µM, varying $[NA]_{tot}$, black), (ii) ($[NA]_{tot}$ = 20 µM, varying $[NFA]_{tot}$, red), and (iii) varying both compounds with $[NA]_{tot}$ = $[NFA]_{tot}$ (blue). (e) Adsorption of NA and NFA ($[NA]_{tot}$ = $[NFA]_{tot}$ = 20 µM) on goethite (0.5 g/L) versus [NaCl] at pH 5. In all graphs, lines correspond to overall adsorption predicted by surface complexation modeling (using the same color as the corresponding symbol).