Supporting Information For

The Role of Charge in the Surfactant Assisted Stabilization of the Natural Product Curcumin

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Curcumin Characterization. Curcumin purity was checked by ^1H NMR and mass spectroscopy. ^1H NMR (DMSO, 300 MHz) ^1H NMR(DMSO)10.04-9.45(m,2H), 7.74-7.51(d,2H), 7.41-7.31(m,2H), 7.30-7.08(d,2H), 6.91-6.81(d,2H), 6.80-6.71(d,2H), 6.18-6.00(m,1H), 4.02-3.75(m,6H). A representative spectrum is shown in Figure S.1.

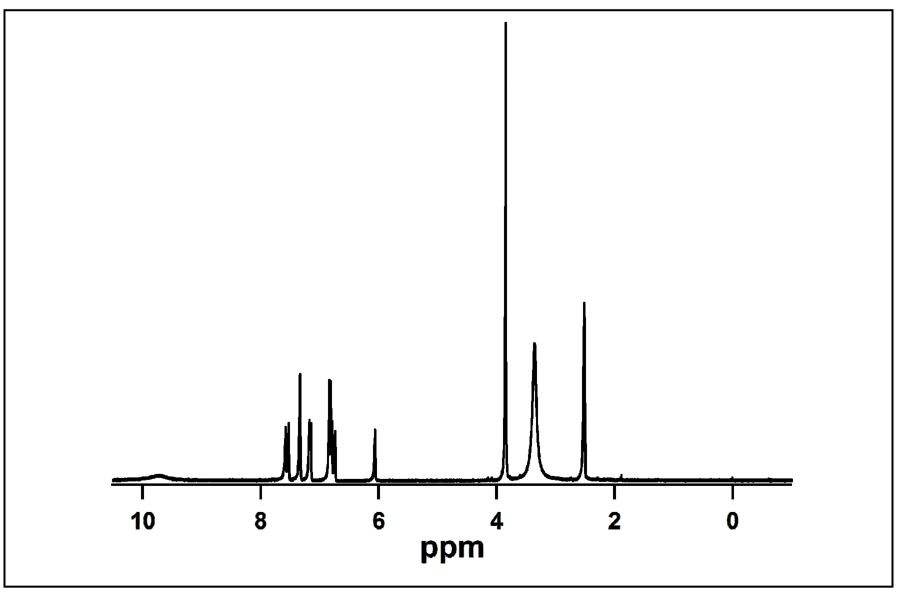

Figure S.1 Proton NMR spectrum of curcumin in DMSO.

Mass spectrometry was performed using a Varian 1200 L Quadrupole Spectrometer with electrospray ionization. The spectrum and major peaks are shown below in Figure S.2.

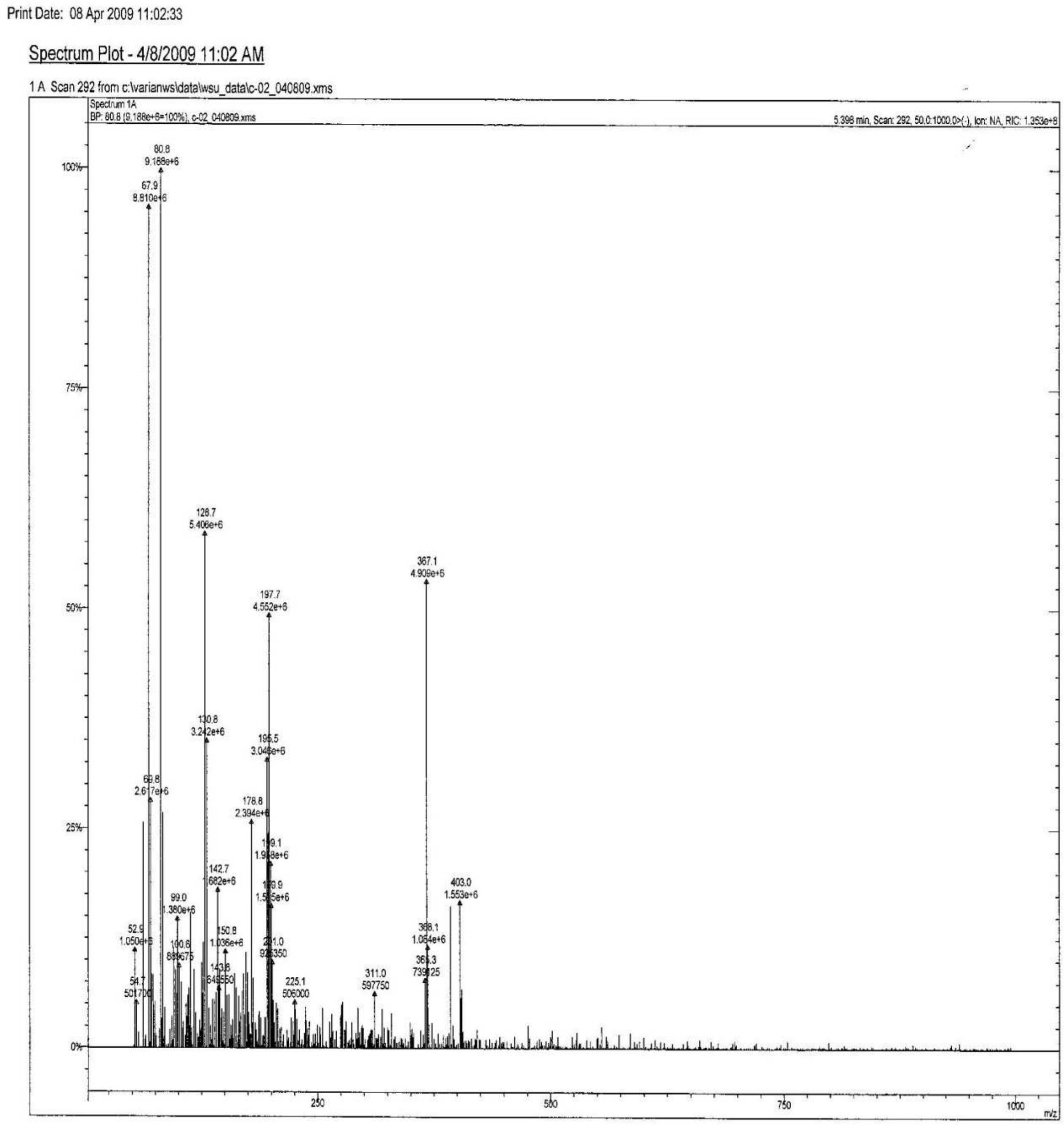

Figure S.2. Mass spectrum of curcumin from ethanol.

Mass spectrum *m/z* (rel intensity): Curcumin 368(M^-,53.7%), 197.7 (48.3%), 128.7 (57.3%), 80.8 (100%), 67.9 (96.5%)

Calculations of Curcumin Hydrolysis Rate

All hydrolysis rates were measured by preparing a curcumin solution of 9.1 μM under the approporiate conditions, i.e. appropriate pH and surfactant concentration. The initial absorbance immediately after mixing was aquired and the degradation process was followed by taking an absorbance spectrum every 3 minutes as shown in Figure S.3A. The initial rate of curcuin degradation was calculated from the slope of the absrobance *vs.* time. A sequence of absorption

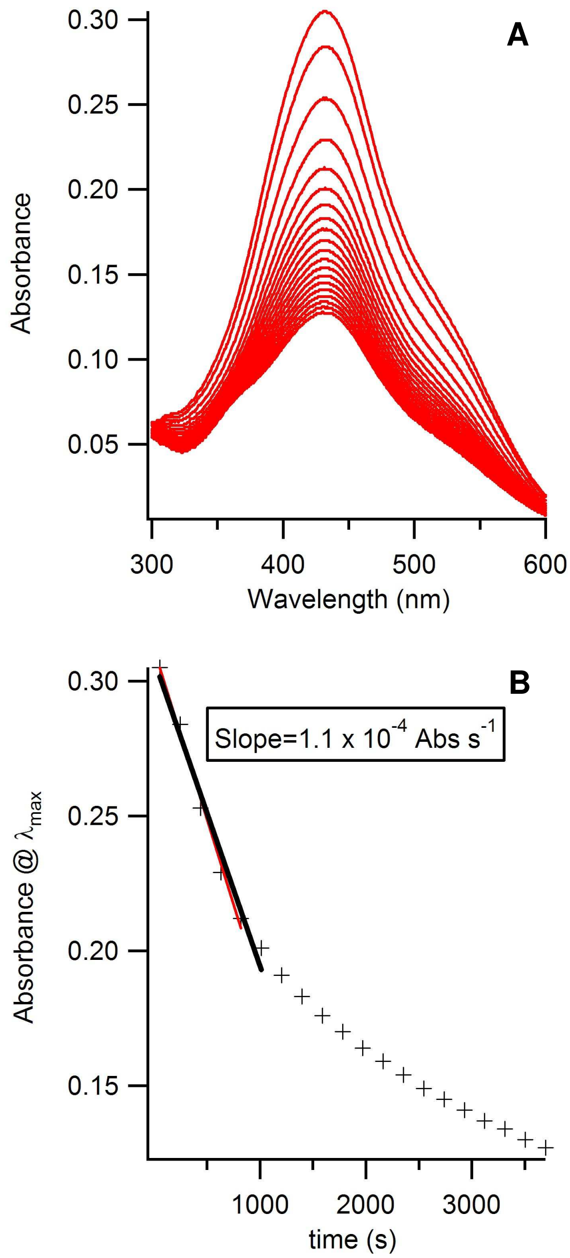

Figure S.3. Measurements of curcumin hydrolysis in water at pH 9.2. A) Absorbance spectra taken at 3 minute intervals. B) Plot of the maximum absorbance as a function of time.

spectra for curcumin in water at pH 9.2 are shown in Figure S.3A and the resulting degradation kinetics are shown in Figure S.3B. The initial rate in units of nM s^{-1} is calculated as:

$$\text{Initial Rate} = -\frac{S_{abs} \times C_{in}}{Abs_{in}}$$

where S_{abs} is the slope obtained from a linear regression of the absorbance *vs.* time (Figure S.3B), C_{in} is the initial concentration in units of nanomolar (9.1 x 10^3 nM in all cases) and Abs_{in} is the initial absorbance value at the maximum absorbance wavelength.

Note that during degradation the absorbance spectrum shape remains unchanged. This is due to formation of degradation products such as vanillin which absorb deeper in the UV, below 300 nm.

Calculations of Curcumin Deprotonation

The Henderson-Hasselbalch equation was used to estimate the proportions of the four different curcumin species:

$$\frac{[\mathrm{A}^-]}{[\mathrm{HA}]} \approx 10^{(\mathrm{pH}-\mathrm{p}K_\mathrm{a})}$$

For the equilibrium

$\mathrm{Cur}^0 \leftrightarrow \mathrm{Cur}^{-1}$

$$R_{-1} = \frac{[\mathrm{Cur}^{-1}]}{[\mathrm{Cur}^0]} = 10^{(\mathrm{pH}-8.3)}$$

The fraction of anion in this equilibrium is

$$f_{-1} = \frac{R_{-1}}{R_{-1}+1}$$

Similarly for the other two equilibria:

$\mathrm{Cur}^{-1} \leftrightarrow \mathrm{Cur}^{-2}$ and $\mathrm{Cur}^{-2} \leftrightarrow \mathrm{Cur}^{-3}$

$$R_{-2} = \frac{[\mathrm{Cur}^{-2}]}{[\mathrm{Cur}^{-1}]} = 10^{(\mathrm{pH}-9.9)}$$

$$R_{-3} = \frac{[\mathrm{Cur}^{-3}]}{[\mathrm{Cur}^{-2}]} = 10^{(\mathrm{pH}-10.5)}$$

$$f_{-2} = \frac{R_{-2}}{R_{-2}+1}$$

$$f_{-3} = \frac{R_{-3}}{R_{-3}+1}$$

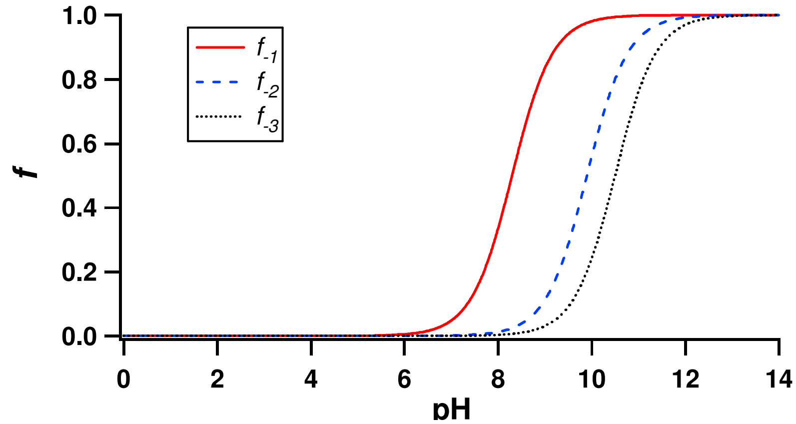

Figure S.4 Fractional ionization for the three different deprotonation events of curcumin

The fraction ionized vs pH is plotted in Figure S.4 for the three diffrerent equilibria. At any given pH we can calculate the fraction of curcumin molecules that are neutral, monoanionic, dianionic or trianionic using the formulae below.

$$\text{Fraction(-3)} = f_{-1}f_{-2}f_{-3}$$

$$\text{Fraction(-2)} = f_{-1}f_{-2} - f_{-1}f_{-2}f_{-3}$$

$$\text{Fraction(-1)} = f_{-1} - f_{-1}f_{-2}$$

$$\text{Fraction(0)} = 1 - f_{-1}$$

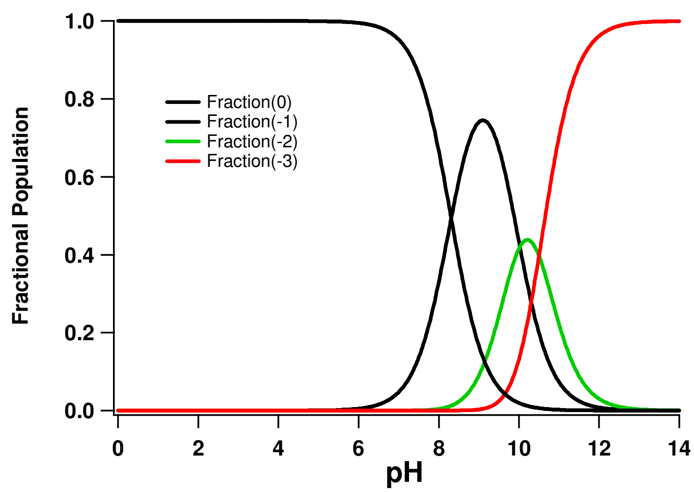

Figure S.5 Speciation diagram for curcumin as a function of pH.

Figure S.5 shows these fractional populations as a function of pH.

The average charge of curcumin is given by

$$\text{Average Net Charge} = -\{\text{Fraction(-1)} + 2*\text{Fraction(-2)} + 3*\text{Fraction(-3)}\}$$

The average net charge as a function of pH is plotted in Figure S.6 on the next page.

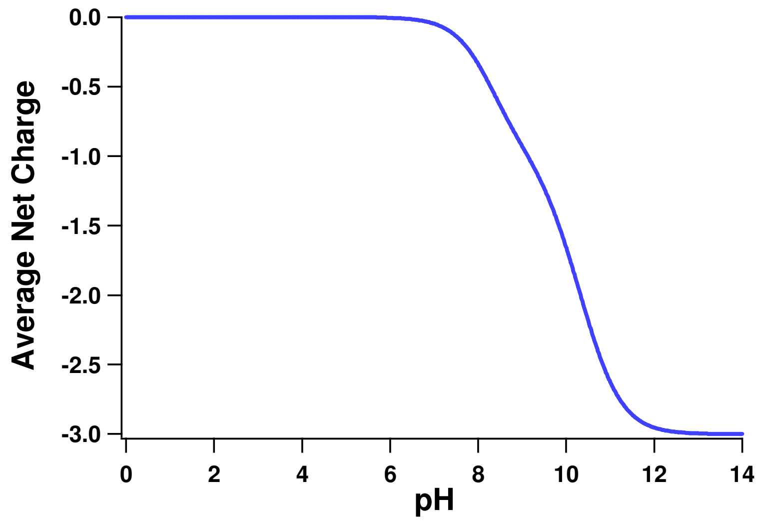

Figure S.5 Average net charge of curcumin as a function of pH.