Electronic Supplemental Information

Life Cycle Analysis and Sustainability Comparison of Reversed Phase High Performance Liquid Chromatography and Carbon Dioxide-Containing Chromatography of Small Molecule Pharmaceuticals

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System Component	Source flow	Waste flow
Electricity	US: electricity, at grid, US	
Carbon Dioxide	US: Carbon Dioxide by-product ammonia (NH ₃)	Inorganic emissions to air
Methanol	US: Methanol from natural gas (combined reforming)	Ecoinvent long-term to air
Ethanol	US: Ethanol (96%) (hydrogenation with nitric acid)	Ecoinvent long-term to air
Isopropanol	US: Isopropanol	Ecoinvent long-term to air
Acetonitrile	US: Acetonitrile	Ecoinvent long-term to air
Water	US: Water deionized (reverse-osmosis/electro-deionization)	Other emissions to fresh water
Diethylamine	DE: Diethylamine (by product Ethylamine, triethylamine (TEA) ts	Ecoinvent long-term to air
Triethylamine	DE: Triethylamine (TEA) ts	Group NMWOC to air
Acetic Acid	US: Acetic acid from methanol (low pressure carbonylation)	Ecoinvent long-term to air

 Table S1 GaBi Database flows used for solvents, additives, electricity for the LCA study.

Power Meter	Prep SFC Components Connected
1	CO ₂ pump chiller
2	Column oven
3	Back Pressure Regulator, 2 Waters SFC heat exchangers
4	Organic modifier pump, CO, pump, Waters SFC heat exchanger, flowmeter
5	Waters gas-liquid separator, Communication module, DAD, Makeup pump (not used)

Table S2 Components connected to each power meter for Preparative Scale SFC Separations

Acronym	Meaning
LCA	Life Cycle Analysis
AMGS	Analytical Greenness Score
EHS	Environmental, Health, and Safety
AMVI	Analytical Mass Volume Intensity
EAT	Environmental Assessment Tool
CED	Cumulative Energy Demand
РСОР	Photochemical Ozone Potential
ACID	Acidification Potential
GHG	Greenhouse Gas Potential
ONGD	Oil and Natural Gas Depletion
EUTR	Eutrophication Potential

Table S3 List of acronyms used and the meaning for each.



Figure S1 Example system design for analytical (A) and preparative scale separations (B)

Solvent Comparisons											
	AMGS Calculator Results LCA Results										
Solvent	Solvent Energy Score	Solvent EHS Score	CED (MJ)	Greenhouse Gas Equivalents (kg of CO ₂ equivalents)	Oil and natural gas depletion (kg)	Acidificaiton potential (kg of SO ₂ equivalents)	Eutrophication potential (kg of (PO ₄) ³⁻)	Photochemical ozone creation potential (kg of ethane equivalents)			
Acetonitrile	58.80	2.24	142	6.27	3.46	1.13E-02	2.79E-03	1.27E-03			
Methanol	18.50	0.36	34.5	0.709	0.835	1.59E-03	1.81E-04	1.40E-01			
Ethanol	18.40	0.97	71.1	2.72	1.73	2.54E-03	5.74E-04	3.99E-01			
Isopropanol	29.10	0.87	59.4	2.07	1.45	2.27E-03	5.22E-04	1.89E-01			
Carbon Dioxide	5.35	0.036	5.25	0.175	0.126	1.68E-04	4.89E-05	2.41E-05			
Water	0.01	0.32	8.13E-03	5.36E-04	1.89E-04	7.47E-07	4.81E-07	5.73E-08			

Table S4 AMGS and LCA results for one kilogram of each solvent.



High Retention Mix 20% MeOH 2 mL/min BPR Comparison

Figure S2 Separations of the high retention mix using SFC. Mobile phase consisted of 80% liquified CO_2 and 20% MeOH. The organic solvent had triethylamine added to it at 0.1% (v/v) concentration. The flow rate was set to 2 mL/min for each, and the column temperature was 40 °C. The retention order was diltiazem, verapamil, amitriptyline, thioridazine.

High Retention Mix 20% MeOH Flow Rate Comparison



Figure S3 Separations of the high retention mix using SFC. Mobile phase consisted of 80% liquified CO_2 and 20% MeOH. The organic solvent had triethylamine added to it at 0.1% (v/v) concentration. The flow rate and BPR pressure is listed for each separation. The column temperature was 40 °C for each. The retention order was diltiazem, verapamil, amitriptyline, thioridazine.



High Retention Mix 20% EtOH 2 mL/min BPR Comparison

Figure S4 Separations of the high retention mix using SFC. Mobile phase consisted of 80% liquified CO_2 and 20% EtOH. The organic solvent had triethylamine added to it at 0.1% (v/v) concentration. The flow rate was set to 2 mL/min for each, and the column temperature was 40°C. The retention order was diltiazem, verapamil, amitriptyline, thioridazine.



High Retention Mix 20% EtOH Flow Rate Comparison

Figure S5 Separations of the high retention mix using SFC. Mobile phase consisted of 80% liquified CO_2 and 20% EtOH. The organic solvent had triethylamine added to it at 0.1% (v/v) concentration. The flow rate and BPR pressure is listed for each separation. The column temperature was 40 °C for each. The retention order was diltiazem, verapamil, amitriptyline, thioridazine.



High Retention Mix 40% IPA 2 mL/min BPR Comparison

Figure S6 Separations of the high retention mix using SFC. Mobile phase consisted of 60% liquified CO_2 and 40% IPA. The organic solvent had triethylamine added to it at 0.1% (v/v) concentration. The flow rate was set to 2 mL/min for each, and the column temperature was 40 °C. The retention order was diltiazem, verapamil, amitriptyline, thioridazine.



High Retention Mix 40% IPA Flow Rate Comparison

Figure S7 Separations of the high retention mix using SFC. Mobile phase consisted of 60% liquified CO_2 and 40% IPA. The organic solvent had triethylamine added to it at 0.1% (v/v) concentration. The flow rate and BPR pressure is listed for each separation. The column temperature was 40 °C for each. The retention order was diltiazem, verapamil, amitriptyline, thioridazine.

High Retention Mix HPLC Separations



Figure S8 Separations of the high retention mix using HPLC. The organic portion of each mobile phase composition for each solvent is listed and water makes up the remaining percentage. The organic solvent had triethylamine added to it at 0.1% (v/v) concentration. The flow rate is listed for each separation and corresponds to a system pressure of approximately 350 bar. The column temperature was 40 °C for all separations. The retention order was diltiazem, verapamil, amitriptyline, thioridazine.

HPEC Network Usage per lipection Instrument Except Consumption (MWN) Separation Trave Paration Trave Paration Trave Paration Trave Paration Trave Colspan="10">Colspan="10" Separation Trave Paration Trave <th></th> <th colspan="10">High Retention Mix Information</th>		High Retention Mix Information									
Separation Trans Pressure Day	HPLC										
Separation Tripe Separation Tripe Present (bar) Mass of Yate (ig) Mass of TAC (ig) Trial) Trial 3 Average 800. M.00.11 S.m./min 10.0 448 2.988 9.494 0.01 0.016	Separatio	on Parameters			Solvent Usage p	er Injection		Instrum	ent Ener	gy Consu	mption (kWh)
BBX ACM 2 CP 1.7.33 5.5.28 0.006 0.016 0.016 0.016 0.016 0.016 0.016 0.016 0.016 0.016 0.016 0.016 0.016 0.016 0.018 0.011 </td <td>Separation Type</td> <td>Separation Time</td> <td>Pressure (bar)</td> <td></td> <td>Mass of Water (g)</td> <td>Mass of Organic (g)</td> <td>Mass of TEA (g)</td> <td>Trial 1</td> <td>Trial 2</td> <td>Trial 3</td> <td>Average</td>	Separation Type	Separation Time	Pressure (bar)		Mass of Water (g)	Mass of Organic (g)	Mass of TEA (g)	Trial 1	Trial 2	Trial 3	Average
BBM MeD 11 SmL/min 10.0 348 2.988 9.494 0.011 0.014 0.036 0.036 0.036 0.036 0.036 0.036 0.036 0.036 0.036 0.036 0.036 0.036	80% ACN 2 mL/min	4.4	227		1.753	5.528	0.006	0.016	0.015	0.016	0.016
27/16 EOH 0.2 mil/min 35.3 351 10.61 11.28 0.012 0.112 </td <td>80% MeOH 1.5 mL/min</td> <td>10.0</td> <td>348</td> <td></td> <td>2.988</td> <td>9.494</td> <td>0.011</td> <td>0.034</td> <td>0.034</td> <td>0.034</td> <td>0.034</td>	80% MeOH 1.5 mL/min	10.0	348		2.988	9.494	0.011	0.034	0.034	0.034	0.034
Bay Inv 0.02, mt/min 38.5 3.44 1.3.64 0.125 0.127 0.027 0.026 0.067	57% EtOH 0.75 mL/min	33.5	351		10.761	11.288	0.018	0.112	0.111	0.112	0.112
SPC tools hold: Instrument Energy Consumption (kg) Separation Time [Pressure (bar) Density of CO, (g/m) Mass of CO, (g/m) Mass of CO, (g/m) Mass of CO, (g/m) MeCH 2 m//min 10b ar 5. Trial 3 Automatic Section (G) Mass of CO, (g/m) MeCH 2 m//min 10b ar 5. MeCH 2 m//min 10b ar 6. 2. MeCH 2 m//min 10b ar 6. MeCH 2 m//min 10b ar 6. 0.0031 MeCH 2 m//min 10b ar MeCH 2 m//min 10b ar 6.	43% IPA 0.625 mL/min	38.5	344		13.661	8.125	0.017	0.129	0.129	0.129	0.129
Job Protection Instrument Energy Consumption (kWh) Separation Time Pressure (bar) Density of CO. (g/mL) Mass of CO. (g/mL) Trial 3 Average MeCh2 mL/min 10b bar 9.5 1.75 0.897 13.534 3.007 0.003 0.066 0.066 0.066 0.066 0.066 0.066 0.066 0.066 0.066 0.066 0.066 0.066 0.066 0.066 0.066 0.066 0.061 </td <td></td> <td></td> <td></td> <td></td> <td>SFC</td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td>					SFC						
Instantine Pressure (bar) Density of C. (grmL) Mass of C. (grmL) Mass of C. (grmL)	Concentia				20% MeOH			In at a second			
Separation type Separation type Separation type Separation type Tests Average Mech2 mL/min 120 bar 15 0.037	Separation Trans		Deserves (here)		Solvent Usage p	er injection		Trial 1	Trial 2	gy Const	mption (kwn)
micro 1. ut/min 120 bar 3.2 1.75 0.207 1.3.6.3 2.007 0.008 0.068	Separation Type	Separation Time	Pressure (bar)	Density of CO ₂ (g/mL)	14 221	viass of Organic (g)	Mass of TEA (g)	1 I I I I I	1 rial 2	1 rial 3	Average
American and Yom 150 Bar 8.5 1.65 0.911 12.277 2.817 0.003 0.065 0.065 0.065 MeXU1 zmir/min 200 Bar 8.1 246 0.941 12.715 2.564 0.002 0.061 0.061 0.061 MeXU1 zmir/min 170 bar 6.6 237 0.936 12.255 2.611 0.002 0.051 <td>MoOH 2 mL/min 100 bar</td> <td>10.2</td> <td>145</td> <td>0.872</td> <td>12.624</td> <td>3.228</td> <td>0.003</td> <td>0.075</td> <td>0.075</td> <td>0.073</td> <td>0.073</td>	MoOH 2 mL/min 100 bar	10.2	145	0.872	12.624	3.228	0.003	0.075	0.075	0.073	0.073
Nex0+2 mir/min 170 bar 8.6 215 0.924 12.714 2.722 0.002 0.084 0.084 0.084 Nex0+2 mir/min 150 bar 6.9 216 0.934 0.2255 2.611 0.002 0.081 0.0631 0.0631 0.0531 0.	MeOH 2 mL/min 150 bar	8.9	195	0.857	12 973	2 817	0.003	0.008	0.008	0.008	0.008
Name Diagnaming 8.1 246 0.941 12.195 2.564 0.002 0.061 0.061 0.061 0.061 0.061 0.061 0.061 0.061 0.061 0.061 0.061 0.061 0.061 0.061 0.063 0.063 0.063 0.063 0.063 0.063 0.063 0.063 0.063 0.063 0.060	MeOH 2 mL/min 130 bar	8.6	215	0.924	12.714	2.722	0.002	0.064	0.064	0.064	0.064
Nicht 25 mi/min 120 bar 6.9 216 0.924 12.751 2.730 0.003 0.003 0.003 0.003 0.003 MeOH 25 mi/min 200 bar 6.3 267 0.951 11.833 2.492 0.002 0.050 0.050 0.050 0.050 0.050 0.050 0.050 0.050 0.056 0.056 0.056 0.056 0.056 0.056 0.056 0.056 0.056 0.056 0.056 0.056 0.056 0.056 0.056 0.056 0.057 0.051 0.051 0.051 0.051 0.056 0.057 0.051 0.056 0.157 0.051 1.158 0.027 0.039 0.039 0.039 0.039 0.039 0.039 0.039 0.031 0.033 <	MeOH 2 mL/min 200 bar	8.1	246	0.941	12.195	2.564	0.002	0.061	0.061	0.061	0.061
Mech 2.5 m//min 20 bar 6.6 237 0.936 12.355 2.611 0.002 0.051 0.050 0.050 Mech 2.5 m//min 20 bar 5.8 252 0.944 13.140 2.733 0.031 0.046 0.046 0.046 0.044 0.040 0.040 0.040 0.040 0.040 0.040 0.040 0.040 0.040 0.040 0.040 0.041 <t< td=""><td>MeOH 2.5 mL/min 150 bar</td><td>6.9</td><td>216</td><td>0.924</td><td>12.751</td><td>2.730</td><td>0.003</td><td>0.053</td><td>0.053</td><td>0.053</td><td>0.053</td></t<>	MeOH 2.5 mL/min 150 bar	6.9	216	0.924	12.751	2.730	0.003	0.053	0.053	0.053	0.053
Meone 2.sm./min 200 bar 6.3 267 0.951 11.983 2.492 0.002 0.050 0.050 0.056 0.064 0.041 0.014 0.018 0.039 0.038 0.039 0.039 </td <td>MeOH 2.5 mL/min 170 bar</td> <td>6.6</td> <td>237</td> <td>0.936</td> <td>12.355</td> <td>2.611</td> <td>0.002</td> <td>0.051</td> <td>0.051</td> <td>0.051</td> <td>0.051</td>	MeOH 2.5 mL/min 170 bar	6.6	237	0.936	12.355	2.611	0.002	0.051	0.051	0.051	0.051
Meod 3 m/min 150 bar 5.8 252 0.944 13.140 2.753 0.003 0.046 0.046 0.044 0.034 0.031 0.033 0.033 0.033 0.033 0.033 0.033 0.033 0.033 0.033 0.033 0.033 0.033 0.033 0.033 0.033 0.033 0.033 0.033 0.031 0.033 0.031 0.033 0.031 0.033	MeOH 2.5 mL/min 200 bar	6.3	267	0.951	11.983	2.492	0.002	0.050	0.050	0.050	0.050
Mec0H 3 mL/min 120 bar 5.4 2.73 0.054 1.2.364 2.564 0.002 0.044 0.044 0.041 0.041 MeOH 3 mL/min 130 bar 4.8 287 0.961 1.1592 2.374 0.002 0.040 0.038 0.038 0.038 0.038 0.038 0.038 0.033 0.034 0.034 0.034 0.034 0.034 0.034 <	MeOH 3 mL/min 150 bar	5.8	252	0.944	13.140	2.753	0.003	0.046	0.046	0.046	0.046
Me:OH 3: ml/min 320 bar 5.0 300 0.966 11.592 2.374 0.002 0.041 0.041 0.041 0.041 0.041 0.041 0.041 0.041 0.041 0.041 0.041 0.041 0.041 0.041 0.041 0.041 0.041 0.041 0.031 0.033 0.032 0.033 0.032 0.032 0.033 0.032 0.033 0.032 0.032 0.032 0.032 0.032 0.032 0.032 0.033 0.032 0.033 0.032 0.033 0.032 0.033 0.032 0.032 0.032 0.032 0.032 0.032 0.033 0.030 0.041 0.011 0.025 0.015 0.015 0.015 </td <td>MeOH 3 mL/min 170 bar</td> <td>5.4</td> <td>273</td> <td>0.954</td> <td>12.364</td> <td>2.564</td> <td>0.002</td> <td>0.044</td> <td>0.044</td> <td>0.044</td> <td>0.044</td>	MeOH 3 mL/min 170 bar	5.4	273	0.954	12.364	2.564	0.002	0.044	0.044	0.044	0.044
Mc 0H 3.5 mL/min 120 bar 4.8 287 0.961 12.916 2.658 0.002 0.039 0.034 0.038 0.033 0.031 0.031 0.031 0.031<	MeOH 3 mL/min 200 bar	5.0	300	0.966	11.592	2.374	0.002	0.041	0.041	0.041	0.041
MeOH 35, mL/min 270 bar 4.6 308 0.970 12.494 2.548 0.002 0.038 0.039 0.039 0.039 0.039 0.039 0.039 0.039 0.039 0.039 0.038 0.038 0.038 0.038 0.038 0.038 0.038 0.038 0.038 0.038 0.038 0.038 0.033 0.034 0.034 0.031 </td <td>MeOH 3.5 mL/min 150 bar</td> <td>4.8</td> <td>287</td> <td>0.961</td> <td>12.916</td> <td>2.658</td> <td>0.002</td> <td>0.040</td> <td>0.040</td> <td>0.040</td> <td>0.040</td>	MeOH 3.5 mL/min 150 bar	4.8	287	0.961	12.916	2.658	0.002	0.040	0.040	0.040	0.040
MEOH 3.5. mL/min 200 bar 4.4. 440 0.983 12.111 2.437 0.002 0.038 0.038 0.038 0.038 0.038 0.038 0.038 0.038 0.038 0.038 0.038 0.038 0.038 0.038 0.038 0.033 0.033 0.033 0.033 0.033 0.032 0.033 0.033 0.033 0.033 0.033 0.033 0.033 0.033 0.033 0.032 0.033 0.032 0.033 0.032 0.033 0.032 0.033 0.032 0.033 0.032 0.032 0.032 0.032 0.032 0.032 0.032 0.032 0.032 0.032 0.032 0.032 0.033 0.034 0.031 0.031 0.031	MeOH 3.5 mL/min 170 bar	4.6	308	0.970	12.494	2.548	0.002	0.039	0.039	0.039	0.039
Michael 1.1.086 2.4.09 0.002 0.034 0.033 0.034 0.035 0.035 0.035 0.035 0.035 0.035 0.036 0.037 0.036 0.036 0.036 0.036 0.036 0.036 0.036 0.036 0.036 0.037 0.037 0.037 0.037 0.037 0.037 0.037 0.037 0.037 0.037 0.037	MeOH 3.5 mL/min 200 bar	4.4	340	0.983	12.111	2.437	0.002	0.038	0.038	0.038	0.038
International 3.a 250 0.003 11.5M 2.405 0.002 0.033 0.032 E(DH 2 m//min 130 bar 14.5 179 0.900 20.880 4.572 0.004 0.091 0.090 0.090 0.090 0.090 0.090 0.094 0.085 0.056 <td>MoOH 4 mL/min 100 bar</td> <td>3.9</td> <td>207</td> <td>0.951</td> <td>11.868</td> <td>2.469</td> <td>0.002</td> <td>0.034</td> <td>0.034</td> <td>0.034</td> <td>0.034</td>	MoOH 4 mL/min 100 bar	3.9	207	0.951	11.868	2.469	0.002	0.034	0.034	0.034	0.034
Intervention Image	MeOH 4 mL/min 150 bar	3.7	316	0.903	11.734	2.403	0.002	0.033	0.033	0.033	0.033
th 2 mL/min 100 bar 15.3 148 0.875 21.420 4.824 0.004 0.105 0.105 0.105 Et0H 2 mL/min 130 bar 14.5 179 0.900 20.880 4.572 0.004 0.099 0.099 0.099 0.099 0.090 0.091 0.091 0.091 0.071 0.072 0.072 0.072 0.070 0.070 0.070 0.070 0.070 0.070 0.070 0.070 0.070 0.070 0.070 0.070		5.7	510	0.575	20% FtOH	2.342	0.002	0.052	0.055	0.052	0.032
tith 14.5 179 0.900 20.880 4.572 0.004 0.099 0.099 0.099 0.099 0.099 0.099 0.099 0.090 0.091 0.084 0.084 0.084 0.084 0.084 0.084 0.081 0.011 0.061 0.067 0.067 0.067 0.067 0.	EtOH 2 mL/min 100 bar	15.3	148	0.875	21.420	4.824	0.004	0.105	0.105	0.105	0.105
EtOH zml/min 150 bar 13.0 202 0.916 19.053 4.099 0.004 0.090 0.090 0.090 EtOH z ml/min 170 bar 112.6 2222 0.928 18.708 3.973 0.004 0.088 0.088 0.088 0.088 0.084 0.087 0.077 0.067 0.067 0.067 0.067 0.067 0.067 0.067 0.067 0.067 0.057 0.057 0.057 0.057 <	EtOH 2 mL/min 130 bar	14.5	179	0.900	20.880	4.572	0.004	0.099	0.099	0.098	0.099
EtOH 2 mL/min 170 bar 12.6 222 0.928 18.708 3.973 0.004 0.088 0.088 0.088 EtOH 2 mL/min 130 bar 12.0 252 0.944 18.125 3.783 0.003 0.084 0.072 0.072 0.072 0.072 0.070 0.070 0.070 0.067 0.067 0.067 0.067 0.067 0.067 0.067 0.067 0.057 0.055 0.055 0.055 0.055 0.057 0.057 0.057 0.057 0.057 0.057 0.057 0.056 0.055 0.055 0.055 0.055 0.055 0.055 0.055 0.055 0.055 0.055 0.055 0.055 0.055 0.055 0.055 0.055 <t< td=""><td>EtOH 2 mL/min 150 bar</td><td>13.0</td><td>202</td><td>0.916</td><td>19.053</td><td>4.099</td><td>0.004</td><td>0.091</td><td>0.090</td><td>0.090</td><td>0.090</td></t<>	EtOH 2 mL/min 150 bar	13.0	202	0.916	19.053	4.099	0.004	0.091	0.090	0.090	0.090
Et0H 2 ml/min 200 bar 12.0 252 0.944 18.125 3.783 0.003 0.084 0.084 0.084 Et0H 2.5 ml/min 150 bar 10.1 225 0.929 18.766 3.980 0.004 0.072 0.072 0.072 0.072 0.072 0.072 0.072 0.072 0.072 0.072 0.072 0.072 0.072 0.072 0.072 0.072 0.072 0.070 0.071 0.051 0.051 0.051 0.051 0.051 0.051 0.051 0.051 0.055 0.055 0.055	EtOH 2 mL/min 170 bar	12.6	222	0.928	18.708	3.973	0.004	0.088	0.088	0.088	0.088
EtOH 2.5 mL/min 150 bar 10.1 225 0.929 18.766 3.980 0.004 0.072 0.072 0.072 0.072 0.072 0.072 0.072 0.072 0.070 0.071 0.061 EtOH 3.5 0.111 0.051 0.055 0.0	EtOH 2 mL/min 200 bar	12.0	252	0.944	18.125	3.783	0.003	0.084	0.084	0.084	0.084
EtOH 2.5 mL/min 170 bar 10.0 245 0.940 18.800 3.941 0.004 0.070 0.070 0.070 EtOH 2.5 mL/min 200 bar 9.6 275 0.955 118.336 3.783 0.003 0.067 0.067 0.067 0.067 0.067 0.067 0.057 0.059 0.059 0.059 0.059 0.059 0.057 0.057 0.057 0.057 0.057 0.057 0.057 0.057 0.057 0.057 0.057 0.057 0.057 0.055	EtOH 2.5 mL/min 150 bar	10.1	225	0.929	18.766	3.980	0.004	0.072	0.072	0.072	0.072
Etch 2, sm //mi 200 Bar 9,6 2/5 0.955 18.36 3.783 0.003 0.067 0.067 0.067 0.067 EtCH 3 m //mi 150 bar 8.0 271 0.953 18.298 3.783 0.003 0.059 0.059 0.059 EtOH 3 m //mi 120 bar 7.7 302 0.967 17.870 3.642 0.003 0.057 0.057 0.056 0.056 EtOH 3.5 m //mi 120 bar 7.3 305 0.9690 19.806 4.085 0.004 0.055 0.055 0.055 0.055 0.051 0.051 0.052 0.052 0.052 0.052 0.052 0.054 0.055 0.055 0.055 0.055 0	EtOH 2.5 mL/min 170 bar	10.0	245	0.940	18.800	3.941	0.004	0.070	0.070	0.070	0.070
Eton B mL/min 130 bar 8.3 252 0.944 18.894 3.925 0.004 0.062 0.061 0.061 0.061 0.061 0.061 0.061 0.061 0.061 0.061 0.061 0.061 0.061 0.059 0.059 0.059 0.057 0.057 0.057 0.057 0.057 0.057 0.057 0.057 0.057 0.057 0.057 0.056 0.056 0.055 <td>EtOH 2.5 mL/min 200 bar</td> <td>9.6</td> <td>275</td> <td>0.955</td> <td>18.336</td> <td>3.783</td> <td>0.003</td> <td>0.067</td> <td>0.067</td> <td>0.067</td> <td>0.067</td>	EtOH 2.5 mL/min 200 bar	9.6	275	0.955	18.336	3.783	0.003	0.067	0.067	0.067	0.067
LCD13 mL/min 120 bar 8.0 27.7 302 0.957 1.783 3.783 0.003 0.035 0.035 0.035 0.035 0.035 0.035 0.035 0.035 0.035 0.035 0.035 0.057 0.057 0.057 0.057 0.057 0.057 0.057 0.057 0.055 0.056 EtOH 3.5 mL/min 170 bar 7.3 305 0.969 19.866 4.085 0.004 0.052 0.055 0.055 0.055 0.055 0	EtOH 3 mL/min 150 bar	8.3	252	0.944	18.804	3.925	0.004	0.062	0.061	0.061	0.061
Eton H, Jim John Job	EtOH 3 mL/min 200 bar	7.7	302	0.955	17.870	3.785	0.003	0.055	0.057	0.055	0.055
EtOH 3.5 mL/min 170 bar 7.3 305 0.963 19.806 4.085 0.001 0.057 0.055 0.055 EtOH 3.5 mL/min 170 bar 7.1 337 0.982 19.522 3.973 0.004 0.054 0.054 0.054 0.054 EtOH 4 mL/min 100 bar 6.9 272 0.954 21.064 4.351 0.004 0.052 0.055 0.056 0.059 0.050 0.050 0.050 0.050 0.050 0.050 0.050 0.050 0.050 0.050 0.050 0.050 0.058 0.058 0.058 0.058 0.058 0.058 0.058 0.058 0.058 0.057 0.057 0.057 0.057 0.057 0.057 0.057 0.057 0.057 0.057 0.057	EtOH 3.5 ml /min 150 bar	7.5	285	0.960	20,160	4,197	0.004	0.057	0.056	0.056	0.056
EtOH 3.5 mL/min 200 bar 7.1 337 0.982 19.522 3.973 0.004 0.054 0.054 0.054 EtOH 4 mL/min 100 bar 6.9 272 0.954 21.064 4.351 0.004 0.053 0.053 0.053 0.052 0.052 0.052 0.052 0.052 0.052 0.052 0.052 0.050 0.058 0.058 0.058 0.058 0.058 0.058 0.057 <t< td=""><td>EtOH 3.5 mL/min 170 bar</td><td>7.3</td><td>305</td><td>0.969</td><td>19.806</td><td>4.085</td><td>0.004</td><td>0.055</td><td>0.055</td><td>0.055</td><td>0.055</td></t<>	EtOH 3.5 mL/min 170 bar	7.3	305	0.969	19.806	4.085	0.004	0.055	0.055	0.055	0.055
EtOH 4 mL/min 130 bar6.92720.95421.0644.3510.0040.0530.0530.0530.053EtOH 4 mL/min 130 bar6.73030.96820.7544.2250.0040.0520.0520.052EtOH 4 mL/min 130 bar6.53250.97720.3224.0990.0040.0500.0500.050EtOH 4 mL/min 130 bar6.53250.97720.3224.0990.0040.0500.0500.050IPA 2 mL/min 100 bar8.01650.8898.5345.0250.0050.0580.0580.058IPA 2 mL/min 130 bar7.81970.9128.5364.9000.00570.0570.0570.057IPA 2 mL/min 150 bar7.72180.9258.5474.8370.0040.0570.0570.057IPA 2 mL/min 120 bar7.52670.9518.5594.7110.0040.0560.0560.056IPA 2.5 mL/min 150 bar6.22350.9358.6964.8680.0050.0480.0480.048IPA 2.5 mL/min 120 bar5.12650.9508.7214.8060.0040.0410.0410.041IPA 3.5 mL/min 120 bar5.12650.9508.7214.8060.0040.0410.0410.041IPA 3.5 mL/min 120 bar5.12650.9508.7214.8060.0040.0410.0410.041IPA 3.5 mL/min 120 bar4.93160.9738.582	EtOH 3.5 mL/min 200 bar	7.1	337	0.982	19.522	3.973	0.004	0.054	0.054	0.054	0.054
EtOH 4 mL/min 130 bar6.73030.96820.7544.2250.0040.0520.0520.0520.052EtOH 4 mL/min 150 bar6.53250.97720.3224.0990.0040.0510.0500.0500.0500.050PA 2 mL/min 100 bar8.01650.8898.5345.0250.0050.0580.0580.0580.0580.0580.0590.0570.0570.0570.0570.0570.0570.0570.0570.0570.0570.0560.05	EtOH 4 mL/min 100 bar	6.9	272	0.954	21.064	4.351	0.004	0.053	0.053	0.053	0.053
EtOH 4 mL/min 150 bar 6.5 325 0.977 20.322 4.099 0.004 0.050 0.050 0.050 0.050 0.050 40% IPA IPA 2 mL/min 130 bar 7.8 197 0.912 8.534 5.025 0.005 0.059 0.059 0.058 IPA 2 mL/min 130 bar 7.8 197 0.912 8.536 4.900 0.004 0.057 0.057 0.057 0.057 IPA 2 mL/min 150 bar 7.7 218 0.925 8.547 4.837 0.004 0.057 0.057 0.057 0.057 IPA 2 mL/min 170 bar 7.6 239 0.937 8.545 4.774 0.004 0.056 0.056 0.056 0.056 IPA 2.5 mL/min 150 bar 6.1 256 0.946 8.656 4.790 0.004 0.047 0.047 0.047 0.047 IPA 2.5 mL/min 170 bar 5.1 265 0.950 8.721 4.806 0.004 0.041 0.041 0.041 0.041 <td< td=""><td>EtOH 4 mL/min 130 bar</td><td>6.7</td><td>303</td><td>0.968</td><td>20.754</td><td>4.225</td><td>0.004</td><td>0.052</td><td>0.052</td><td>0.052</td><td>0.052</td></td<>	EtOH 4 mL/min 130 bar	6.7	303	0.968	20.754	4.225	0.004	0.052	0.052	0.052	0.052
40% IPA IPA 2 mL/min 100 bar 8.0 165 0.889 8.534 5.025 0.005 0.059 0.059 0.059 0.058 0.058 IPA 2 mL/min 130 bar 7.8 197 0.912 8.536 4.900 0.005 0.058 0.058 0.058 0.058 0.058 0.057 IPA 2 mL/min 150 bar 7.7 218 0.925 8.547 4.837 0.004 0.057 0.057 0.057 0.057 IPA 2 mL/min 170 bar 7.6 239 0.937 8.545 4.774 0.004 0.057 0.057 0.057 0.057 IPA 2.5 mL/min 150 bar 6.2 235 0.935 8.696 4.868 0.005 0.048 0.048 0.048 0.048 0.048 0.048 0.048 0.048 0.046 0.466 0.4655 4.790 0.004 0.041 0.041 0.041 0.041 0.041 0.041 0.041 0.041 0.041 0.041 0.041 0.041 0.041	EtOH 4 mL/min 150 bar	6.5	325	0.977	20.322	4.099	0.004	0.050	0.050	0.050	0.050
IPA 2 mL/min 100 bar 8.0 165 0.889 8.534 5.025 0.005 0.059 0.057 <td></td> <td></td> <td>4.65</td> <td>0.000</td> <td>40% IPA</td> <td>5.005</td> <td>0.005</td> <td>0.050</td> <td>0.050</td> <td>0.050</td> <td>0.050</td>			4.65	0.000	40% IPA	5.005	0.005	0.050	0.050	0.050	0.050
IPA 2 mL/min 150 bar 7.8 197 0.912 8.336 4.900 0.003 0.038 0.057 <td>IPA 2 mL/min 100 bar</td> <td>8.0</td> <td>165</td> <td>0.889</td> <td>8.534</td> <td>5.025</td> <td>0.005</td> <td>0.059</td> <td>0.059</td> <td>0.059</td> <td>0.059</td>	IPA 2 mL/min 100 bar	8.0	165	0.889	8.534	5.025	0.005	0.059	0.059	0.059	0.059
IPA 2 mL/min 170 bar 7.6 239 0.937 8.547 4.637 0.004 0.057 <td>IPA 2 mL/min 150 bar</td> <td>7.8</td> <td>218</td> <td>0.912</td> <td>8.530</td> <td>4.900</td> <td>0.005</td> <td>0.058</td> <td>0.058</td> <td>0.058</td> <td>0.058</td>	IPA 2 mL/min 150 bar	7.8	218	0.912	8.530	4.900	0.005	0.058	0.058	0.058	0.058
Internmin 200 bar 7.5 267 0.951 8.559 4.771 0.004 0.056 0.056 0.056 IPA 2.5 mL/min 150 bar 6.2 235 0.935 8.696 4.868 0.005 0.048 0.048 0.048 0.048 0.048 0.048 0.048 0.048 0.048 0.048 0.048 0.048 0.048 0.047 0.041 0.041 0.041 0.041 0.041 0.041 0.041 0.041 0.041 0.041 0.041 0.041 0.041 0.041 0.041 0	IPA 2 mL/min 130 bar	7.6	218	0.925	8 545	4.837	0.004	0.057	0.057	0.057	0.057
IPA 2.5 mL/min 150 bar 6.2 235 0.935 8.696 4.868 0.005 0.048 0.048 0.048 IPA 2.5 mL/min 170 bar 6.1 256 0.946 8.656 4.790 0.004 0.047 0.047 0.047 0.047 IPA 2.5 mL/min 170 bar 5.9 287 0.961 8.505 4.633 0.004 0.046 0.046 0.046 0.046 0.046 0.046 0.046 0.046 0.046 0.047 0.041 0.041 0.041 0.041 0.041 0.041 0.041 0.040 0.040 0.040 0.040 0.040 0.040 0.040 0.040	IPA 2 mL/min 200 bar	7.5	267	0.951	8.559	4.711	0.004	0.056	0.056	0.056	0.056
PA 2.5 mL/min 170 bar 6.1 256 0.946 8.656 4.790 0.004 0.047 0.047 0.047 IPA 2.5 mL/min 200 bar 5.9 287 0.961 8.505 4.633 0.004 0.046 0.046 0.046 0.046 0.046 0.046 0.046 0.046 0.046 0.046 0.046 0.041 0.040 0.040 0.040 0.040 0.040 0.040 0.040 0.040 0.043 0.337 0.337 0	IPA 2.5 mL/min 150 bar	6.2	235	0.935	8.696	4.868	0.005	0.048	0.048	0.048	0.048
PA 2.5 mL/min 200 bar 5.9 287 0.961 8.505 4.633 0.004 0.046 0.046 0.046 PA 3 mL/min 150 bar 5.1 265 0.950 8.721 4.806 0.004 0.041 0.041 0.041 0.041 PA 3 mL/min 170 bar 5.0 286 0.960 8.640 4.711 0.004 0.041 0.041 0.041 0.041 PA 3 mL/min 170 bar 4.9 316 0.973 8.582 4.617 0.004 0.040 0.037 0.037 0.037 0.037 0.037 0.037 0.037 0.037 0.037 0.037 0.037 0.037 0.037 0.037 0.036 0.036 0.036 0.036 0.036 0.036	IPA 2.5 mL/min 170 bar	6.1	256	0.946	8.656	4.790	0.004	0.047	0.047	0.047	0.047
IPA 3 mL/min 150 bar 5.1 265 0.950 8.721 4.806 0.004 0.041 0.041 0.041 IPA 3 mL/min 170 bar 5.0 286 0.960 8.640 4.711 0.004 0.041 0.041 0.041 0.041 IPA 3 mL/min 120 bar 4.9 316 0.973 8.582 4.617 0.004 0.040 0.041 0.041 0.041 0.041 0.041 0.041 0.041 0.041 0.041 0.041 0.041 0.040 0.040 0.041 0.041 0.041 0.041 0.041 0.041 0.041 <	IPA 2.5 mL/min 200 bar	5.9	287	0.961	8.505	4.633	0.004	0.046	0.046	0.046	0.046
IPA 3 mL/min 170 bar 5.0 286 0.960 8.640 4.711 0.004 0.041 0.041 0.040 0.041 IPA 3 mL/min 200 bar 4.9 316 0.973 8.582 4.617 0.004 0.040 0.037 0.037 0.037 0.037 0.037 0.037 0.036 0.03	IPA 3 mL/min 150 bar	5.1	265	0.950	8.721	4.806	0.004	0.041	0.041	0.041	0.041
IPA 3 mL/min 200 bar 4.9 316 0.973 8.582 4.617 0.004 0.040 0.037 0.036 0.036 0.036 0.036 0.036 0.036 0.036 0.036 0.036 0.036 0.034 0.033 0.033 0.033 0.034 0.034 0.033 0.033 0.033 0.033 0.033 0.033 0.033 0.033 0.033 0.033	IPA 3 mL/min 170 bar	5.0	286	0.960	8.640	4.711	0.004	0.041	0.041	0.040	0.041
IPA 3.5 mL/min 120 bar 4.4 268 0.952 8.796 4.837 0.004 0.037 0.037 0.037 0.037 IPA 3.5 mL/min 150 bar 4.3 301 0.967 8.732 4.727 0.004 0.036 0.034 0.034 0.034 0.034 0.034 0.034 0.034 0.034 0.034 0.034 0.034 0.034 0.034 0.034 0.034 0.034 0.034 0.034 0.033 0.033 0.033 0.033 0.033 0.033 0.032	IPA 3 mL/min 200 bar	4.9	316	0.973	8.582	4.617	0.004	0.040	0.040	0.040	0.040
IIPA 3.5 mL/min 150 bar 4.3 301 0.967 8.732 4.727 0.004 0.036 0.034 0.033 0.033 0.034 0.034 0.033 0.033 0.033 0.033 0.033 0.033 0.033 0.032 <td>IPA 3.5 mL/min 120 bar</td> <td>4.4</td> <td>268</td> <td>0.952</td> <td>8.796</td> <td>4.837</td> <td>0.004</td> <td>0.037</td> <td>0.037</td> <td>0.037</td> <td>0.037</td>	IPA 3.5 mL/min 120 bar	4.4	268	0.952	8.796	4.837	0.004	0.037	0.037	0.037	0.037
IPA A:s.mL/min 1/0 bar 4.3 321 0.975 8.804 4.727 0.004 0.036 0.037 0.034 0.034 0.034 0.034 0.034 0.034 0.034 0.034 0.034 0.034 0.034 0.034 0.034 0.033 0.033 0.033 0.033 0.033 0.033 0.033 0.033 0.032 <td>IPA 3.5 mL/min 150 bar</td> <td>4.3</td> <td>301</td> <td>0.967</td> <td>8.732</td> <td>4.727</td> <td>0.004</td> <td>0.036</td> <td>0.036</td> <td>0.036</td> <td>0.036</td>	IPA 3.5 mL/min 150 bar	4.3	301	0.967	8.732	4.727	0.004	0.036	0.036	0.036	0.036
Incrementation 5.7 267 0.502 9.004 4.900 0.005 0.034	IPA 3.5 mL/min 1/0 bar	4.3	321	0.975	8.804	4./2/	0.004	0.036	0.036	0.036	0.036
Brack mining for boar 3.7 344 0.984 8,738 4,648 0.004 0.032	IPA 4 mL/min 100 bar	3.9	209	0.902	9.004	4.900	0.005	0.034	0.034	0.033	0.034
	IPA 4 mL/min 150 bar	3.7	344	0.984	8,738	4.648	0.004	0.032	0.032	0.032	0.032

Table S5 Solvent consumption and energy consumption information for the high retention mix separations.

	High Retention Mix Information										
HPLC											
Separation Parameters		AMGS Calcula	tor Results					LCA Results			
Separation Type	Instrument Energy Score	Solvent Energy Score	Solvent EHS Score	Greenness Score	CED (MJ)	GHG (kg of CO ₂ eq.)	ONGD (kg eq.)	ACID (kg of SO ₂ eq.)	EUTR (kg of (PO ₄) ³⁻ eq.)	PCOP (kg of ethane eq.)	
80% ACN 2 mL/min	94.45	420.98	49.27	564.69	50.2	2.40	1.20	8.88E-03	9.70E-04	9.13E-04	
80% MeOH 1.5 mL/min	214.67	234.25	70.90	519.82	41.3	1.74	0.967	1.28E-02	5.00E-04	0.0678	
57% EtOH 0.75 mL/min	719.13	274.41	64.16	1057.70	116	5.97	2.72	4.25E-02	1.79E-03	0.229	
43% IPA 0.625 mL/min	826.47	310.35	57.82	1194.64	112	5.94	2.59	4.82E-02	1.88E-03	0.0813	
					SFC						
MaOH 2 ml /min 100 har	254.22	102.16	40.05	477 54		2 1 2	1 27	2 705 02	1.015.02	2 525 02	
MeOH 2 mL/min 100 bar	234.32	171.60	40.05	4/7.54	55.6	3.13	1.37	2.70E-02	9.385-04	2.53E-02	
MeOH 2 mL/min 150 bar	230.87	161.69	36.82	440.78	53.0	2.32	1.20	2.52L-02	8.96E-04	2.33E-02	
MeOH 2 mL/min 130 bar MeOH 2 mL/min 170 bar	214.43	156.73	36.07	407.23	52.1	2.74	1.20	2.37E-02	8.82E-04	2.14E-02	
MeOH 2 mL/min 200 bar	201.96	148.47	34.82	385.25	49.6	2.61	1.14	2.26E-02	8.40E-04	2.02E-02	
MeOH 2.5 mL/min 150 bar	172.04	157.14	36.13	365.31	44.7	2.31	1.03	1.96E-02	7.39E-04	2.11E-02	
MeOH 2.5 mL/min 170 bar	164.56	150.95	35.20	350.71	43.0	2.22	0.991	1.89E-02	7.11E-04	2.01E-02	
MeOH 2.5 mL/min 200 bar	157.08	144.75	34.26	336.10	42.0	2.18	0.967	1.85E-02	6.96E-04	1.93E-02	
MeOH 3 mL/min 150 bar	144.61	158.38	36.32	339.31	40.1	2.04	0.925	1.71E-02	6.49E-04	2.10E-02	
MeOH 3 mL/min 170 bar	134.64	148.47	34.82	317.93	38.1	1.95	0.881	1.63E-02	6.20E-04	1.96E-02	
MeOH 3 mL/min 200 bar	124.67	138.56	33.33	296.56	35.5	1.82	0.820	1.52E-02	5.78E-04	1.81E-02	
MeOH 3.5 mL/min 150 bar	119.68	153.43	35.57	308.68	35.8	1.80	0.827	1.49E-02	5.70E-04	2.01E-02	
MeOH 3.5 mL/min 170 bar	114.69	147.64	34.70	297.03	34.8	1.76	0.803	1.45E-02	5.55E-04	1.93E-02	
MeOH 3.5 mL/min 200 bar	109.71	141.86	33.83	285.40	33.8	1.70	0.780	1.41E-02	5.41E-04	1.85E-02	
MoOH 4 mL/min 100 bar	97.24	143.51	34.08	2/4.83	31.0	1.55	0.718	1.27E-02	4.88E-04	1.85E-02	
MeOH 4 mL/min 150 bar	97.75	136.90	33.08	262.24	29.6	1.30	0.685	1.23E-02	4.746-04	1.812-02	
Meon 4 mL/mm 150 bar	52.25	150.50	55.00	202.24	20% EtOH	1.47	0.005	1.201-02	4.052-04	1.702-02	
EtOH 2 mL/min 100 bar	381.48	266.39	45.11	692.98	94.300	4.99	2.18	3.94E-02	1.57E-03	0.100	
EtOH 2 mL/min 130 bar	361.53	253.23	43.52	658.28	88.900	4.71	2.06	3.70E-02	1.48E-03	9.49E-02	
EtOH 2 mL/min 150 bar	324.13	228.55	40.53	593.21	88.100	4.29	1.88	3.39E-02	1.35E-03	8.51E-02	
EtOH 2 mL/min 170 bar	314.16	221.97	39.73	575.86	79.000	4.18	1.83	3.30E-02	1.31E-03	8.25E-02	
EtOH 2 mL/min 200 bar	299.20	212.09	38.54	549.83	75.400	3.99	1.75	3.15E-02	1.25E-03	7.86E-02	
EtOH 2.5 mL/min 150 bar	251.83	222.38	39.78	513.99	68.200	3.55	1.58	2.71E-02	1.11E-03	8.21E-02	
EtOH 2.5 mL/min 170 bar	249.33	220.32	39.54	509.19	66.700	3.47	1.55	2.64E-02	1.08E-03	8.13E-02	
EtOH 2.5 mL/min 200 bar	239.36	212.09	38.54	489.99	64.000	3.32	1.48	2.53E-02	1.03E-03	7.80E-02	
EtOH 3 mL/min 150 bar	206.95	219.50	39.44	465.88	60.800	3.13	1.41	2.32E-02	9.66E-04	8.06E-02	
EtOH 3 mL/min 170 bar	199.47	212.09	38.54	450.10	58.500	3.02	1.36	2.23E-02	9.30E-04	7.77E-02	
EtOH 3 5 mL/min 200 bar	191.99	204.05	41.04	454.52	58 700	2.91	1.32	2.16E-02	9.13E-04	7.48E-02 8.59E-02	
EtOH 3.5 mL/min 150 bar	187.00	226.17	40.33	400.00	57.300	2.91	1.37	2.14L-02	8.19F-04	8.35E-02	
EtOH 3.5 mL/min 200 bar	177.03	220.37	39.63	437.03	56.100	2.85	1.31	2.05E-02	8.74E-04	8.13E-02	
EtOH 4 mL/min 100 bar	172.04	241.71	42.12	455.87	57.200	2.88	1.34	2.02E-02	8.77E-04	8.88E-02	
EtOH 4 mL/min 130 bar	167.05	235.13	41.33	443.51	56.000	2.82	1.31	1.98E-02	8.59E-04	8.63E-02	
EtOH 4 mL/min 150 bar	162.07	228.55	40.53	431.15	54.100	2.72	1.26	1.91E-02	8.28E-04	8.37E-02	
					40% IPA						
IPA 2 mL/min 100 bar	199.47	252.66	44.75	496.88	57.400	2.93	1.34	2.23E-02	9.16E-04	4.95E-02	
IPA 2 mL/min 130 bar	194.48	246.71	44.00	485.19	56.300	2.88	1.31	2.19E-02	9.00E-04	4.83E-02	
IPA 2 mL/min 150 bar	191.99	243.74	43.62	479.35	55.500	2.83	1.29	2.15E-02	8.85E-04	4.77E-02	
IPA 2 mL/min 170 bar	189.49	240.76	43.25	473.50	55.300	2.83	1.29	2.15E-02	8.84E-04	4.71E-02	
IPA 2 mL/min 200 bar	187.00	237.79	42.87	467.66	54.400	2.78	1.2/	2.11E-02	8.69E-04	4.65E-02	
IPA 2.5 mL/min 150 bar	152.00	245.22	43.81	443.62	49.500	2.49	1.15	1.82E-02	7.70E-04	4.77E-02	
IPA 2.5 mL/min 200 bar	147 11	234.07	43.54	430.33	47.400	2.44	1 11	1.75E-02	7.332-04	4.092-02	
IPA 3 mL/min 150 bar	127.16	242.25	43.43	412.84	44.600	2.20	1.04	1.57E-02	6.77E-04	4.68E-02	
IPA 3 mL/min 170 bar	124.67	237.79	42.87	405.33	44.000	2.19	1.03	1.55E-02	6.70E-04	4.59E-02	
IPA 3 mL/min 200 bar	122.17	233.32	42.30	397.80	43.300	2.15	1.01	1.53E-02	6.59E-04	4.50E-02	
IPA 3.5 mL/min 120 bar	109.71	243.74	43.62	397.07	42.000	2.06	0.983	1.42E-02	6.26E-04	4.70E-02	
IPA 3.5 mL/min 150 bar	107.21	238.53	42.96	388.70	41.000	2.00	0.959	1.38E-02	6.10E-04	4.59E-02	
IPA 3.5 mL/min 170 bar	107.21	238.53	42.96	388.70	41.000	2.00	0.960	1.38E-02	6.11E-04	4.59E-02	
IPA 4 mL/min 100 bar	97.24	246.71	44.00	387.95	40.000	1.93	0.938	1.30E-02	5.85E-04	4.74E-02	
IPA 4 mL/min 120 bar	94.75	240.76	43.25	378.76	39.100	1.90	0.917	1.27E-02	5.73E-04	4.62E-02	
IPA 4 mL/min 150 bar	92.25	234.81	42.49	369.55	38.000	1.74	0.892	1.23E-02	5.56E-04	4.50E-02	

 Table S6 LCA and AMGS Calculator results for the high retention mix separations.



Figure S9 Metric results for the high retention mixture of the 150bar BPR SFC separations and HPLC for the different metrics calculated. The displayed impact factors/greenness metrics are the greenness score (A), CED (B), GHG (C), ONGD (D), ACID (E), EUTR (F), and PCOP (G).



Figure S10 Percent contribution to each impact factor from each portion of the system for the LCA analysis. Example SFC separations are for the high retention mix, and each are for the 3 mL/min and 150bar BPR separations. The separation with methanol, ethanol, and isopropanol in SFC are shown in A, B, and C respectively. TEA had a contribution of less than 0.5% of the total of each.



Figure S11 Percent contribution to each impact factor from each portion of the system for the LCA analysis. HPLC separations are for the high retention mix. The separation with methanol, ethanol, isopropanol, acetonitrile in HPLC is shown in A, B, C, and D respectively. The contribution of TEA and water was less than 0.5% and 0.02% of the total respectively.



Low Retention Mix 7% MeOH 2 mL/min BPR Comparison

Figure S12 Separations of the low retention mix using SFC. Mobile phase consisted of 93% liquified CO_2 and 7% MeOH. The organic solvent had acetic acid added to it at 0.1% (v/v) concentration. The flow rate was set to 2mL/min for each and the column temperature was 40°C. The retention order was ketoprofen, hydrocortisone, prednisone, indapamide.



Low Retention Mix 7% MeOH Flow Rate Comparison

Figure S13 Separations of the low retention mix using SFC. Mobile phase consisted of 93% liquified CO₂ and 7% MeOH. The organic solvent had acetic acid added to it at 0.1% (v/v) concentration. The flow rate and BPR pressure is listed for each. The column temperature was 40°C for all separation. The retention order was ketoprofen, hydrocortisone, prednisone, indapamide.

Low Retention Mix 7% EtOH 2 mL/min BPR Comparison



Figure S14 Separations of the low retention mix using SFC. Mobile phase consisted of 93% liquified CO_2 and 7% EtOH. The organic solvent had acetic acid added to it at 0.1% (v/v) concentration. The flow rate was set to 2mL/min for each and the column temperature was 40°C. The retention order was ketoprofen, hydrocortisone, prednisone, indapamide.



Figure S15 Separations of the low retention mix using SFC. Mobile phase consisted of 93% liquified CO₂ and 7% EtOH. The organic solvent had acetic acid added to it at 0.1% (v/v) concentration. The flow rate and BPR pressure is listed for each. The column temperature was 40°C for all separation. The retention order was ketoprofen, hydrocortisone, prednisone, indapamide.



Low Retention Mix 10% IPA 2 mL/min BPR Comparison

Figure S16 Separations of the low retention mix using SFC. Mobile phase consisted of 90% liquified CO_2 and 10% IPA. The organic solvent had acetic acid added to it at 0.1% (v/v) concentration. The flow rate was set to 2mL/min for each and the column temperature was 40°C. The retention order was ketoprofen, hydrocortisone, prednisone, indapamide.



Low Retention Mix 10% IPA Flow Rate Comparison

Figure S17 Separations of the low retention mix using SFC. Mobile phase consisted of 90% liquified CO₂ and 10% IPA. The organic solvent had acetic acid added to it at 0.1% (v/v) concentration. The flow rate and BPR pressure is listed for each. The column temperature was 40°C for all separation. The retention order was ketoprofen, hydrocortisone, prednisone, indapamide.

Low Retention Mix HPLC Comparison



Figure S18 Separations of the high retention mix using HPLC. The organic portion of each mobile phase composition for each solvent is listed and water makes up the remaining percentage. The organic solvent had triethylamine added to it at 0.1% (v/v) concentration. The flow rate is listed for each separation and corresponds to a system pressure of approximately 300, 350, 400 bar respectively. The column temperature was 40°C for all separations. The retention order was indapamide, prednisone, hydrocortisone, ketoprofen for the alcohol separation. The retention order for the ACN separation was prednisone, hydrocortisone, indapamide, ketoprofen.

Low Retention Mix Separation Information											
				HPLC							
Separati	on Parameters			Solvent Usa	ge per Injection		Instrumen	t Energy Co	onsumption	h (kWh)	
Separation Type	Separation Time	Pressure (bar)		Mass of Water (g)	Mass of Organic (g)	Mass of Acetic Acid (g)	Trial 1	Trial 2	Trial 3	Average	
28% ACN 1.8 mL/min	24.0	341		30.980	9.498	0.0453	0.081	0.081	0.081	0.081	
28% ACN 1.8 mL/min	8.0	340		10.327	3.166	0.0151	0.028	0.028	0.027	0.028	
60% MeOH 1 mL/min	8.2	291		3.267	3.893	0.0086	0.034	0.034	0.034	0.034	
60% MeOH 1.2 mL/min	7.3	346		3.490	4.159	0.0092	0.025	0.025	0.025	0.025	
60% MeOH 1.4 mL/min	6.3	396		3.514	4.187	0.0093	0.023	0.023	0.022	0.023	
40% EtOH 0.7 mL/min	14.0	305		5.856	3.090	0.0103	0.046	0.046	0.046	0.046	
40% EtOH 0.8 mL/min	12.5	350		5.976	3.153	0.0105	0.042	0.042	0.042	0.042	
40% EtOH 0.95 mL/min	11.2	401		6.358	3.355	0.0112	0.039	0.038	0.038	0.038	
33% IPA 0.6 mL/min	12.0	294		5.522	1.866	0.0076	0.04	0.04	0.04	0.040	
33% IPA 0.725 mL/min	10.5	349		5.838	1.973	0.0080	0.035	0.035	0.035	0.035	
33% IPA 0.85 mL/min	9.2	396		5.997	2.026	0.0082	0.032	0.031	0.031	0.031	
				SFC							
				7% MeOH							
Separati	on Parameters			Solvent Usa	ge per Injection		Instrumen	t Energy Co	onsumption	h (kWh)	
Separation Type	Separation Time	Pressure (bar)	Density of CO ₂ (g/mL)	Mass of CO ₂ (g)	Mass of Organic (g)	Mass of TEA (g)	Trial 1	Trial 2	Trial 3	Average	
MeOH 2 mL/min 100 bar	11.8	145	0.872	19.139	1.307	0.0017	0.083	0.083	0.083	0.083	
MeOH 2 mL/min 130 bar	10.0	176	0.898	16.703	1.108	0.0015	0.071	0.071	0.071	0.071	
MeOH 2 ml /min 150 bar	9.2	196	0.912	15.606	1.019	0.0014	0.066	0.066	0.066	0.066	
MeOH 2 mL/min 170 bar	8.8	217	0.925	15,140	0.975	0.0013	0.064	0.064	0.063	0.064	
MeOH 2 mL/min 200 bar	8.0	247	0.941	14.002	0.886	0.0012	0.058	0.058	0.058	0.058	
MeOH 2.5 mL/min 150 bar	6.8	217	0.925	14.624	0.942	0.0012	0.051	0.051	0.051	0.051	
MeOH 2.5 ml /min 170 bar	6.5	238	0.937	14 160	0.900	0.0012	0.049	0.049	0.049	0.049	
MeOH 2.5 ml /min 200 bar	6.1	268	0.952	13 502	0.845	0.0011	0.046	0.046	0.046	0.046	
MeOH 3 ml /min 150 bar	5.5	251	0.943	14 470	0.914	0.0012	0.044	0.044	0.044	0.044	
MeOH 3 ml /min 170 bar	5.2	270	0.953	13,826	0.864	0.0011	0.042	0.042	0.042	0.042	
MeOH 3 ml /min 200 bar	4.8	298	0.966	12 937	0.798	0.0011	0.039	0.039	0.039	0.039	
MeOH 3 5 ml /min 150 bar	4.6	265	0.950	14 224	0.897	0.0011	0.038	0.038	0.038	0.038	
MeOH 3.5 mL/min 170 bar	4.0	286	0.960	13 7/9	0.852	0.0011	0.037	0.036	0.036	0.036	
MeOH 3.5 mL/min 200 bar	4.4	316	0.973	12 668	0.355	0.0011	0.034	0.034	0.034	0.034	
MeOH 4 ml /min 100 bar	4.0	283	0.959	14 270	0.886	0.0010	0.034	0.034	0.034	0.034	
MeOH 4 ml /min 130 bar	2.0	306	0.969	12 609	0.800	0.0012	0.034	0.034	0.032	0.034	
MeOH 4 ml /min 150 bar	3.6	325	0.977	13.084	0.798	0.0011	0.032	0.032	0.032	0.032	
Meon 4 meynin 150 bar	3.0	325	0.377	70/ 5404	0.758	0.0011	0.032	0.032	0.032	0.032	
Et Old 2 mail (main 100 has	15.5	143	0.870	25.092	1 710	0.0013	0.105	0.105	0.105	0.105	
EtOH 2 mL/min 100 bar	13.5	145	0.870	25.062	1.710	0.0025	0.105	0.105	0.105	0.105	
EtOH 2 mL/min 150 bar	13.0	1/4	0.096	21.005	1.435	0.0019	0.089	0.089	0.089	0.089	
EtOH 2 mL/min 130 bar	12.0	215	0.911	18.005	1.524	0.0016	0.085	0.085	0.065	0.065	
EtOH 2 mL/min 170 bar	10.2	215	0.924	17.905	1.214	0.0016	0.078	0.070	0.078	0.077	
EtOH 2 Eml (min 150 bar	10.2	247	0.941	10.460	1.120	0.0013	0.075	0.075	0.075	0.075	
EtOH 2.5 mL/min 130 bar	9.0	220	0.950	19.400	1.241	0.0017	0.068	0.060	0.060	0.060	
EtOH 2.5 mL/min 200 bar	0.4	244	0.940	17 201	1.159	0.0013	0.062	0.062	0.062	0.062	
EtOH 2 ml /min 150 bar	7.0	2/2	0.934	19.660	1.076	0.0014	0.059	0.058	0.059	0.059	
EtOH 3 mL/min 130 bar	7.1	240	0.942	17.520	1.173	0.0015	0.054	0.054	0.034	0.054	
EtOH 2 mL/min 200 bar	6.0	209	0.952	16.070	1.032	0.0013	0.031	0.03	0.03	0.030	
EtOH 3 5 mL/min 150 bar	6.0	300	0.960	10.373	1.043	0.0014	0.049	0.045	0.045	0.049	
EtOH 3.5 mL/min 150 bar	5.0	207	0.901	17 600	1.133	0.0013	0.047	0.040	0.047	0.04/	
EtOH 3.5 mL/min 170 bar	5.0	342	0.971	16.075	1.001	0.0014	0.043	0.044	0.044	0.044	
EtOH 4 mL/min 100 bar	5.5	277	0.564	19 540	1.025	0.0014	0.042	0.042	0.042	0.042	
EtOH 4 mL/min 120 bar	5.5	217	0.930	19.300	1.214	0.0015	0.043	0.043	0.043	0.043	
EtOH 4 mL/min 150 bar	5.0	220	0.972	19 265	1.120	0.0015	0.042	0.042	0.042	0.042	
Lton 4 me/mm 150 bar	5.0	339	0.982	10% IDA	1.105	0.0015	0.041	0.041	0.041	0.041	
	12.2	140	0.070	10% IPA	1.010	0.0026	0.000	0.000	0.000	0.000	
IPA 2 mL/min 100 bar	12.2	146	0.873	19.171	1.916	0.0026	0.086	0.086	0.086	0.086	
IPA 2 mL/min 130 bar	11.0	1/8	0.899	17.800	1.727	0.0023	0.078	0.078	0.078	0.078	
IPA 2 mL/min 150 bar	9.8	192	0.909	16.035	1.539	0.0021	0.071	0.071	0.071	0.071	
IPA 2 mL/min 170 bar	9.2	219	0.926	15.335	1.445	0.0019	0.066	0.067	0.067	0.067	
IPA 2 mL/min 200 bar	8.8	249	0.942	14.921	1.382	0.0018	0.065	0.065	0.065	0.065	
IPA 2.5 mL/min 150 bar	7.8	216	0.924	16.216	1.531	0.0020	0.059	0.059	0.059	0.059	
IPA 2.5 mL/min 1/0 bar	/.5	23/	0.936	15./95	1.4/2	0.0020	0.057	0.057	0.057	0.057	
IPA 2.5 mL/min 200 bar	/.2	269	0.952	15.422	1.413	0.0019	0.055	0.055	0.055	0.055	
IPA 3 mL/min 150 bar	6.2	224	0.929	15.551	1.460	0.0020	0.048	0.049	0.049	0.049	
IPA 3 mL/min 170 bar	6.0	266	0.951	15.406	1.413	0.0019	0.047	0.048	0.047	0.047	
IPA 3 mL/min 200 bar	5.8	301	0.967	15.143	1.366	0.0018	0.046	0.046	0.046	0.046	
IPA 3.5 mL/min 150 bar	5.4	288	0.961	16.347	1.484	0.0020	0.044	0.045	0.045	0.045	
IPA 3.5 mL/min 170 bar	5.2	306	0.969	15.872	1.429	0.0019	0.043	0.043	0.043	0.043	
IPA 3.5 mL/min 200 bar	4.9	334	0.980	15.126	1.347	0.0018	0.041	0.041	0.041	0.041	
IPA 4 mL/min 100 bar	4.8	270	0.953	16.468	1.508	0.0020	0.04	0.04	0.04	0.040	
IPA 4 mL/min 130 bar	4.5	303	0.968	15.682	1.413	0.0019	0.038	0.038	0.039	0.038	
IPA 4 mL/min 150 bar	1 44	1 325	0 977	15/176	1 1 2 8 2	0.0018	0.038	0.038	I 0.038	0.038	

 Table S7 Solvent consumption and energy consumption information for the low retention mix separations.

Low Retention Mix LCA and AMGS Results											
HPLC											
Separation Parameters		AMGS Calcul	ator Results					LCA Results			
Separation Type	Instrument Energy Score	Solvent Energy Score	Solvent EHS Score	Greenness Score	CED (MJ)	GHG (kg of CO ₂ eq.)	ONGD (kg eq.)	ACID (kg of SO₂ eq.)	EUTR (kg of (PO4) ³⁻ eq.)	PCOP (kg of ethane eq.)	
28% ACN 1.8 mL/min	515.20	713.14	75.18	1303.51	123	6.25	2.90	3.51E-02	2.37E-03	3.73E-03	
28% ACN 1.8 mL/min	171.73	247.48	34.83	454.04	41.4	2.11	0.978	1.19E-02	7.99E-04	1.27E-03	
60% MeOH 1 mL/min	176.03	104.71	37.79	318.53	30.5	1.50	0.706	1.26E-02	4.65E-04	2.85E-02 3.01E-02	
60% MeOH 1.4 mL/min	135.24	111.52	39.54	286.30	23.4	1.10	0.545	8.44E-03	3.20E-04	3.02E-02	
40% EtOH 0.7 mL/min	300.53	85.79	28.31	414.63	42.3	2.24	0.982	1.73E-02	6.91E-04	6.34E-02	
40% EtOH 0.8 mL/min	268.33	87.24	28.59	384.16	39.8	2.09	0.926	1.58E-02	6.41E-04	6.45E-02	
40% EtOH 0.95 mL/min	240.43	91.89	29.48	361.80	38.1	1.98	0.887	1.45E-02	6.00E-04	6.48E-02	
33% IPA 0.6 mL/min	257.60	82.58	24.65	364.84	32.7	1.77	0.755	1.49E-02	5.67E-04	1.91E-02	
33% IPA 0.725 mL/min 33% IPA 0.85 mL/min	225.40	88.43	25.23	337.10	29.7	1.59	0.686	1.31E-02 1.17E-02	4 58E-04	2.03E-02	
5576 IF A 0.05 IT L/ III II	157.45	00.45	23.32	511.44	SEC	1.45	0.000	1.172 02	4.562.04	2.032.02	
				7	/% MeOH						
MeOH 2 mL/min 100 bar	294.21	171.11	30.87	496.19	64.0	3.48	1.47	3.07E-02	1.14E-03	1.22E-02	
MeOH 2 mL/min 130 bar	249.33	147.24	28.40	424.97	54.8	2.99	1.26	2.62E-02	9.73E-04	1.03E-02	
MeOH 2 mL/min 150 bar	229.39	136.63	27.30	393.32	50.9	2.77	1.17	2.44E-02	9.05E-04	9.54E-03	
MeOH 2 mL/min 170 bar	219.41	131.33	26.75	377.49	49.1	2.67	1.13	2.35E-02	8.73E-04	9.15E-03	
MeOH 2 mL/min 200 bar	199.47	120.72	25.65	345.84	44.8	2.44	1.03	2.14E-02 1.89E-02	7.96E-04	8.32E-03	
MeOH 2.5 mL/min 150 bar	162.07	127.35	25.82	310.27	38.8	2.09	0.891	1.81E-02	6.80E-04	8.09E-03	
MeOH 2.5 mL/min 200 bar	152.09	115.75	25.13	292.98	36.4	1.97	0.837	1.70E-02	6.39E-04	7.60E-03	
MeOH 3 mL/min 150 bar	137.13	124.04	25.99	287.16	35.5	1.90	0.816	1.63E-02	6.16E-04	8.01E-03	
MeOH 3 mL/min 170 bar	129.65	118.07	25.37	273.10	33.9	1.81	0.779	1.56E-02	5.88E-04	7.59E-03	
MeOH 3 mL/min 200 bar	119.68	110.12	24.55	254.35	31.5	1.68	0.723	1.45E-02	5.46E-04	7.01E-03	
MeOH 3.5 mL/min 150 bar	114.69	121.39	25.72	261.79	31.3	1.66	0.721	1.41E-02	5.37E-04	7.64E-03	
MeOH 3.5 mL/min 170 bar	99.73	107.46	25.24	251.69	27.9	1.58	0.690	1.35E-02 1.26E-02	5.14E-04 4.80E-04	6.68E-03	
MeOH 4 mL/min 100 bar	99.73	120.72	25.65	246.10	28.6	1.50	0.659	1.25E-02	4.85E-04	7.46E-03	
MeOH 4 mL/min 130 bar	94.75	115.42	25.10	235.27	27.7	1.46	0.638	1.23E-02	4.70E-04	7.11E-03	
MeOH 4 mL/min 150 bar	89.76	110.12	24.55	224.43	26.7	1.41	0.615	1.19E-02	4.55E-04	6.76E-03	
					7% EtOH						
EtOH 2 mL/min 100 bar	386.47	219.80	33.25	639.52	84.0	4.59	1.93	3.90E-02	1.48E-03	3.80E-02	
EtOH 2 mL/min 130 bar	324.13	186.71	30.25	541.09	71.3	3.89	1.64	3.31E-02	1.26E-03	3.19E-02	
EtOH 2 mL/min 130 bar	299.20	160.24	29.05	462.36	61.4	3.98	1.35	2.85E-02	1.08E-03	2.70E-02	
EtOH 2 mL/min 200 bar	254.32	149.65	26.89	430.86	58.3	3.18	1.34	2.71E-02	1.03E-03	2.51E-02	
EtOH 2.5 mL/min 150 bar	224.40	163.55	28.15	416.10	54.4	2.94	1.25	2.46E-02	9.47E-04	2.72E-02	
EtOH 2.5 mL/min 170 bar	209.44	153.62	27.25	390.31	51.1	2.76	1.18	2.31E-02	8.89E-04	2.54E-02	
EtOH 2.5 mL/min 200 bar	194.48	143.70	26.35	364.53	48.3	2.61	1.11	2.18E-02	8.41E-04	2.36E-02	
EtOH 3 mL/min 150 bar	177.03	155.61	27.43	360.07	45.8	2.45	1.06	2.01E-02	7.87E-04	2.54E-02	
EtOH 3 mL/min 170 bar	157.08	145.00	25.99	322.80	41.5	2.28	0.958	1.83E-02	7.13E-04	2.26E-02	
EtOH 3.5 mL/min 150 bar	149.60	153.62	27.25	330.47	40.8	2.16	0.943	1.75E-02	6.91E-04	2.49E-02	
EtOH 3.5 mL/min 170 bar	139.63	144.36	26.41	310.40	38.7	2.05	0.894	1.66E-02	6.56E-04	2.32E-02	
EtOH 3.5 mL/min 200 bar	132.15	137.41	25.78	295.34	36.7	1.94	0.848	1.57E-02	6.22E-04	2.20E-02	
EtOH 4 mL/min 100 bar	137.13	160.24	27.85	325.22	38.8	2.03	0.897	1.61E-02	6.48E-04	2.58E-02	
EtOH 4 mL/min 130 bar	127.16	149.65	26.89	303.70	37.5	1.97	0.866	1.57E-02	6.29E-04	2.40E-02	
ELOH 4 ML/ININ 150 bar	124.67	147.01	20.05	290.33	10% IDA	1.55	0.646	1.546-02	0.152-04	2.336-02	
IPA 2 ml /min 100 har	304.19	210.64	33.21	548.04	69.2	3 75	1 59	3 19E-02	1 22E-03	2 12E-02	
IPA 2 mL/min 130 bar	274.27	191.36	31.38	497.02	62.8	3.41	1.45	2.90E-02	1.10E-03	1.19E-02	
IPA 2 mL/min 150 bar	244.35	172.09	29.56	445.99	57.0	3.10	1.31	2.64E-02	1.00E-03	1.71E-02	
IPA 2 mL/min 170 bar	229.39	162.45	28.65	420.48	53.6	2.90	1.23	2.48E-02	9.43E-04	1.61E-02	
IPA 2 mL/min 200 bar	219.41	156.02	28.04	403.47	52.2	2.83	1.20	2.41E-02	9.19E-04	1.54E-02	
IPA 2.5 mL/min 150 bar	194.48	171.28	29.48	395.25	48.9	2.63	1.13	2.20E-02	8.48E-04	1.66E-02	
IPA 2.5 mL/min 170 bar	187.00	165.26	28.91	381.17	48.6	2.61	1.12	2.20E-02	8.46E-04	1.60E-02	
IPA 3 mL/min 150 bar	154.59	164.05	28.80	347.44	41.5	2.45	0,959	1.82F-02	7.10F-04	1.56F-02	
IPA 3 mL/min 170 bar	149.60	159.23	28.34	337.18	40.5	2.15	0.934	1.77E-02	6.92E-04	1.51E-02	
IPA 3 mL/min 200 bar	144.61	154.41	27.89	326.91	39.3	2.08	0.908	1.72E-02	6.72E-04	1.46E-02	
IPA 3.5 mL/min 150 bar	134.64	166.46	29.03	330.13	39.1	2.06	0.904	1.67E-02	6.61E-04	1.56E-02	
IPA 3.5 mL/min 170 bar	129.65	160.84	28.49	318.98	37.7	1.99	0.871	1.61E-02	6.37E-04	1.51E-02	
IPA 3.5 mL/min 200 bar	122.17	152.41	27.70	302.27	35.9	1.89	0.830	1.53E-02	6.0/E-04	1.42E-02	
IPA 4 mL/min 100 bar	112.08	159.23	29.25	299 78	34.4	1.88	0.797	1.50E-02	5.76F-04	1.57E-02	
IPA 4 mL/min 150 bar	109.71	156.02	28.04	293.77	34.1	1.78	0.788	1.42E-02	5.70E-04	1.44E-02	

 Table S8 LCA and AMGS Calculator results for the low retention mix separations



Figure S19 Metric results for the low retention mixture of the 150bar BPR SFC separations and HPLC for the different metrics calculated. The displayed are the greenness score (A), CED (B), GHG (C), ONGD (D), ACID (E), EUTR (F), and PCOP (G).



Figure S20 Percent contribution to each impact factor from each portion of the system for the LCA analysis. Example SFC separations are for the low retention mix and each are for the 3mL/min and 150bar BPR separations. Separations with methanol, ethanol, and isopropanol are shown in A, B, C respectively.



Figure S21 Percent contribution to each impact factor from each portion of the system for the LCA analysis. Example HPLC separations are for the low retention mix at the flow rate that gave a pressure of approximately 350bar. The separation with methanol, ethanol, isopropanol, acetonitrile in HPLC is shown in A, B, C, and D respectively. The ACN separation is for the 8 min for the hypothetical separation.



Figure S22 Separations of the gradient mix using SFC. TEA was added to the organic solvent at 0.1% (v/v) concentration. The flow rate and BPR pressure is listed for each. The column temperature was 40°C for all separation. The gradients for the gradient mix separations were scaled based on the 2mL/min gradient. The resulting gradients were as follows. 2mL/min: 0-8min, 5-50%B; 8-10min, 50%B; 3min equilibration time. 2.5mL/min: 0-6.4min, 5-50%B; 6.4-8min, 50%B; 2.4min equilibration time. 3mL/min: 0-5.3min, 5-50%B; 5.3-6.7min, 50%B; 2min equilibration time. 3.5mL/min: 0-4.6min, 5-50%B; 4.6-5.8min, 50%B; 1.7min equilibration time. 4mL/min: 0-4min, 5-50%B; 4-5min, 50%B; 1.5min equilibration time. The retention order was indapamide, diltiazem, verapamil, thioridazine.



Figure S23 Separations of the gradient mix using SFC. TEA was added to the organic solvent at 0.1% (v/v) concentration. The flow rate and BPR pressure is listed for each. The column temperature was 40°C for all separation. The gradients for the gradient mix separations were scaled based on the 2mL/min gradient. The resulting gradients were as follows. 2mL/min: 0-8min, 5-50%B; 8-10min, 50%B; 3min equilibration time. 2.5mL/min: 0-6.4min, 5-50%B; 6.4-8min, 50%B; 2.4min equilibration time. 3mL/min: 0-5.3min, 5-50%B; 5.3-6.7min, 50%B; 2min equilibration time. 3.5mL/min: 0-4.6min, 5-50%B; 4.6-5.8min, 50%B; 1.7min equilibration time. 4mL/min: 0-4min, 5-50%B; 4-5min, 50%B; 1.5min equilibration time. The retention order was indapamide, diltiazem, verapamil, thioridazine.



Figure S24 Separations of the gradient mix using SFC. TEA was added to the organic solvent at 0.1% (v/v) concentration. The flow rate and BPR pressure is listed for each. The column temperature was 40°C for all separation. The gradients for the gradient mix separations were scaled based on the 2mL/min gradient. The resulting gradients were as follows. 2mL/min: 0-8min, 5-50%B; 8-11.3min, 50%B; 3min equilibration time. 2.5mL/min: 0-6.4min, 5-50%B; 6.4-9.1min, 50%B; 2.4min equilibration time. 3mL/min: 0-5.3min, 5-50%B; 5.3-7.5min, 50%B; 2min equilibration time. 3.5mL/min: 0-4.6min, 5-50%B; 4.6-6.5min, 50%B; 1.7min equilibration time. 4mL/min: 0-4min, 5-50%B; 4-5.7min, 50%B; 1.5min equilibration time. The retention order was indapamide, diltiazem, verapamil, thioridazine.

Gradient Mix HPLC Comparison



Figure S25 Separations of the gradient mix using HPLC. TEA was added to the mobile phase at 0.1% (v/v) concentration. The flow rate for each solvent is listed. The column temperature was 40°C for all separation. The gradients used were as follows. ACN Gradient: 0-5min, 5-95%B; 5-8.5min, 95%B; 2.2min equilibration time. MeOH Gradient: 0-7min, 5-95%B; 7-12min, 95%B; 3min equilibration time. EtOH Gradient: 0-15min, 5-95%B; 15-19min, 95%B; 5min equilibration time. IPA Gradient: 0-19min, 5-95%B; 19-21min, 95%B; 6min equilibration time. The retention order was thioridazine, verapamil, diltiazem, indapamide.

Gradient Mix Information												
HPLC												
Separatio	n Parameters			Solvent Usage	per Injection		Instrument Energy Consumption (kWh)					
Separation Type	Separation Time	Pressure (bar)		Mass of CO ₂ (g)	Mass of MeOH (g)	Mass of TEA (g)	Trial 1	Trial 2	Trial 3	Average		
ACN Gradient 1.7 mL/min	10.7	144-319		12.652	4.318	0.0040	0.036	0.036	0.036	0.036		
MeOH Gradient 1.2 mL/min	15.0	244-364		12.472	4.344	0.0040	0.050	0.050	0.050	0.050		
EtOH Gradient 0.8 mL/min	24.0	164-362		14.058	4.020	0.0037	0.078	0.078	0.078	0.078		
IPA Gradient 0.6 mL/min	27.0	138-387		11.949	3.310	0.0031	0.087	0.087	0.087	0.087		
	•			SFC	•							
MeOH Gradient												
Separatio	n Parameters			Solvent Usage	per Injection		Instrume	nt Energy C	Consumptio	on (kWh)		
Separation Type	Separation Time	Pressure (bar)	Density of CO ₂ (g/mL)	Mass of CO_2 (g)	Mass of MeOH (g)	Mass of TEA (g)	Trial 1	Trial 2	Trial 3	Average		
MeOH 2 mL/min 130 bar	13.0	172-208	0.919	17.737	5.301	0.0049	0.091	0.091	0.091	0.091		
MeOH 2.5 mL/min 130 bar	10.4	193-232	0.933	18.007	5.301	0.0049	0.075	0.075	0.075	0.075		
MeOH 3 mL/min 100 bar	8.7	193-228	0.931	17.994	5.358	0.0049	0.065	0.065	0.065	0.065		
MeOH 3 mL/min 130 bar	8.7	227-260	0.948	18.322	5.358	0.0049	0.065	0.065	0.065	0.065		
MeOH 3 mL/min 150 bar	8.7	246-281	0.958	18.516	5.358	0.0049	0.066	0.065	0.065	0.065		
MeOH 3.5 mL/min 130 bar	7.5	261-289	0.962	18.687	5.400	0.0050	0.058	0.058	0.058	0.058		
MeOH 4 mL/min 130 bar	6.5	301-326	0.977	18.856	5.301	0.0049	0.051	0.051	0.051	0.051		
			Et	OH Gradient								
EtOH 2 mL/min 130 bar	13.0	172-215	0.924	17.833	5.281	0.0049	0.091	0.092	0.091	0.091		
EtOH 2.5 mL/min 130 bar	10.4	196-240	0.938	18.103	5.281	0.0049	0.076	0.075	0.075	0.075		
EtOH 3 mL/min 100 bar	8.7	193-236	0.936	18.091	5.338	0.0049	0.065	0.065	0.065	0.065		
EtOH 3 mL/min 130 bar	8.7	229-269	0.952	18.400	5.338	0.0049	0.065	0.065	0.065	0.065		
EtOH 3 mL/min 150 bar	8.7	250-290	0.962	18.593	5.338	0.0049	0.065	0.065	0.065	0.065		
EtOH 3.5 mL/min 130 bar	7.5	261-298	0.966	18.765	5.380	0.0050	0.058	0.058	0.058	0.058		
EtOH 4 mL/min 130 bar	6.5	306-335	0.981	18.933	5.281	0.0049	0.052	0.051	0.051	0.051		
			IF	PA Gradient								
IPA 2 mL/min 130 bar	14.3	173-206	0.918	18.911	6.282	0.0058	0.107	0.107	0.107	0.107		
IPA 2.5 mL/min 130 bar	11.5	197-230	0.932	19.269	6.341	0.0059	0.088	0.088	0.088	0.088		
IPA 3 mL/min 100 bar	9.5	194-223	0.928	19.050	6.260	0.0058	0.073	0.073	0.073	0.073		
IPA 3 mL/min 130 bar	9.5	226-254	0.945	19.398	6.260	0.0058	0.069	0.069	0.069	0.069		
IPA 3 mL/min 150 bar	9.5	248-276	0.956	19.624	6.260	0.0058	0.071	0.072	0.072	0.072		
IPA 3.5 mL/min 130 bar	8.2	265-287	0.961	19.845	6.321	0.0058	0.065	0.066	0.066	0.066		
IPA 4 mL/min 130 bar	7.2	306-332	0.980	20.286	6.360	0.0059	0.060	0.060	0.060	0.060		

Table S9 Solvent consumption and energy consumption information for the gradient mix separations. The maximum pressure was used to determine the density of CO₂ used.

Gradient Mix Information												
HPLC												
Separation Parameters		AMGS Calcula	tor Results					LCA Results				
Separation Type	Instrument	Solvent Energy	Solvent EHS	Greenness	CED	GHG	ONGD	ACID	EUTR	РСОР		
Separation Type	Energy Score	Score	Score	Score	(MJ)	(kg of CO ₂ eq.)	(kg eq.)	(kg of SO ₂ eq.)	(kg of (PO ₄) ³⁻ eq.)	(kg of ethane eq.)		
ACN Gradient 1.7 mL/min	229.69	332.20	186.17	748.07	55.3	2.81	1.31	1.57E-02	1.07E-03	1.57E-03		
MeOH Gradient 1.2 mL/min	322.00	115.26	83.98	521.24	42.2	2.15	0.975	1.85E-02	6.76E-04	3.22E-02		
EtOH Gradient 0.8 mL/min	515.20	107.28	119.62	742.11	67.4	3.62	1.56	2.92E-02	1.14E-03	8.31E-02		
IPA Gradient 0.6 mL/min	579.60	135.19	98.44	813.23	68.9	3.77	1.59	3.23E-02	1.21E-03	3.44E-02		
					SFC							
MeOH Gradient												
MeOH 2 mL/min 130 bar	324.13	248.24	45.84	618.21	76.8	3.96	1.77	3.37E-02	1.26E-03	4.04E-02		
MeOH 2.5 mL/min 130 bar	259.31	248.24	45.84	553.39	66.0	3.34	1.53	2.78E-02	1.05E-03	3.99E-02		
MeOH 3 mL/min 100 bar	216.19	249.72	46.11	512.02	59.3	2.95	1.37	2.42E-02	9.25E-04	3.99E-02		
MeOH 3 mL/min 130 bar	216.19	249.72	46.11	512.02	59.4	2.95	1.38	2.42E-02	9.25E-04	3.99E-02		
MeOH 3 mL/min 150 bar	216.19	249.72	46.11	512.02	59.7	2.96	1.38	2.43E-02	9.30E-04	3.99E-02		
MeOH 3.5 mL/min 130 bar	187.00	251.24	46.33	484.58	54.9	2.69	1.27	2.16E-02	8.36E-04	4.00E-02		
MeOH 4 mL/min 130 bar	162.07	248.24	45.84	456.15	50.0	2.41	1.16	1.90E-02	7.45E-04	3.90E-02		
		-		E	tOH Gradient			-				
EtOH 2 mL/min 130 bar	324.13	247.11	86.15	657.40	85.7	4.49	1.99	3.44E-02	1.39E-03	1.09E-01		
EtOH 2.5 mL/min 130 bar	259.31	247.11	86.15	592.58	74.9	3.86	1.74	2.85E-02	1.19E-03	1.08E-01		
EtOH 3 mL/min 100 bar	216.19	248.59	86.86	551.63	68.1	3.47	1.59	2.47E-02	1.05E-03	1.09E-01		
EtOH 3 mL/min 130 bar	216.19	248.59	86.86	551.63	68.2	3.47	1.59	2.47E-02	1.06E-03	1.09E-01		
EtOH 3 mL/min 150 bar	216.19	248.59	86.86	551.63	68.3	3.47	1.59	2.48E-02	1.06E-03	1.09E-01		
EtOH 3.5 mL/min 130 bar	187.00	250.10	87.40	524.50	63.7	3.20	1.49	2.22E-02	9.67E-04	1.10E-01		
EtOH 4 mL/min 130 bar	162.07	247.11	86.15	495.34	58.9	2.93	1.38	1.97E-02	8.78E-04	1.07E-01		
			1	I	PA Gradient							
IPA 2 mL/min 130 bar	356.55	361.63	90.94	809.11	96.5	5.04	2.24	4.01E-02	1.60E-03	6.31E-02		
IPA 2.5 mL/min 130 bar	286.73	364.20	91.61	742.54	83.9	4.32	1.95	3.32E-02	1.35E-03	6.30E-02		
IPA 3 mL/min 100 bar	236.87	360.42	90.67	687.97	73.4	3.72	1.71	2.77E-02	1.16E-03	6.17E-02		
IPA 3 mL/min 130 bar	236.87	360.42	90.67	687.97	72.6	3.66	1.69	2.72E-02	1.14E-03	6.17E-02		
IPA 3 mL/min 150 bar	236.87	360.42	90.67	687.97	72.7	3.67	1.69	2.72E-02	1.14E-03	6.17E-02		
IPA 3.5 mL/min 130 bar	204.45	363.34	91.38	659.17	68.8	3.44	1.61	2.50E-02	1.07E-03	6.20E-02		
IPA 4 mL/min 130 bar	179.52	365.06	91.83	636.41	65.2	3.23	1.52	2.29E-02	9.94E-04	6.22E-02		

Table S10 LCA and AMGS Calculator results for the gradient mix separation



Figure S26 Metric results for the gradient mixture of the 130bar BPR SFC separations and HPLC for the different metrics calculated. The displayed are the greenness score (A), CED (B), GHG (C), ONGD (D), ACID (E), EUTR (F), and PCOP (G).



Figure S27 Percent contribution to each impact factor from each portion of the system for the LCA analysis. Example SFC separations are for the gradient mix and each are the 3 mL/min and 130bar BPR separations. The separation with methanol, ethanol, and isopropanol in SFC is shown in A, B, and C respectively.



Figure S28 Percent contribution to each impact factor from each portion of the system for the LCA analysis. Data is for the gradient HPLC separations. The separation with methanol, ethanol, isopropanol, acetonitrile in HPLC are shown in A, B, C, and D respectively.

Prep SFC Solvent Comparison



Figure S29 Preparative SFC separations of the preparative scale mix. The gradients were scaled with flow rate. The 40 mL/min gradient was 0-15 min, 5-50% B, 15-18 min, 50% B, 2 min post time. The 60 mL/min gradient was 0-10 min, 5-50% B, 10-12 min, 50% B. The 80 mL/min gradient was 0-7.5 min, 5-50% B, 7.5-9 min, 50% B, 1 min post time. Each separation was completed at 40 °C and a BPR pressure of 120 bar. Organic portions had diethylamine added at a concentration of 0.1% (v/v). The retention order was prednisone, hydrocortisone, indapamide, chlorthalidone.



Prep SFC Solvent Comparison

Figure S30 Preparative HPLC separations of the preparative scale mix. The methanol and ethanol gradients were a 30min gradient form 5-95% B with a 5min hold at the end. The flow rate for methanol was 10 mL/min with a post time of 7 mins. The flow rate for ethanol was 8 mL/min with a post time of 8 mins. The acetonitrile gradient was a 19 min gradient from 5-95% B with a 4 min hold at the end. The flow rate was 16 mL/min with a 5 min post time. The isopropanol gradient was a 30 min gradient form 5-80% B with a 5 min hold. The flow rate was 8 mL/min with a post time of 8.5 min. The mobile phases had acetic acid added at 0.1% (v/v). The retention order for methanol was chlorthalidone, indapamide, hydrocortisone, prednisone. Indapamide was remove from the mix for isopropanol and ethanol. Prednisone was removed from the mix for acetonitrile.

Preparative Scale Separation Information											
HPLC											
Separation Parameters Solvent Usage per Injection Instrument Energy Consumption (kWh)											
Separation Type	Separation Time	Mass of Water (g)	Mass of Organic (g)	Mass of Acetic Acid (g)	Trial 1	Trial 2	Trial 3	Average			
ACN Gradient 16 mL/min	28.0	230.506	170.234	0.2276	0.066	0.067	0.068	0.067			
MeOH Gradient 10 mL/min	42.0	218.343	159.033	0.2111	0.096	0.097	0.097	0.097			
EtOH Gradient 8 mL/min	43.0	182.252	127.060	0.1693	0.100	0.100	0.100	0.100			
IPA Gradient 8 mL/min	43.5	186.040	126.734	0.1695	0.101	0.101	0.101	0.101			
SFC											
MeOH Gradients											
Separation Parame	eters	S	olvent Usage per Inj	ection	Instrume	nt Energy Co	nsumption	(kWh)			
Separation Type	Separation Time	Mass of CO_2 (g)	Mass of MeOH (g)	Mass of DEA (g)	Trial 1	Trial 2	Trial 3	Average			
MeOH 40 mL/min 120 bar BPR	20.0	551.586	181.187	0.1619	0.475	0.465	0.465	0.468			
MeOH 60 mL/min 120 bar BPR	13.3	549.751	181.108	0.1618	0.333	0.331	0.333	0.332			
MeOH 80 mL/min 120 bar BPR	10.0	551.586	181.187	0.1619	0.267	0.268	0.265	0.267			
			EtOH Gradier	nts							
EtOH 40 mL/min 120 bar BPR	20.0	551.586	180.500	0.1619	0.473	0.459	0.46	0.464			
EtOH 60 mL/min 120 bar BPR	13.3	549.751	180.421	0.1618	0.329	0.335	0.327	0.330			
IPA Gradients											
IPA 40 mL/min 120 bar BPR	20.0	551.586	179.814	0.1619	0.453	0.454	0.45	0.452			
IPA 60 mL/min 120 bar BPR	13.3	549.751	179.735	0.1618	0.325	0.327	0.324	0.325			

Table S11: Separation information for the preparative scale separations. The mass of CO₂ was calculated using a pressure of 300 bar at 25°C.

Preparative Scale SFC Fraction Information										
MeOH Gradients										
Fraction	Fraction Volume (mL)	Methanol mass (g)	DEA Mass (g)	Energy to Remove (kWhr)						
		MeOH 40 mL/min	-							
Prednisone	1	0.791	0.001	2.42E-04						
Hydrocortisone	1.3	1.029	0.001	3.14E-04						
Indapamide	2.7	2.136	0.002	6.53E-04						
Chlorthalidone	3.8	3.007	0.003	9.19E-04						
		MeOH 60 mL/min								
Prednisone	1.1	0.870	0.001	2.66E-04						
Hydrocortisone	1.3	1.029	0.001	3.14E-04						
Indapamide	2.4	1.899	0.002	5.80E-04						
Chlorthalidone	3.4	2.690	0.002	8.22E-04						
		MeOH 80 mL/min								
Prednisone	1.1	0.870	0.001	2.66E-04						
Hydrocortisone	1.3	1.029	0.001	3.14E-04						
Indapamide	2.4	1.899	0.002	5.80E-04						
Chlorthalidone	3.4	2.690	0.002	8.22E-04						
EtOH Gradients										
EtOH 40 mL/min										
Prednisone	1.8	1.419	0.001	3.34E-04						
Hydrocortisone	2.0	1.576	0.001	3.71E-04						
Indapamide	3.3	2.601	0.002	6.11E-04						
Chlorthalidone	5.2	4.099	0.004	9.64E-04						
		EtOH 60 mL/min								
Prednisone	1.8	1.419	0.001	3.34E-04						
Hydrocortisone	2.0	1.576	0.001	3.71E-04						
Indapamide	3.2	2.522	0.002	5.93E-04						
Chlorthalidone	4.9	3.862	0.003	9.08E-04						
		IPA Gradients								
		IPA 40 mL/min								
Prednisone	3.0	2.356	0.002	4.34E-04						
Hydrocortisone	3.1	2.434	0.002	4.49E-04						
Indapamide	4.5	3.533	0.003	6.51E-04						
Chlorthalidone	10.0	7.852	0.007	1.45E-03						
		IPA 60 mL/min								
Prednisone	3.0	2.356	0.002	4.34E-04						
Hydrocortisone	3.1	2.434	0.002	4.49E-04						
Indapamide	4.4	3.455	0.003	6.37E-04						
Chlorthalidone	9.6	7.538	0.007	1.39E-03						

Table S12: Preparative SFC fraction information. All SFC separations were done with a BPR pressure of 120 bar.

Preparative Scale HPLC Fraction Information									
Fraction	Fraction Volume (mL)	Water mass (g)	Organic mass (g)	Acetic Acid Mass (g)	Energy to Remove (kWhr)				
ACN Gradient 16 mL/min									
Chlorthalidone	11.0	6.211	3.653	0.012	0.0047				
Hydrocortisone	14.7	7.156	5.615	0.015	0.0058				
Indapamide	14.1	8.511	5.205	0.015	0.0065				
MeOH Gradient 10 mL/min									
Chlorthalidone	3.2	1.471	1.351	0.003	0.0013				
Indapamide	6.0	1.968	3.146	0.006	0.0022				
Prednisone	6.6	1.977	3.575	0.007	0.0023				
Hydrocortisone	5.9	1.565	3.388	0.006	0.0020				
		EtOH	Gradient 8 mL/min						
Chlorthalidone	10.2	5.695	3.384	0.011	0.0044				
Prednisone	5.4	2.579	2.181	0.006	0.0021				
Hydrocortisone	5.4	2.386	2.308	0.006	0.0020				
IPA Gradient 8 mL/min									
Chlorthalidone	10.0	6.583	2.516	0.010	0.0046				
Prednisone	5.1	3.069	1.533	0.005	0.0022				
Hydrocortisone	5.4	3.163	1.719	0.006	0.0023				

Table S13: Preparative HPLC fraction information. Fraction volume was converted to organic mass using dwell volume and elution time.

r											
		Prepara	ative Scale	Lowest R	etained	Compound	Results				
				HF	PLC	-					
Separation Parameters		AMGS Calculator	Results	-				LCA Results			
Separation Type	Instrument Energy Score	Solvent Energy Score	Solvent EHS Score	Greenness Score	CED (MJ)	GHG (kg of CO ₂ eq.)	ONGD (kg eq.)	ACID (kg of SO ₂ eq.)	EUTR (kg of (PO ₄) ³⁻ eq.)	PCOP (kg of ethane eq.)	
ACN Gradient 16 mL/min	1465	12517	1074	15056	1261	56.2	30.6	0.123	2.47E-02	0.0145	
MeOH Gradient 10 mL/min	2198	5139	1040	8377	372	10.70	8.90	0.0406	2.25E-03	1.12	
EtOH Gradient 8 mL/min	2250	2926	561	5737	523	21.4	12.6	0.0544	5.02E-03	2.54	
IPA Gradient 8 mL/min	2277	4176	834	7287	448	17.2	10.8	0.0531	4.68E-03	1.20	
		1	1	S	FC	1					
				MeOH	Gradient						
MeOH 40 mL/min	1224	7475	1294	9993	819	31.3	19.3	0.182	8.65E-03	1.29	
MeOH 60 mL/min	814	7463	1293	9569	718	25.7	17.0	0.132	6.77E-03	1.28	
MeOH 80 mL/min	612	7475	1294	9381	683	23.5	16.2	0.108	6.04E-03	1.28	
	EtOH Gradient										
EtOH 40 mL/min	1224	7437	1008	9669	1114	48.8	26.6	0.201	1.30E-02	3.62	
EtOH 60 mL/min	814	7424	1007	9245	1010	42.3	24.2	0.149	1.08E-02	3.62	
				IPA Gr	adient						
IPA 40 mL/min	1224	9826	1166	12217	995	42.2	23.7	0.191	1.19E-02	1.71	
IPA 60 mL/min	814	9812	1165	11792	899	36.2	21.6	0.144	1.03E-02	1.71	
		Prepara	tive Scale	Highest R	Retained	l Compound	Results				
		•		 HF	PLC	•					
Separation Parameters		AMGS Calculator	Results					LCA Results			
Separation Type	Instrument Energy	Solvent Energy	Solvent EHS	Greenness	CED	GHG	ONGD	ACID	EUTR	РСОР	
	Score	Score	Score	Score	(MJ)	(kg of CO ₂ eq.)	(kg eq.)	(kg of SO ₂ eq.)	(kg of (PO ₄) ^{3*} eq.)	(kg of ethane eq.)	
ACN Gradient 16 mL/min	1465	12517	1074	15056	1263	56.3	30.6	0.123	2.47E-02	0.0145	
MeOH Gradient 10 mL/min	2198	5139	1040	8377	372	10.70	8.91	0.0408	2.26E-03	1.12	
EtOH Gradient 8 mL/min	2250	2926	561	5737	521	21.3	12.6	0.0536	4.99E-03	2.54	
IPA Gradient 8 mL/min	2277	4176	834	7287	447	17.2	10.8	0.0523	4.65E-03	1.20	
				S	FC						
MeOH Gradient											
MeOH 40mL/min	1224	7475	1294	9993	819	31.4	19.4	0.182	8.66E-03	1.29	
MeOH 60mL/min	814	7463	1293	9569	718	25.7	17.0	0.132	6.78E-03	1.28	
MeOH 80mL/min	612	7475	1294	9381	683	23.5	16.3	0.109	6.05E-03	1.28	
				EtOH G	iradient						
EtOH 40mL/min	1224	7437	1008	9669	1113	48.7	26.6	0.200	1.30E-02	3.62	
EtOH 60mL/min	814	7424	1007	9245	1011	42.3	24.2	0.149	1.08E-02	3.62	
		1		IPA Gr	adient						
IPA 40mL/min	1224	9826	1166	12217	996	42.30	23.70	0.191	1.19E-02	1.71	
IPA 60mL/min	814	9812	1165	11792	900	36.20	21.60	0.144	1.03E-02	1.71	

Table S14 AMGS and LCA results for the highest and lowest retained compound in the preparative HPLC and SFC separations. All SFC separations were completed with a BPR pressure of 120 bar.



Figure S31 Percent contribution to each impact factor from each portion of the system for the LCA analysis for preparative SFC. All separation are for 60 mL/min. Lowest retained compounds are on the left (A, C, E) and highest retained is on the right (B, D, F). Separation for methanol (A, B), ethanol (C, D), and isopropanol (E, F) are shown.



Figure S32 Percent contribution to each impact factor from the portions of the system for the LCA analysis. Data shown is for preparative HPLC with methanol (A, C) and ethanol (B, D). The lowest retained analyte (A, B) is shown on top, and the highest retained analyte (C, D) is shown on the bottom.



Figure S33 Percent contribution to each impact factor from the portions of the system for the LCA analysis. Data shown is for preparative HPLC with isopropanol (A, B) and acetonitrile (C, D). The lowest retained analyte (A, C) is shown on left, and the highest retained analyte (B, D) is shown on the right.

Prep SFC BPR Comparison at 15% MeOH 60 mL/min



Figure S34 Preparative SFC separation for the BPR study. The mobile phase was made of 15% MeOH and 85% liquified CO₂. The organic portion had diethylamine added at a concentration of 0.1% (v/v). The flow rate was 60 mL/min, and the column temperature was held at 40°C for all separations. The BPR pressure is listed for each. The retention order was ibuprofen, prednisone, hydrocortisone, indapamide, and chlorthalidone.

Preparative Scale BPR Study Separation Information									
15% MeOH 60 mL/min									
Separation Paramet	Solv	vent Usage per Injec	Instrument Energy Consumption (kWh)						
Separation Type	Separation Time	Mass of CO ₂ (g) Mass of MeOH (g) Mass of DEA (g)		Average					
120 bar BPR Pressure	11	541.926	78.330	0.0700	0.312				
160 bar BPR Pressure	9.5	468.027	67.648	0.0604	0.280				
200 bar BPR Pressure	8.5	418.761	60.527	0.0541	0.254				
240 bar BPR Pressure	8.0	394.128	56.967	0.0509	0.241				

Table S15 Separation information for the preparative scale BPR study. The mass of CO₂ was determined using a pressure of 300 bar and 25°C.

Preparative Scale SFC BPR Study Fraction Information									
15% MeOH 60 mL/min									
Fraction	Fraction Volume (mL)	Methanol mass (g)	DEA Mass (g)	Energy to Remove (kWhr)					
120 bar BPR Pressure									
Ibuprofen	5.9	4.629	0.004	1.41E-03					
Prednisone	6.5	5.127	0.005	1.57E-03					
Hydrocortisone	5.2	4.130	0.004	1.26E-03					
Indapamide	6.6	5.198	0.005	1.59E-03					
Chlorthalidone	10.2	8.047	0.007	2.46E-03					
	140 bar BPR Pressure								
Ibuprofen	5.0	3.916	0.003	1.20E-03					
Prednisone	5.7	4.486	0.004	1.37E-03					
Hydrocortisone	4.4	3.489	0.003	1.07E-03					
Indapamide	5.9	4.700	0.004	1.44E-03					
Chlorthalidone	9.5	7.477	0.007	2.29E-03					
		200 bar BPR Pressur	e						
Ibuprofen	4.4	3.489	0.003	1.07E-03					
Prednisone	4.6	3.632	0.003	1.11E-03					
Hydrocortisone	3.8	2.991	0.003	9.14E-04					
Indapamide	5.6	4.415	0.004	1.35E-03					
Chlorthalidone	8.9	7.050	0.006	2.15E-03					
		240 bar BPR Pressur	e						
Ibuprofen	4.0	3.133	0.003	9.58E-04					
Prednisone	3.7	2.920	0.003	8.92E-04					
Hydrocortisone	3.7	2.920	0.003	8.92E-04					
Indapamide	5.1	4.059	0.004	1.24E-03					
Chlorthalidone	8.6	6.836	0.006	2.09E-03					

 Table S16 Fraction information for the preparative scale BPR study.

Preparative Scale BPR Study 15% MeOH 60 mL/min										
Separation Parameters	s AMGS Calculator Results					LCA Results				
BPR Pressure	Instrument Energy	Solvent Energ	gy Solvent EHS	Greenness	CED	GHG	ONGD	ACID	EUTR	PCOP
	Score	Score	Score	Score	(MJ)	(kg of CO ₂ eq.)	(kg eq.)	(kg of SO ₂ eq.)	(kg of (PO ₄) ³⁻ eq.)	(kg of ethane eq.)
			Ibuprofen Fr	action (Low	est Retain	ed Compound)				
120 bar	673	5039	682	6394	510	20.6	12.0	0.122	5.99E-03	0.561
160 bar	581	4352	589	5523	448	18.2	10.6	0.109	5.31E-03	0.485
% Decrease	14%	1	14% 14%	14%	12%	12%	12%	11%	11%	14%
200 bar	520	3894	527	4942	403	16.5	9.50	0.0992	4.80E-03	0.434
% Decrease	23%	2	23% 23%	23%	21%	20%	21%	19%	20%	23%
240 bar	490	3665	496	4651	380	15.5	8.96	0.0938	4.53E-03	0.408
% Decrease	27%	2	27% 27%	27%	25%	25%	25%	23%	24%	27%
			Chlorthalidone	Fraction (Hi	ghest Reta	ained Compour	nd)			
120 bar	673	5039	682	6394	511	20.7	12.0	0.123	6.01E-03	0.561
160 bar	581	4352	589	5523	449	18.3	10.6	0.110	5.33E-03	0.485
% Decrease	14%	1	14% 14%	14%	12%	12%	12%	11%	11%	14%
200 bar	520	3894	527	4942	404	16.5	9.51	0.100	4.81E-03	0.434
% Decrease	23%	2	23% 23%	23%	21%	20%	21%	19%	20%	23%
240 bar	490	3665	496	4651	381	15.6	8.98	0.095	4.55E-03	0.408
% Decrease	27%	2	27% 27%	27%	25%	25%	25%	23%	24%	27%

Table S17 AMGS and LCA results for the ibuprofen and chlorthalidone fraction of the BPR study.



Fig. S35 Energy consumption by the different parts of the preparative SFC. The description of what is attached to each power meter can be found in Table S2. A: energy consumption vs flow rate B: energy consumption vs BPR pressure



Figure S36 Example system design for NWPP energy (A) and wind energy (B).



Figure S37 Percent contribution to each impact factor for the analytical scale HPLC gradient separations using NWPP energy mix (A, C) and wind energy (B, D). HPLC separations utilizing methanol (A, B) and acetonitrile (C, D) are shown.



Figure S38 Percent contribution for the preparative scale separations using methanol. The SFC separation (A) is for the 60 mL/min separation at 120 bar BPR. The separation for HPLC is shown in B.

Impact Factor										
	CED	GHGP	ONGD	ACID	EUTR	РСОР				
Separation Type	(MJ)	(kg of CO ₂ eq.)	(kg of oil eq.)	(kg of SO ₂)	$(kg of (PO_4)^{3-}$	(kg of ethane ec	ן.)			
HPLC MeOH Gradient										
US Average	42.2	2.15	0.975	1.85E-02	6.76E-04	3.22E-02				
NWPP	23.7	1.17	0.556	9.43E-03	3.26E-04	3.11E-02				
% Decrease	-44%	-46%	-43%	-49%	-52%	-:	3%			
Wind	8.6	0.205	0.207	1.71E-04	3.21E-05	3.04E-02				
% Decrease	-80%	-90%	-79%	-99%	-95%	-(6%			
SFC MeOH Gradient 4 mL/min										
US Average	50	2.41	1.16	1.90E-02	7.45E-04	3.90E-02				
NWPP	30.8	1.40	0.726	9.80E-03	3.83E-04	3.78E-02				
% Decrease	-38%	-42%	-37%	-48%	-49%	-:	3%			
Wind	15.3	0.407	0.370	3.58E-04	8.39E-05	3.72E-02				
% Decrease	-69%	-83%	-68%	-98%	-89%	-!	5%			
		Pre	eparative HPLC	C MEOH						
US Average	372	10.7	8.91	4.08E-02	2.26E-03	1.12				
NWPP	335	8.81	8.08	2.29E-02	1.57E-03	1.12				
% Decrease	-10%	-18%	-9%	-44%	-31%		0%			
Wind	306	6.90	7.39	4.68E-03	9.88E-04	1.12				
% Decrease	-18%	-36%	-17%	-89%	-56%		0%			
Prep SFC MeOH Gradient 80 mL/min										
US Average	683	23.5	16.3	1.09E-01	6.05E-03	1.28				
NWPP	575	17.9	13.8	5.97E-02	4.06E-03	1.27				
% Decrease	-16%	-24%	-15%	-45%	-33%	-	1%			
Wind	494	12.8	11.9	1.01E-02	2.49E-03	1.27				
% Decrease	-28%	-46%	-27%	-91%	-59%	-:	1%			

Table S18 Reductions in impact factors from changing the source of energy. All separations are using methanol.The analytical SFC had a BPR pressure of 130 bar and the preparative scale SFC was for the 120 bar BPRseparations.