Supplementary Information

Dimethyl carbonate as a mobile phase modifier for normal phase and hydrophilic interaction liquid chromatography

Philip D. Boes, Sophie R. Elleman, Neil D. Danielson*

Department of Chemistry and Biochemistry

Miami University

Oxford, OH 45056

*danielnd@miamioh.edu

Table S1. Solvent properties for ethyl acetate (EA), acetonitrile (MeCN), dimethyl carbonate (DMC), and propylene carbonate (PC)

Parameter	**Ethyl Acetate**	**Acetonitrile**	**Dimethyl Carbonate**	**Propylene Carbonate**
Viscosity (cP)	0.43	0.38	0.66	2.4
Solubility in water g/100 mL	8.7 N/A for normal phase	Completely miscible	13.9	17.5
Dipole moment	2.9	3.7	0.93	4.9
Dielectric constant	5.9	35.7	3.17	65
Surface tension	24	26.6	29.4	41.9
Polarity parameter P'	4.4	5.8	?	6.1
Hildebrand solubility parameter	9.1	11.9	9.5	27.2
Hanson solubility parameter (dispersion, polar, H bonding) Total	15.8, 5.3, 7.2 28.3	15.3, 18, 6.1 39.4	15.5, 8.6, 9.7 33.8	20, 18, 4.1 42.1

Table S2. Fit of the log k (y) versus log Φ (x) plots in Figure 4 for EA and DMC modifiers in hexane

Ethyl Acetate	**Phthalate**	**Linear least squares regression equation**	**Correlation coefficient**
	Dioctyl	y = -1.301x - 2.286	0.9767
	Dibutyl	y = -1.079x - 1.498	0.9889
	Benzyl butyl	y = -1.033x - 1.254	0.9898
	Diethyl	y = -0.977x - 1.036	0.9922
	Dimethyl	y = -0.803x - 0.693	0.9974
Dimethyl Carbonate	**Phthalate**	**Linear least squares regression equation**	**Correlation coefficient**
	Dioctyl	y = -1.347x - 2.090	0.8389
	Dibutyl	y = -1.302x - 1.614	0.9325
	Benzyl butyl	y = -1.247x - 1.316	0.9475
	Diethyl	y = -1.201x - 1.166	0.9492
	Dimethyl	y = -0.918x - 0.784	0.9935

Table S3. Comparison of benzoic acid derivative retention factors using MeCN and DMC on the silica column

Benzoic Acid Compound	**Retention factor (k) MeCN**	**Retention factor (k) DMC**
o-HBA	0.6	3.5
m-HBA	5.6	5.3
p-HBA	4.2	2.5
2,4-DHBA	1.2	5.1
2,5-DHBA	1.0	6.6
2,6-DHBA	0.0	1.9
3,5-DHBA	8.0	8.9

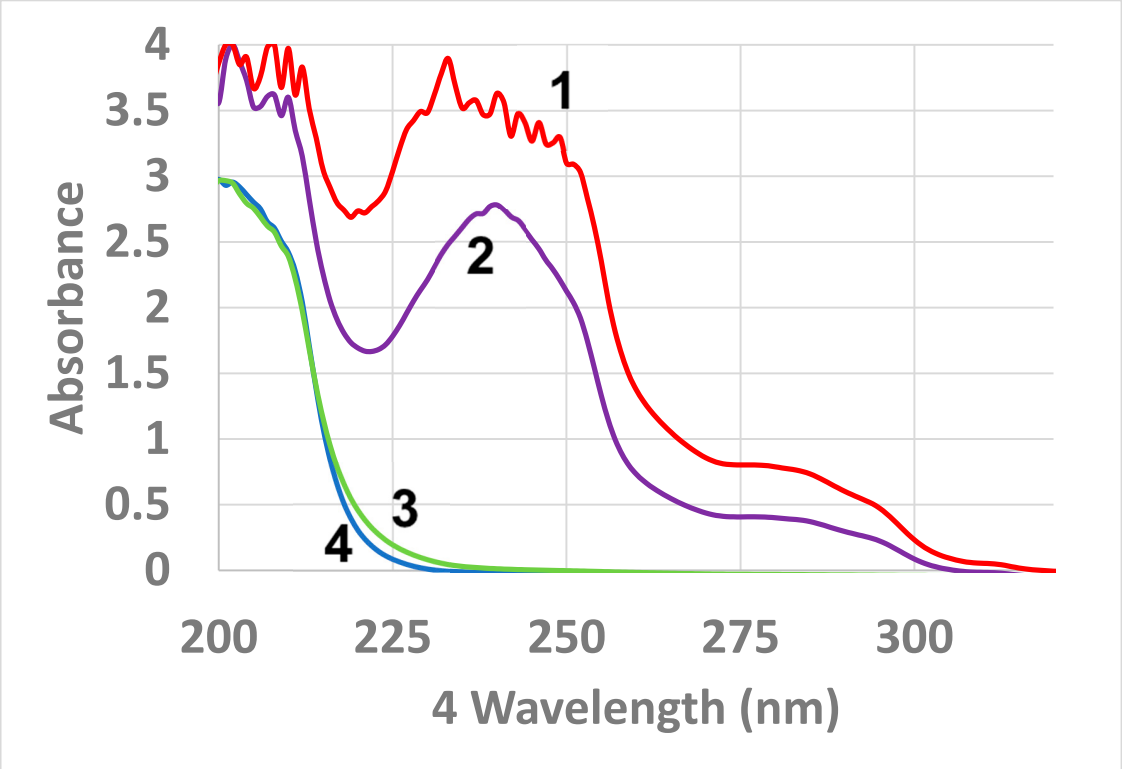


Figure S1: UV-Vis spectra on neat DMC, before and after distillation. Comparison between distilled DMC and DMC obtained from Sigma shows similar UV absorbance. There is decent correlation between the bottoms of the distillation and the DMC before distillation. An increase in absorbance indicates potential concentration. This impurity was not observed in GC-MS analysis. 1 (red): Bottoms in flask remaining after distillation of DMC from Company X; 2 (purple): DMC purchased from Company X before distillation; 3 (green): Distillate from Company X DMC; 4 (blue): Sigma-Aldrich DMC directly from bottle.

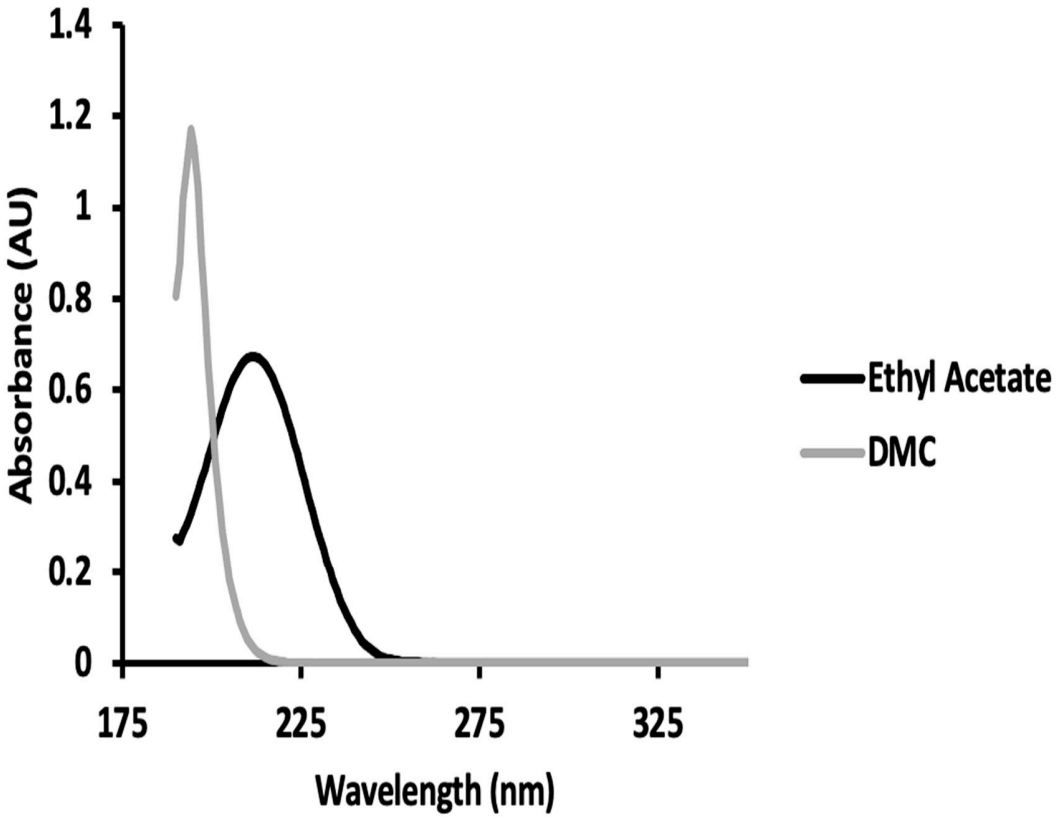


Figure S2. UV spectra for 2% ethyl acetate with 98% hexane (black trace) and 5% dimethyl carbonate (DMC) with 95% hexane (gray trace).

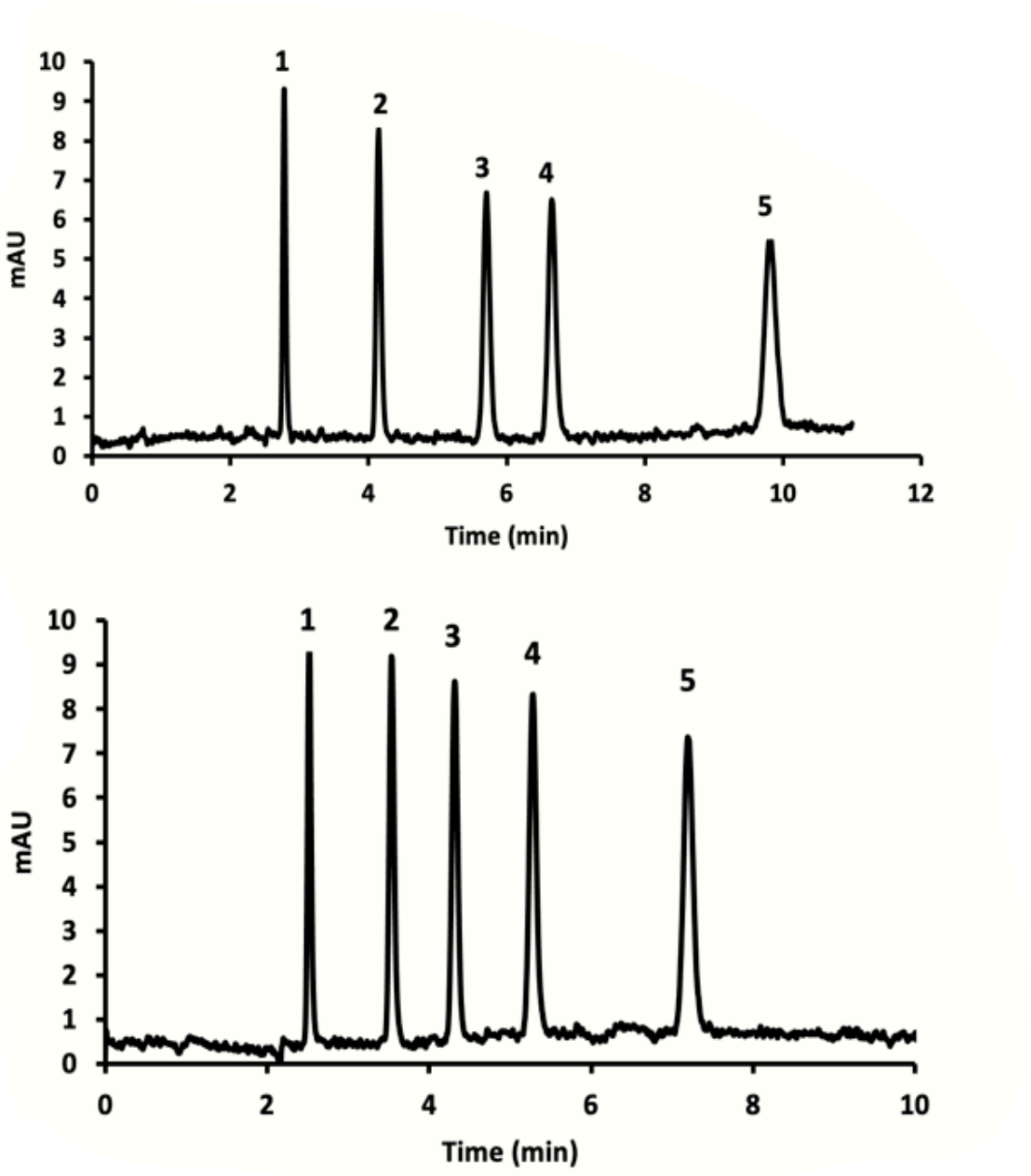


Figure S3. Chromatograms of phthalates comparing 4% DMC (top) and 4% ethyl acetate (bottom) as the modifier solvent with 96% hexane at 275 nm.

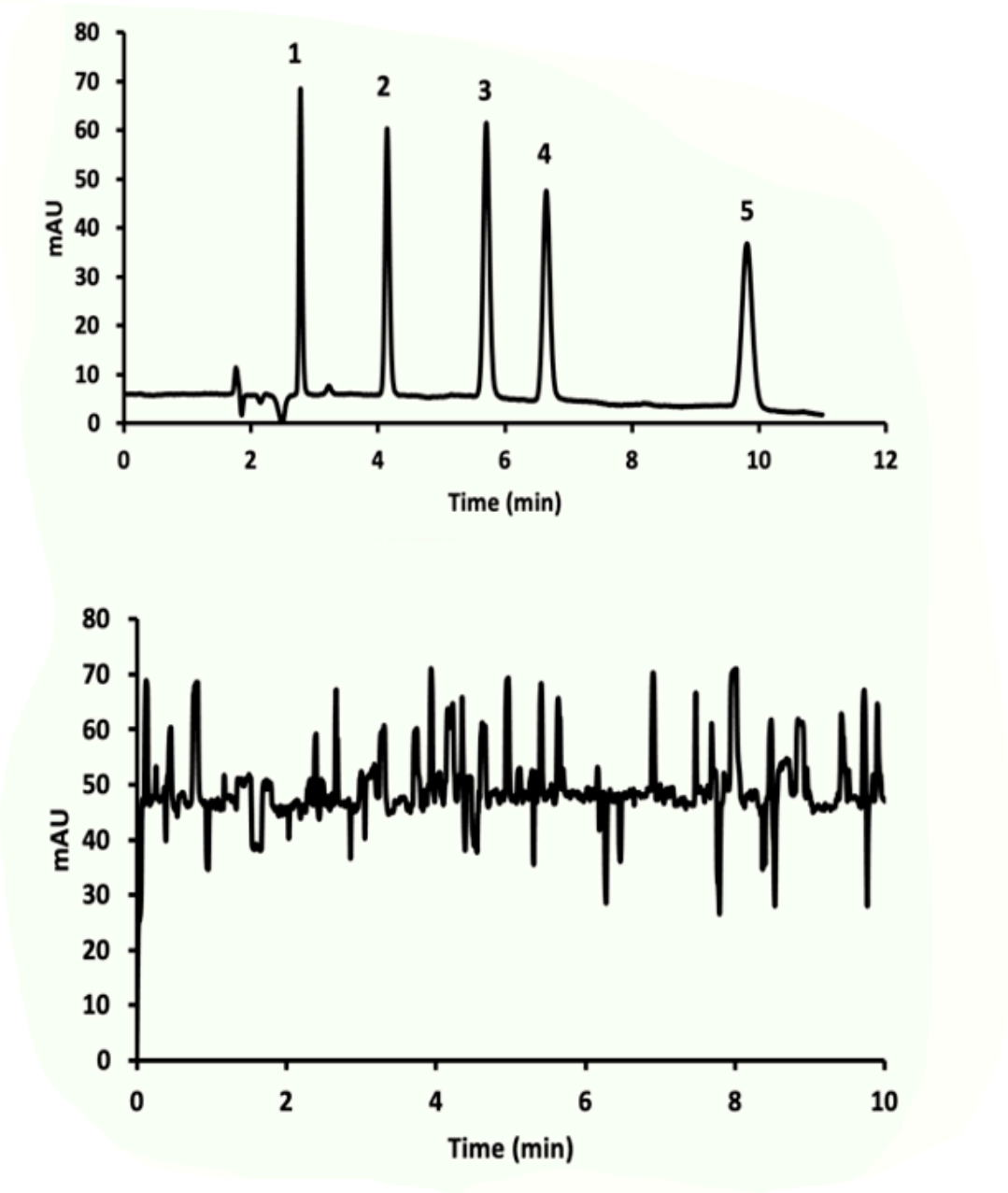


Figure S4. Chromatograms of phthalates comparing 4% DMC (top) and 4% ethyl acetate (bottom) as the modifier solvent with 96% hexane at 220 nm.

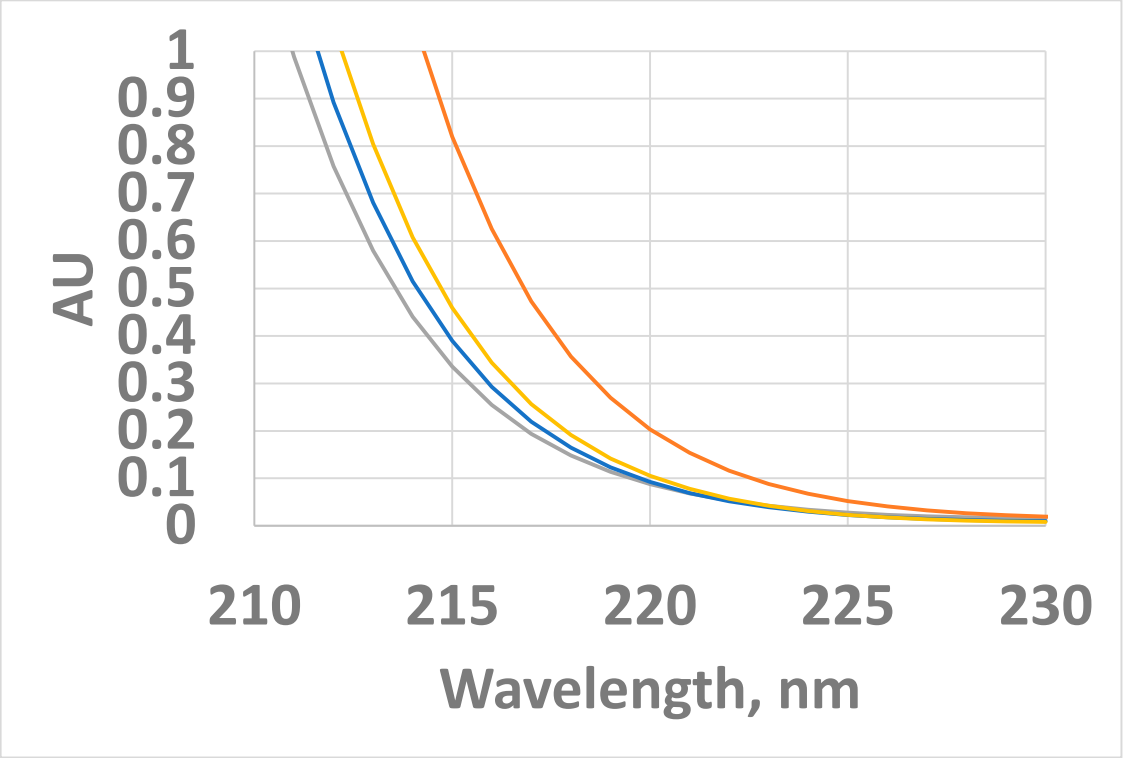


Figure S5. Absorbance spectra of HILIC mobile phases with different % DMC in 2:1 ethanol/water. Top to bottom: (90, 80, 70, 60% DMC).

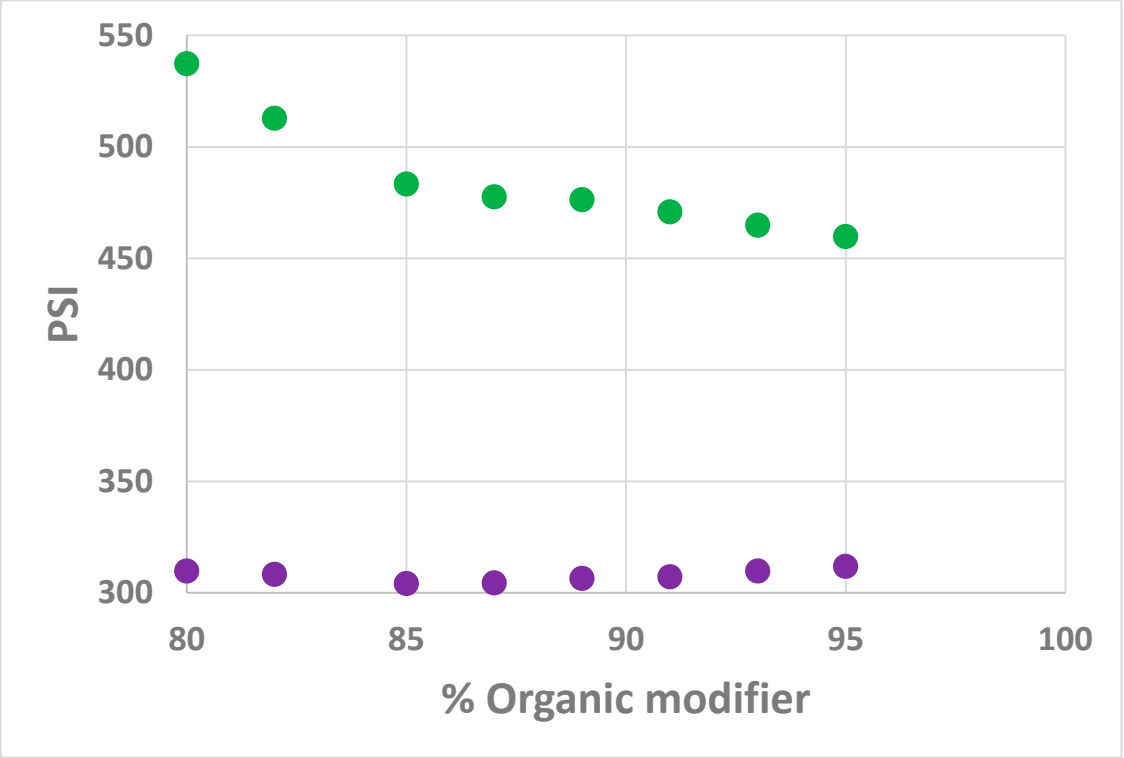
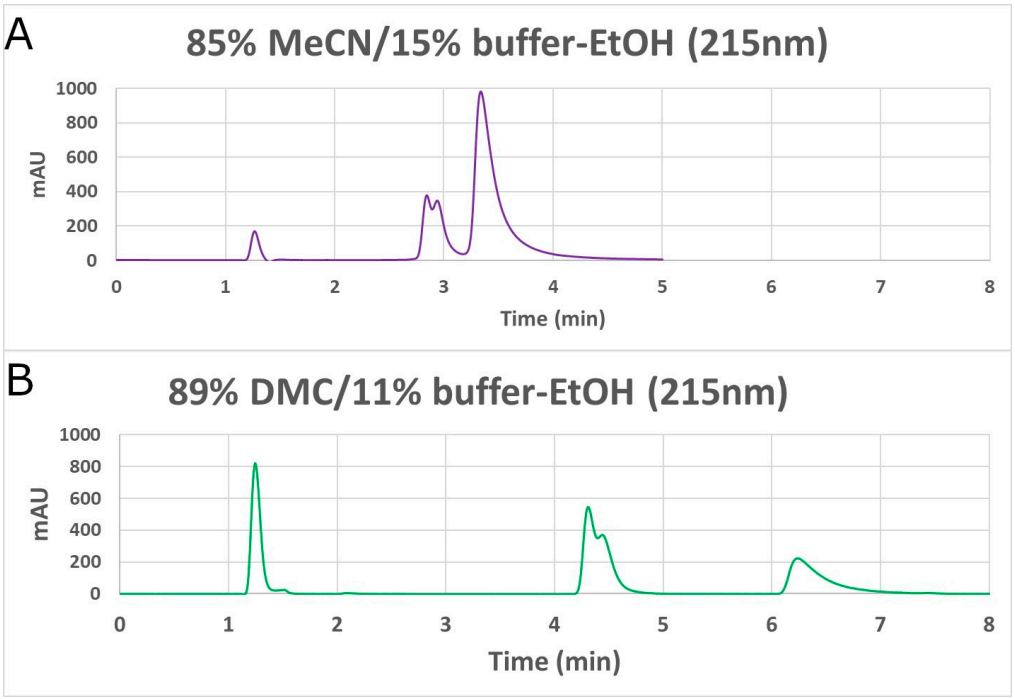


Figure S6. Plot of column pressure compared with % organic solvent. Top (green) –dimethyl carbonate. Bottom (purple) – acetonitrile. Flow rate – 0.5 mL/min.



C

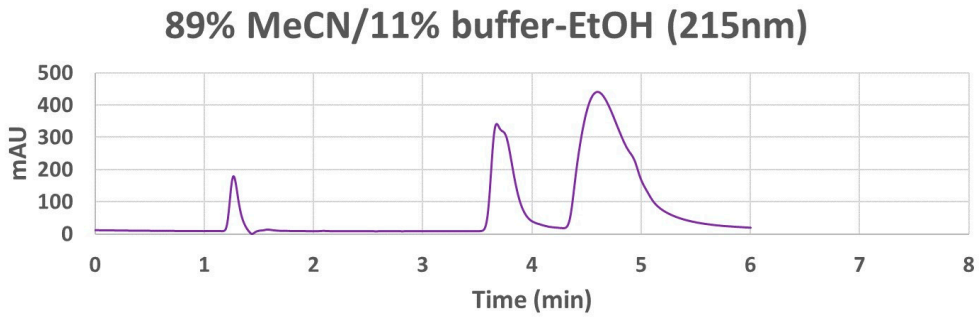


Figure S7: Sample chromatograms comparing MeCN and DMC as mobile phase modifier solvents. Mixture of toluene (1), *t*-ferulic acid (2), vanillic acid (3), and syringic acid (4) in order of retention time. Peaks 2 and 3 overlap.

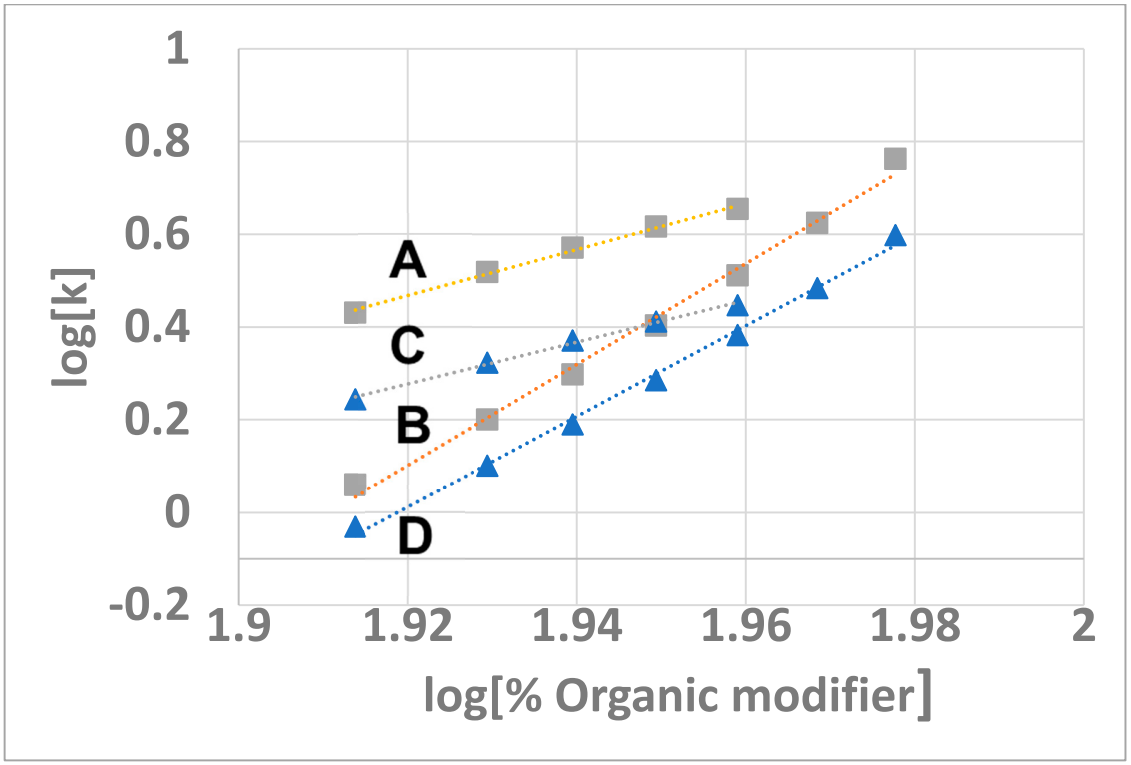


Figure S8. Log retention factor of syringic acid (more retained) and vanillic acid (less retained) versus log % modifier solvent for acetonitrile (C, D – blue triangles) and dimethyl carbonate (A, B – gray squares). Linear regression equations: (A) y = 4.98(x) – 9.09, R^2=0.9949; (B) y = 10.89(x) -20.81, R^2=0.9927; (C) y = 4.51(x) – 8.38, R^2=0.9954; (D) y = 9.79(x) – 18.78, R^2=0.9955.

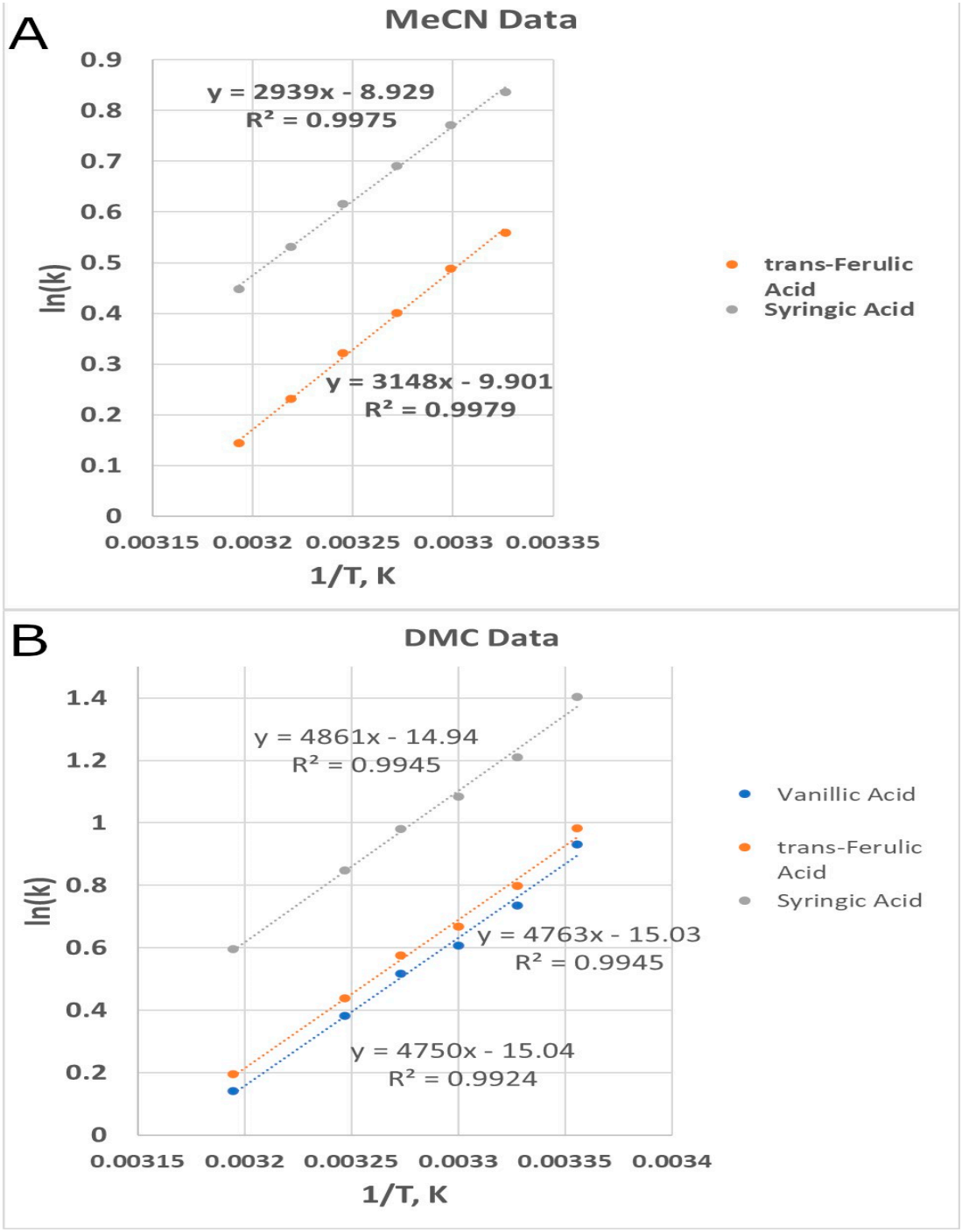


Figure S9: van't Hoff plots for MeCN and DMC mobile phases

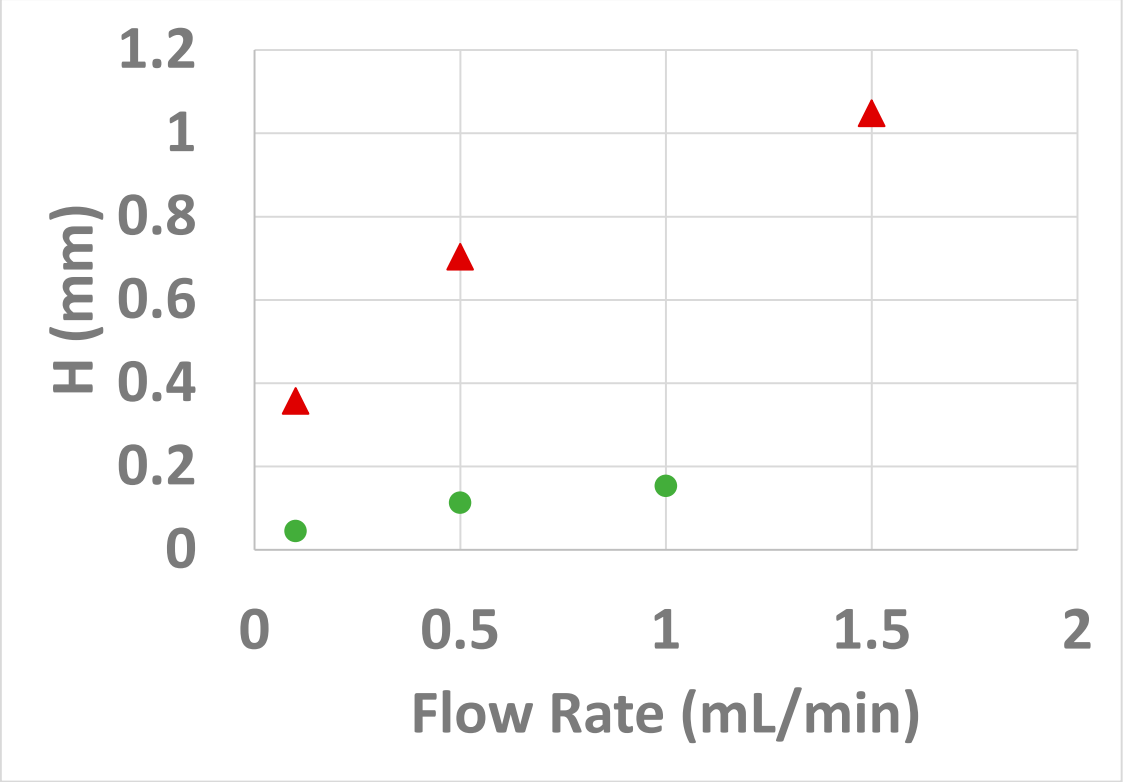


Figure S10: Height equivalent of theoretical plates for syringic acid with a mobile phase of 89% organic modifier in 11% buffer-ethanol. The column used was SeQuant ZIC-HILIC 5μm, 200˚A with dimensions 150 × 2.1mm. Top (red triangles) – MeCN; Bottom (green circles) – DMC.

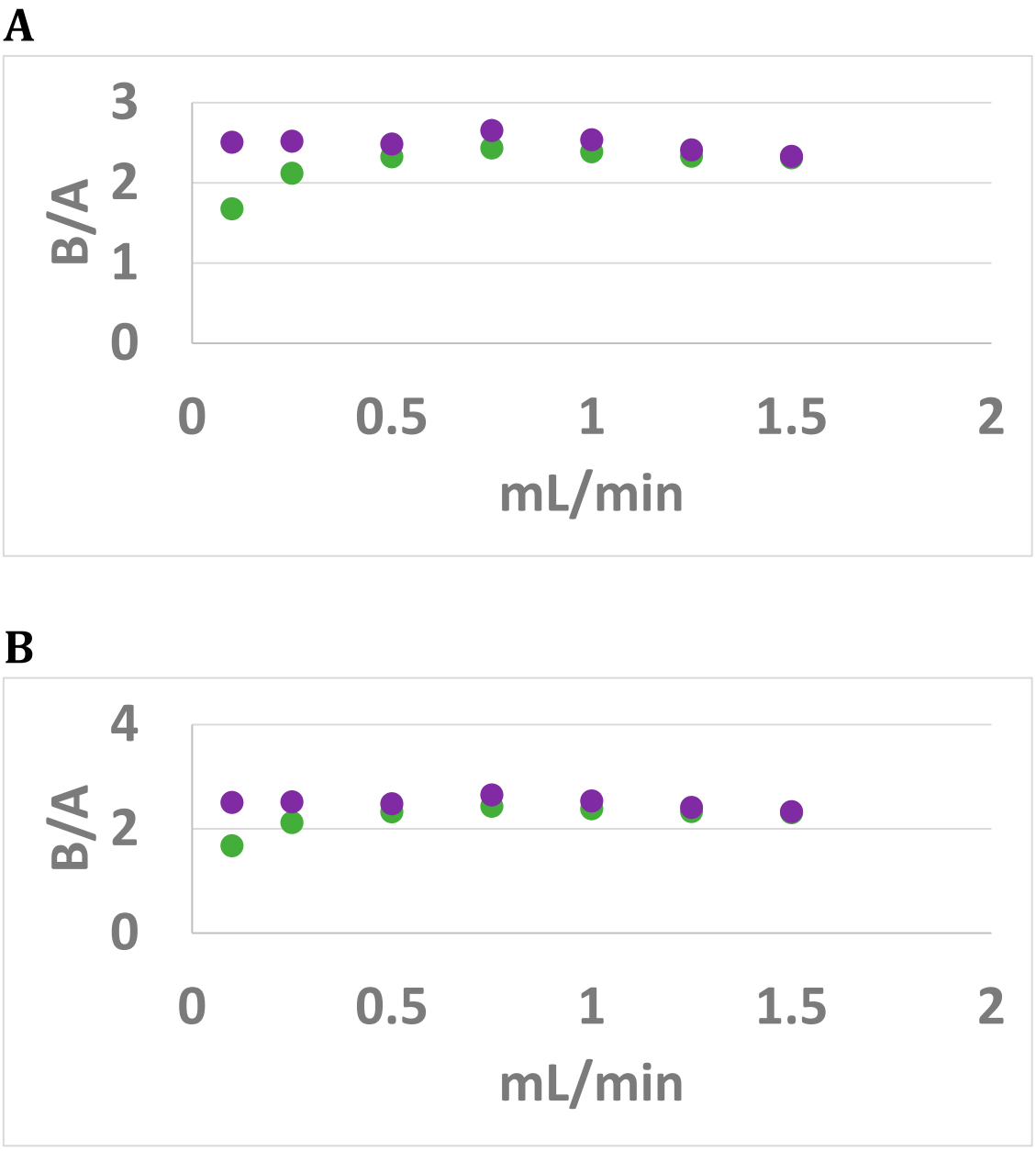
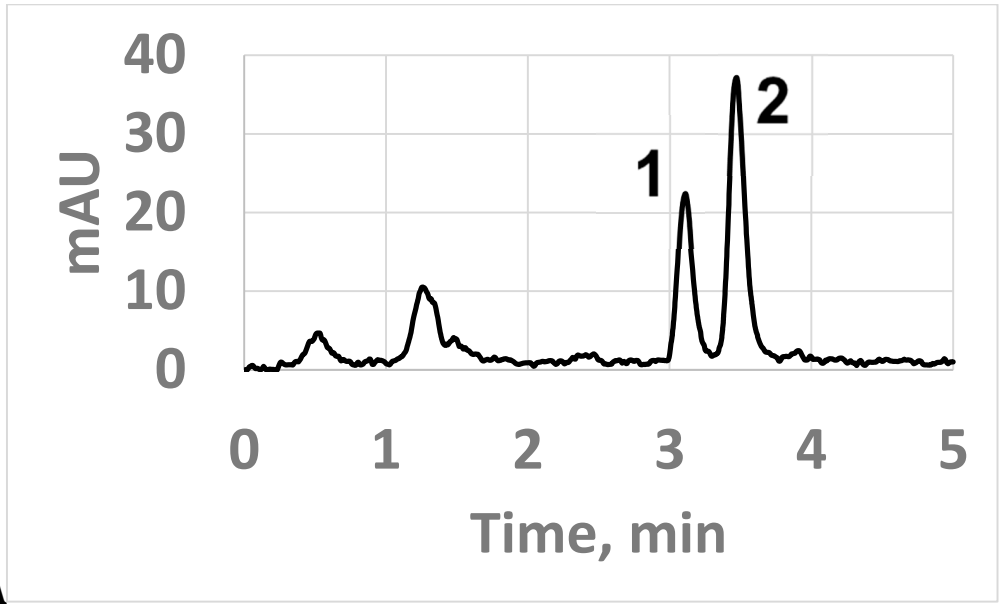
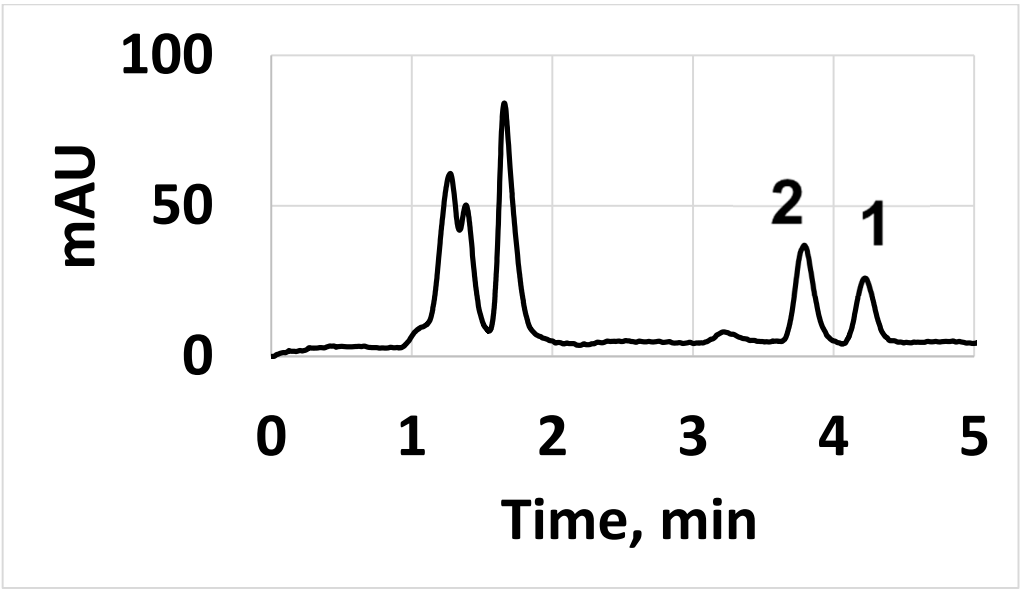


Figure S11: Peak asymmetry between the Halo silica column (A) and the ZIC zwitterion column (B). MeCN –purple (darker) points; DMC – green (lighter) points.



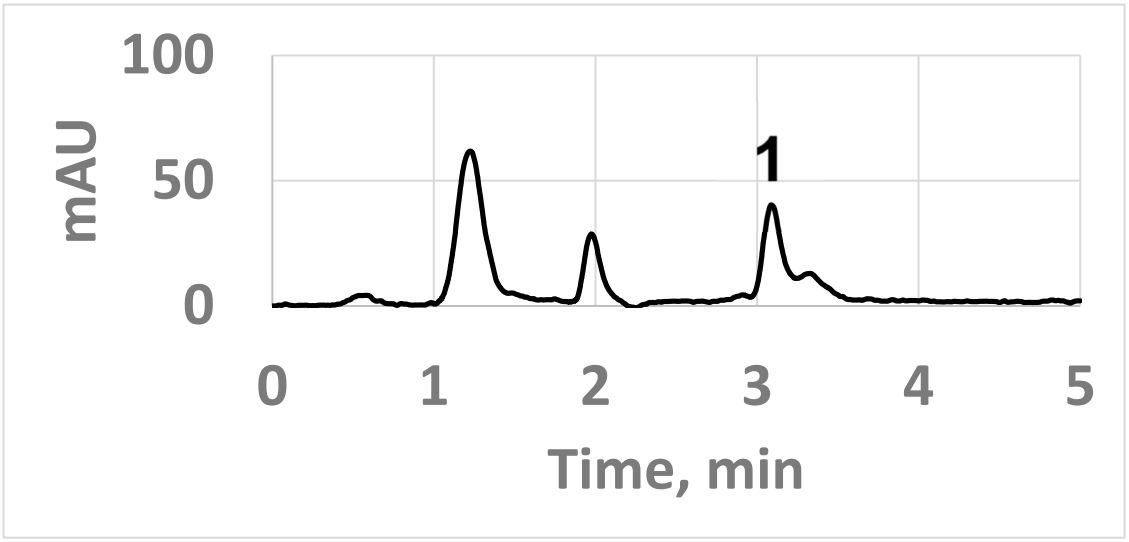
A



B

Figure S12. Chromatograms of Jose Cuervo Classic Lime Margarita. A) 85% DMC – 15% 10 mM buffer/ethanol and B) 85 % MeCN – 15% 100 mM buffer/ethanol. Peak 1 sorbate and peak 2 benzoate. Wavelength: 215 nm.

A



B

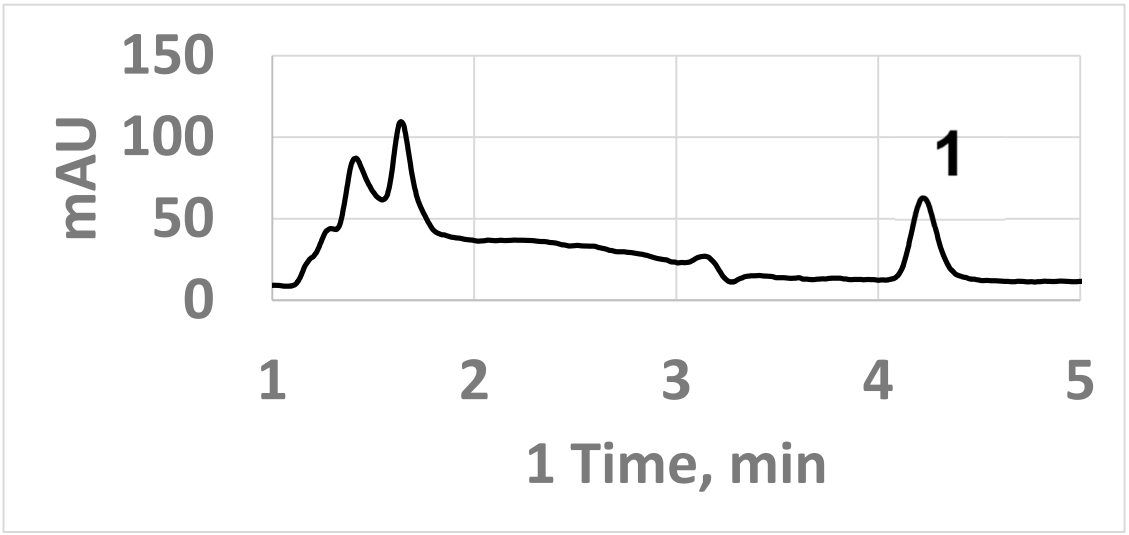
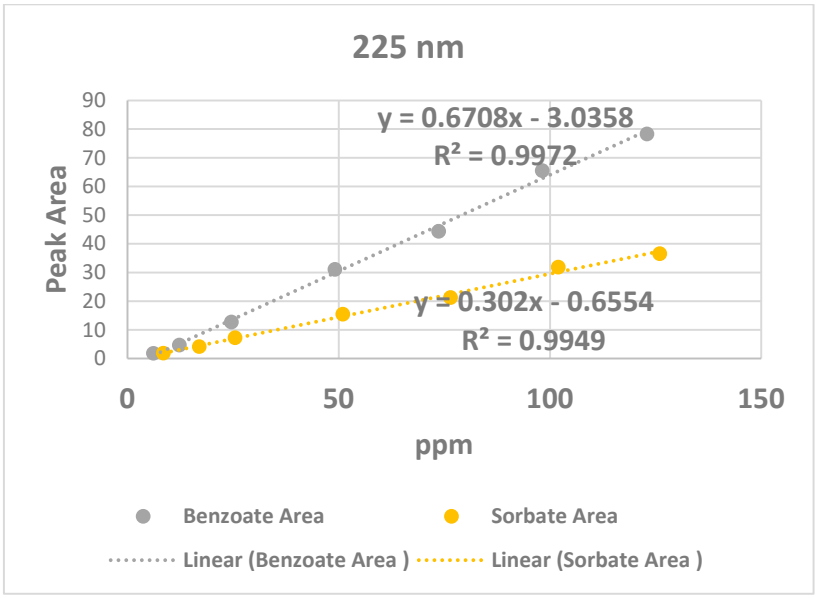


Figure S13. Chromatograms of Sunny D Orange Strawberry. A) 85% DMC – 15% 10 mM buffer/ethanol and B) 85 % MeCN – 15% 100 mM buffer/ethanol. Peak 1 sorbate. Wavelength: 215 nm.

A



B

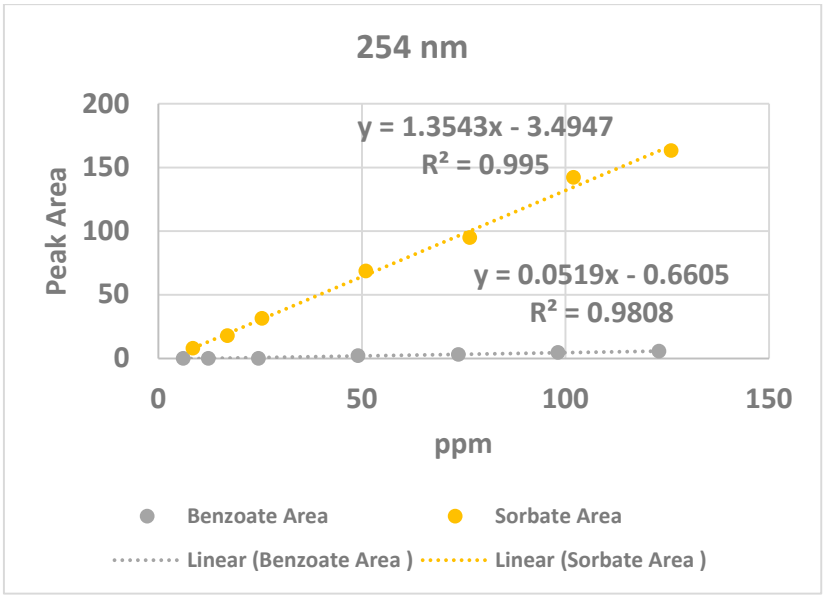
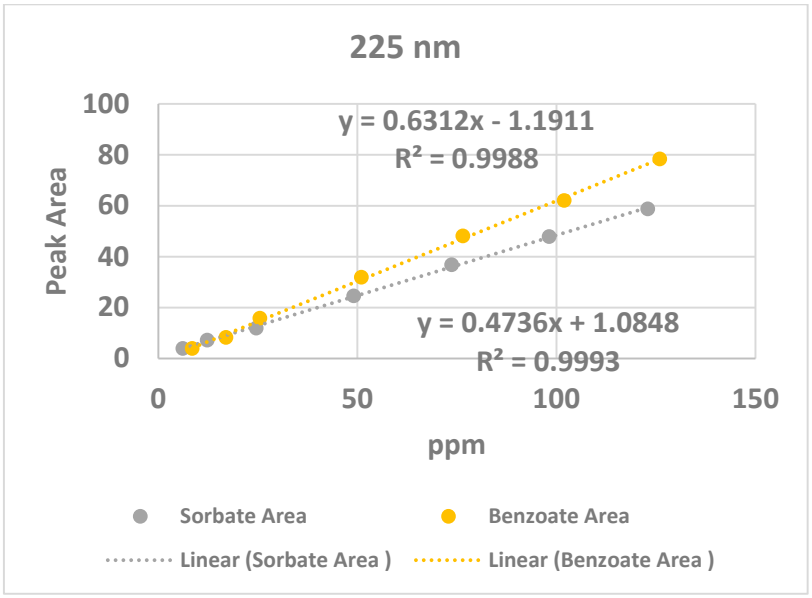


Figure S14. Peak area calibration curves (n=4) for benzoate and sorbate at 225 nm (top plot, spectral absorbance max for benzoate) and sorbate at 254 nm (top plot, spectral absorbance max for sorbate) using dimethyl carbonate mobile phase.

A



B

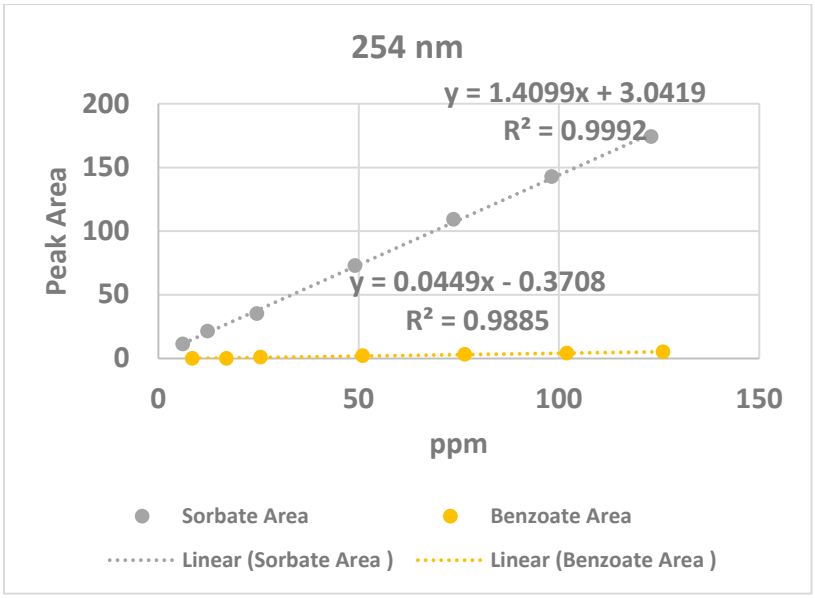


Figure S15. Peak area calibration curves (n=4) for benzoate and sorbate at 225 nm (top plot, spectral absorbance max for benzoate) and sorbate at 254 nm (top plot, spectral absorbance max for sorbate) using acetonitrile mobile phase.

Figure S16. AGREE Greenness assessment circle for HILIC using DMC. Segment 3 indicates the HPLC method is a potential at-line analytical method. Segment 7 considers amount of solvent waste generated by HPLC. DMC is a fairly good biodegradable solvent. There is the possibility of fire concern for DMC.