Supporting Information

Integrated Extraction, Enrichment, and Formulation of Parthenolide Using Thermoreversible Aqueous Biphasic Systems toward Antitumoral Applications

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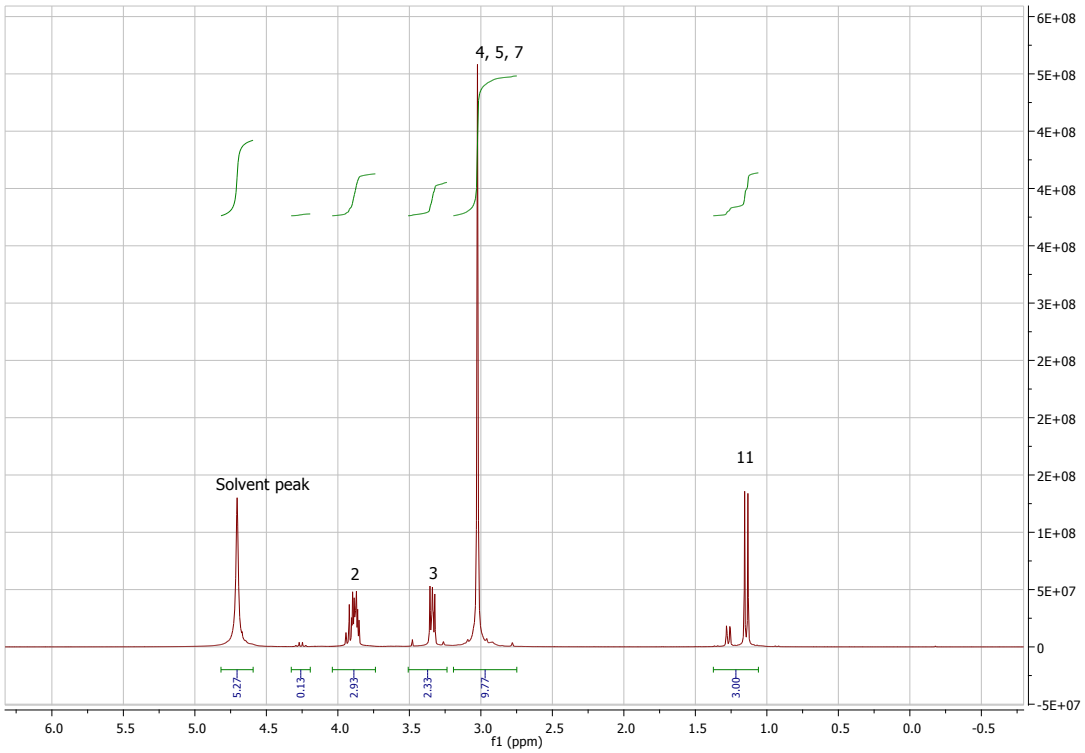

Figure S1. NMR spectra ^{1}H of ionic liquid [Ch][Lac]

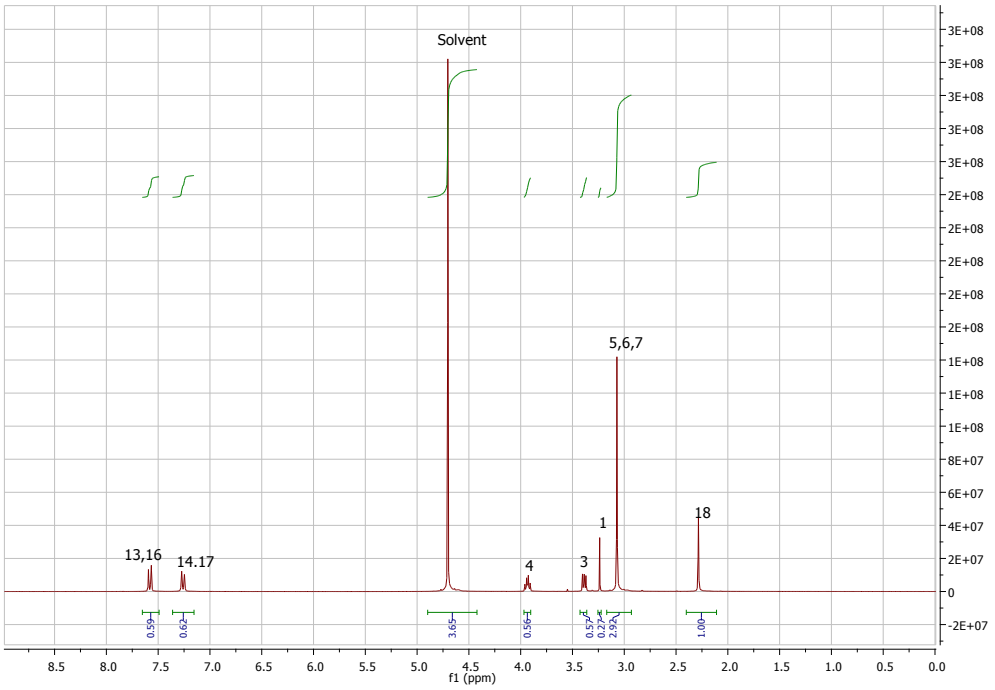

Figure S2. NMR spectra ^{1}H of ionic liquid [Ch][Tos]

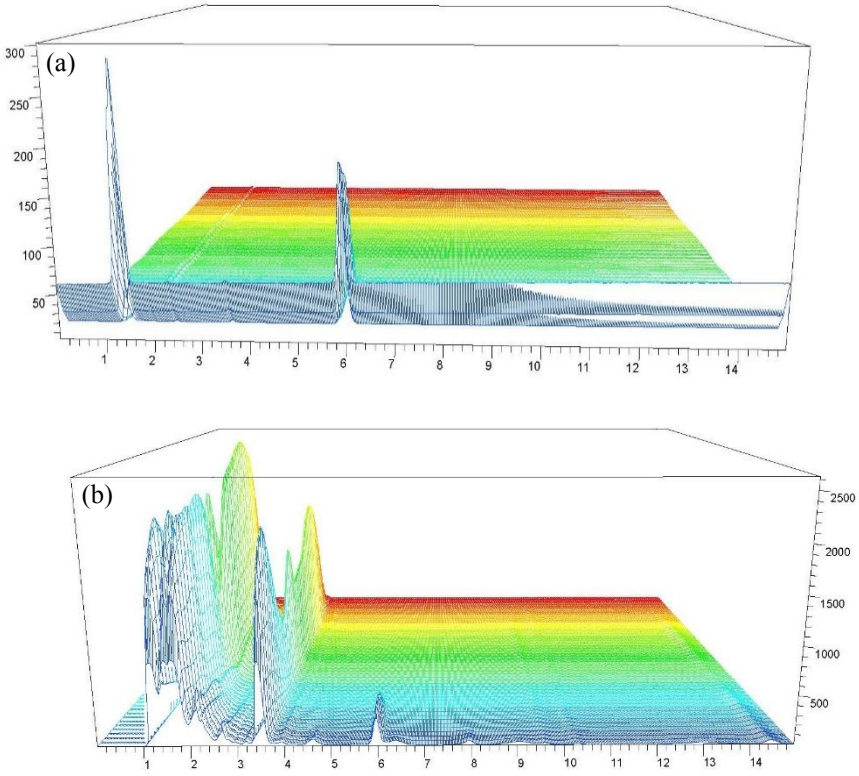

Figure S3. 3D HPLC chromatograms of (a) pure PAR and (b) PAR extracted from feverfew biomass in this study, recorded in the wavelength range 190–400 nm

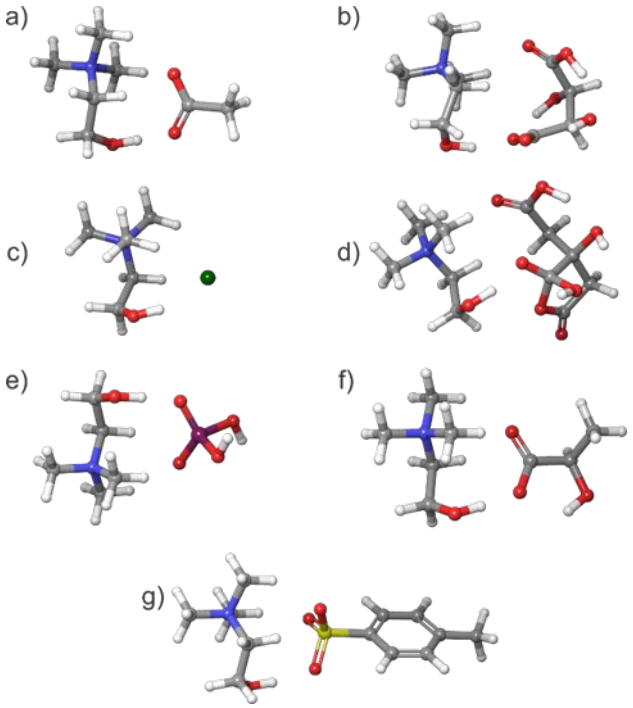

Figure S4. Optimized ion pairs of ILs investigated in this study: a) [Ch][Ac]; b) [Ch][Bit]; c) [Ch]Cl; d) [Ch][DHCit]; e) [Ch][DHP]; f) [Ch][Lac], and f) [Ch][Tos]

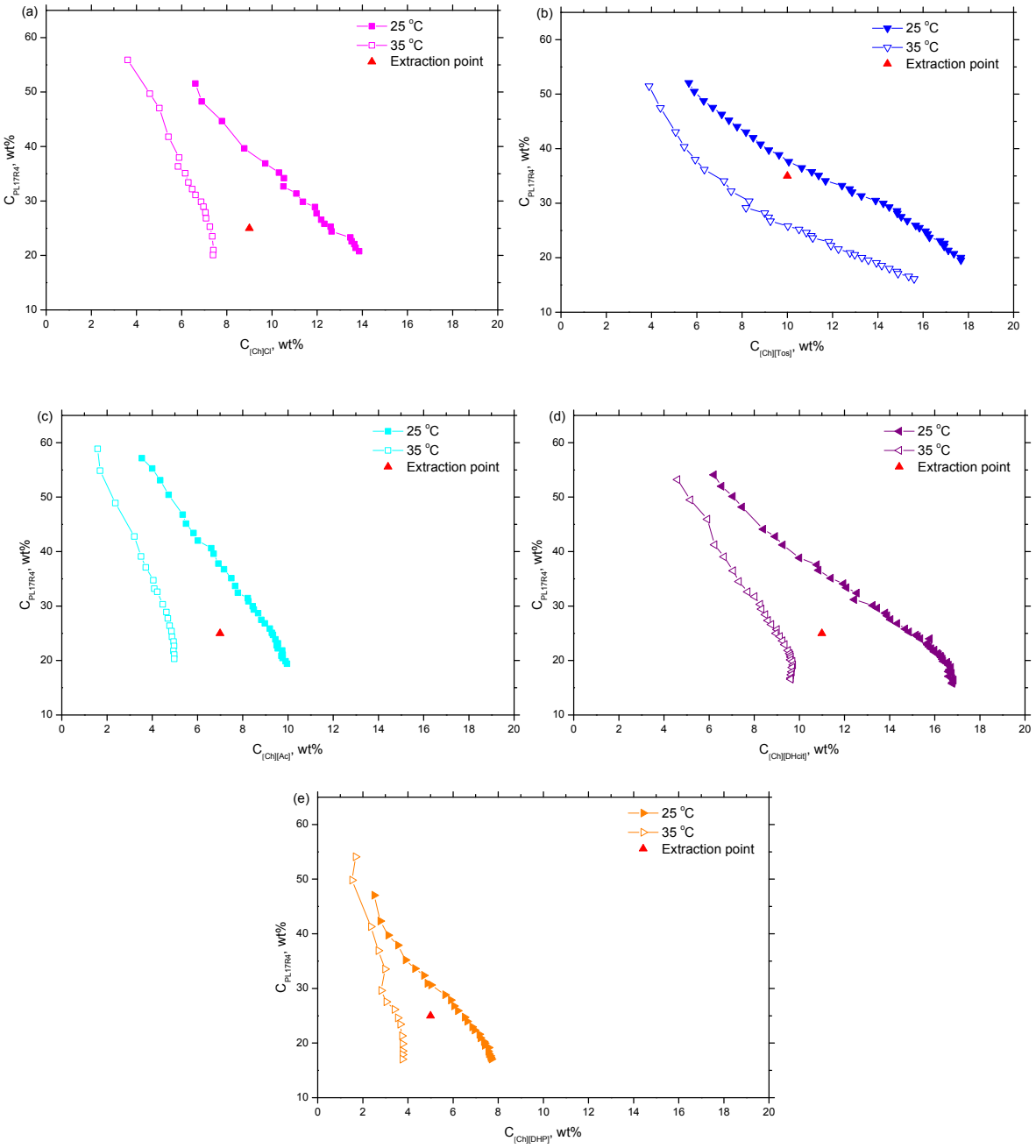

Figure S5. Phase diagrams at 25 °C and 35 °C with selected extraction points for systems composed of {IL/salt + PL17R4 + H_2O}

Table S1. pH values of studied IL, ABS and both IL and polymer rich phases

Compound	IL	ABS	IL-rich phase	PL-rich phase
[Ch]Cl	5.2	4.1	4	4.1
[Ch][Lac]	8.5	7.9	8	8
[Ch][Bit]	3.4	3.7	3.5	3.9
[Ch][Tos]	8.8	8.6	8.6	8.7
[Ch][Ac]	8.6	8.2	8.2	8.4
[Ch][DHCit]	3.7	4	3.8	4.2
[Ch][DHP]	3.5	3.6	3.4	4.0

Table S2a. Weight fraction composition for binodal data for the {IL (Y) + Polymer (X) + Water} ABS at 25 °C and at p = 0.1MPa

[Ch][Cl]		[Ch][Bit]		[Ch][Lac]		[Ch][Ac]	
100Y	**100X**	**100Y**	**100 X**	**100Y**	**100X**	**100Y**	**100X**
6.6119	51.5487	3.3969	52.0163	5.3680	50.5307	3.5385	57.1284
6.8925	48.2785	3.5959	50.8278	5.5634	49.4842	4.0028	55.2505
7.7908	44.6484	3.8923	49.2698	5.7927	48.5213	4.3509	53.0994
8.7744	39.6663	4.3939	46.9419	5.9501	47.7363	4.7283	50.4216
9.7045	36.8918	4.5460	45.8141	6.1398	46.7142	5.3503	46.7735
10.3105	35.1979	4.7494	44.6026	6.2777	45.5858	5.4970	45.1175
10.5356	34.1727	5.1499	42.8203	6.4411	44.2629	5.8246	43.4076
10.5100	32.6569	5.3074	41.6780	6.5818	43.5542	6.0192	42.0146
11.0858	31.3722	5.4552	40.3390	6.7052	42.6005	6.6132	40.6250
11.3697	29.8414	5.7420	39.5670	6.8423	41.6960	6.7156	39.5989
11.9058	28.8807	5.9201	38.7822	7.1365	40.3001	6.9289	37.7871
11.9759	27.7223	6.1718	37.7196	7.2624	39.4972	7.1760	36.7423
12.1817	26.5480	6.2720	36.8216	7.3935	38.7614	7.5010	35.1217
12.3224	25.8091	6.4351	36.1432	7.5195	38.1658	7.6707	33.6945
12.5963	25.2849	6.7002	35.4299	7.6294	37.5119	7.7859	32.4413
12.6431	24.3972	6.8267	34.1035	7.7356	36.7314	8.2276	31.4472
13.4741	23.2851	7.1389	32.5781	7.7987	36.2713	8.2550	30.8773
13.5278	22.6099	7.3417	31.5082	8.1124	35.1631	8.4431	29.9682
13.6507	22.0687	7.6984	30.4111	8.1545	34.5826	8.4962	29.3487
13.7107	21.3721	7.9625	29.1562	8.2211	34.1763	8.6863	28.6907
13.8657	20.7603	8.0368	28.4549	8.3451	33.7396	8.8271	27.4533
13.9600	20.3731	8.2972	27.4794	8.4093	33.1575	8.9784	26.8338
		8.5453	26.7807	8.5069	32.6679	9.2009	25.8511
		8.6775	25.6700	8.6372	32.2538	9.2908	25.0756
		8.8562	25.0878	8.7015	31.7101	9.3386	24.7080
		9.0387	24.1704	8.7368	30.9954	9.4474	23.8742
		9.1375	23.6045	8.9133	30.3692	9.5568	23.1594
		9.3510	22.8244	9.0607	29.5801	9.4996	22.7952
		9.4416	21.9890	9.1474	29.2238	9.5545	22.2250
		9.5153	21.4057	9.1894	28.3881	9.7507	21.8436
		9.6742	20.9221	9.2999	27.9886	9.7672	21.0649
		9.7795	20.1914	9.3780	27.6865	9.7145	20.8593
		9.8215	19.5991	9.4199	27.2035	9.7637	20.4411
		9.9246	18.9969	9.4090	26.6497	9.8988	19.8665
		9.0387	24.1704	9.6018	25.9605	9.9588	19.3914
		9.1375	23.6045	9.6943	25.5884	9.9258	18.8295
		9.3510	22.8244	9.6796	25.1219		
		9.4416	21.9890	9.8403	24.5392		
		9.5153	21.4057	9.9222	23.8355		
		9.6742	20.9221	9.9296	23.2655		
		9.7795	20.1914	10.0977	22.8725		
		9.8215	19.5991	10.1043	22.2837		
		9.9246	18.9969	10.1407	22.0097		
				10.1233	21.6294		
				10.2040	21.3263		
				10.2102	20.8259		
				10.2317	20.3623		
				10.2679	19.8999		

10.3311	19.3081
10.3896	18.9135
10.4319	18.5074
10.4130	18.0845

Table S2b. Weight fraction composition for binodal data for the {IL (Y) + Polymer (X) + Water} ABS at 25 °C and at p = 0.1MPa

[Ch][DHCit]		[Ch][DHP]		[Ch][Tos]	
100Y	**100X**	**100Y**	**100 X**	**100Y**	**100X**
6.2128	54.0826	2.5054	47.0324	5.6524	52.0727
6.5522	51.9805	2.7753	42.3168	5.8910	50.4648
7.0544	50.1194	3.1262	39.7416	6.3060	48.7506
7.4659	48.1833	3.5564	37.8986	6.7096	47.5512
8.4008	44.1014	3.8952	35.2050	7.1022	46.2890
8.9319	42.7544	4.3100	33.6172	7.4194	45.2064
9.2721	41.2238	4.7062	32.3906	7.7787	44.0361
10.0052	38.8491	4.8612	30.9178	8.1754	43.0433
10.7786	37.5903	5.0252	30.6221	8.4923	42.0065
10.8557	36.5626	5.6465	28.8247	8.8208	40.8119
11.3986	35.1056	5.8955	27.8686	9.1842	39.7314
11.9579	34.1003	6.0376	26.7873	9.6362	38.8536
12.0909	33.3775	6.2084	25.9307	10.0670	37.6243
12.5508	32.3706	6.5091	24.7223	10.6391	36.4917
12.4408	31.1801	6.6222	23.9780	11.0858	35.7560
13.2544	30.1186	6.8415	22.9403	11.3878	35.0947
13.4551	29.6256	6.9521	22.3664	11.6922	34.1092
13.8099	28.7258	7.1605	21.5974	12.4171	33.2269
13.9007	28.2289	7.2071	20.9361	12.7524	32.6193
14.0453	27.5318	7.3549	20.2746	12.8586	32.0384
14.3395	26.8020	7.3979	19.9675	13.2787	31.3404
14.6942	25.7997	7.4014	19.5636	13.9057	30.4849
14.8612	25.2536	7.5760	19.1645	14.2399	29.9525
15.1764	24.6787	7.5558	18.5013	14.5020	29.2989
15.2584	24.3968	7.5838	18.0303	14.8527	28.6048
15.3626	23.9880	7.6467	17.6510	14.8631	28.1394
15.7858	24.0072	7.6639	17.3279	15.0358	27.5228
15.6681	23.1581	7.7055	17.0757	15.3048	26.7963
15.6875	22.9038	7.6987	16.6968	15.6758	25.9121
15.7604	22.5496	7.7191	16.3021	15.8353	25.5097
15.8530	22.1585	7.7644	15.8513	16.1032	24.8834
15.9930	21.9012	7.7396	15.4338	16.1994	24.3648
15.9819	21.5971	7.7445	15.1324	16.2825	23.7367
16.1235	21.2732	7.7745	14.6341	16.7566	23.0829
16.1871	21.0662	7.5962	14.0661	16.9458	22.6376
16.2770	20.7668			16.9343	22.0741
16.3013	20.5601			17.1121	21.3618
16.3506	20.2521			17.3647	20.7443
16.3775	19.8594			17.6687	20.0443
16.5589	19.6475			17.6689	19.5344
16.5459	19.4901				
16.6281	19.1442				
16.7292	18.7414				

Table S3a. Weight fraction composition for binodal data for the {IL (Y) + Polymer (X) + Water} ABS at 35 °C and at p = 0.1MPa

[Cl][Cl]		[Ch][Bit]		[Ch][Lac]		[Ch][Ac]	
100Y	**100X**	**100Y**	**100 X**	**100Y**	**100X**	**100Y**	**100X**
3.6099	55.8891	2.6089	53.9240	2.9347	56.4747	1.5867	58.8627
4.5949	49.6986	2.8294	51.5302	3.1729	55.0509	1.6925	54.8398
5.0172	47.0505	3.3039	46.9439	3.3906	51.9609	2.3695	48.9140
5.4199	41.7642	3.4144	44.7079	3.4853	49.6160	3.2109	42.7531
5.8907	37.9611	3.5534	42.7257	3.6158	47.1558	3.5089	39.0953
5.8405	36.3465	3.7700	41.2089	3.7663	44.9505	3.7154	37.0788
6.1595	35.0851	3.8404	40.0222	3.8509	43.2923	4.0510	34.7396
6.3020	33.3877	3.9675	38.5787	3.9783	42.2333	4.0923	33.2030
6.4725	32.1762	4.0499	37.3651	4.0404	40.2531	4.2290	32.6068
6.6176	31.1012	4.2053	36.5387	4.1180	38.8627	4.4676	30.3146
6.8630	29.8510	4.3155	35.5614	4.2488	37.5202	4.6304	28.8741
6.9710	28.9446	4.4140	34.6134	4.3734	36.5189	4.6896	27.7077
7.0544	27.9101	4.5300	33.5909	4.4874	35.5131	4.7709	26.3914
7.0838	26.8151	4.6093	32.6427	4.5541	34.2085	4.8520	25.3992
7.2500	25.2858	4.5839	32.2783	4.6807	33.2767	4.8749	24.3367
7.3551	23.4905	4.6944	31.3584	4.7487	32.4144	4.9424	23.4615
7.4052	20.9787	4.9112	30.4426	4.8802	31.3726	4.9631	22.6561
7.3906	20.0695	4.8370	29.7683	4.8773	29.9212	4.9417	21.7631
7.2954	19.4880	4.9391	29.1607	4.8333	29.2714	4.9762	21.0896
7.4098	19.1830	4.9776	28.5442	5.0078	28.1764	4.9749	20.2946
7.3861	18.5725	5.0516	27.8819	5.0983	27.5194	4.9734	19.5635
7.3924	18.1831	5.2890	27.1423	5.1751	26.7249	4.9278	18.7223
7.3754	17.5877	5.2471	26.5854	5.2619	25.3663	4.9013	18.1438
7.3406	17.0055	5.3092	25.8575	5.2164	25.1364	4.8410	17.3434
7.1893	16.0685	5.3444	25.2056	5.3002	24.6849	4.8630	16.8107
7.1248	15.6387	5.3951	24.3756	5.3463	24.1661	4.6159	15.5470
7.0715	15.2580	5.4474	23.7669	5.3216	23.4272		
		5.5582	23.1484	5.4127	22.2605		
		5.6292	22.3295	5.4750	21.2031		
		5.6321	21.7171	5.4724	20.8109		
		5.6737	21.2260	5.5403	19.6643		
		5.7154	20.7369	5.4924	19.0591		
		5.7499	20.3021	5.4430	18.1673		
		5.8583	19.8813	5.4050	17.6809		
		5.8617	19.4386				
		5.8785	19.0259				
		5.8252	18.7776				
		5.7641	18.2802				
		5.7819	17.9101				
		5.7763	17.5380				
		5.8141	16.9840				

Table S3b. Weight fraction composition for binodal data for the {IL (Y) + Polymer (X) + Water} ABS at 35 °C and at p = 0.1MPa

[Ch][DHCit]		[Ch][DHP]		[Ch][Tos]	
100Y	**100X**	**100Y**	**100 X**	**100Y**	**100X**
4.6011	53.2191	1.6787	54.0892	1.5867	58.8627
5.1745	49.4885	1.5264	49.7950	1.6925	54.8398
5.9288	45.9404	2.3582	41.3053	2.3695	48.9140
6.2399	41.2628	2.6909	36.9141	3.2109	42.7531
6.6572	39.0477	2.9875	33.5351	3.5089	39.0953
7.0710	36.4821	2.8152	29.6262	3.7154	37.0788
7.3243	34.5131	3.0381	27.5555	4.0510	34.7396
7.7086	32.6190	3.4010	26.1445	4.0923	33.2030
8.0185	31.7334	3.5488	24.5998	4.2290	32.6068
8.2677	30.3152	3.6514	23.4578	4.4676	30.3146
8.3271	29.4456	3.7346	21.3162	4.6304	28.8741
8.4913	28.4302	3.7607	19.8785	4.6896	27.7077
8.6116	27.3524	3.7606	18.5623	4.7709	26.3914
8.7632	26.6300	3.7631	17.8812	4.8520	25.3992
9.0123	25.6726	3.7560	17.0555	4.8749	24.3367
8.9675	24.9800	3.7116	15.9781	4.9424	23.4615
9.1434	24.4037	3.6736	14.8013	4.9631	22.6561
9.2584	23.6240			4.9417	21.7631
9.3567	22.9128			4.9762	21.0896
9.5032	21.8568			4.9749	20.2946
9.5760	21.3032			4.9734	19.5635
9.6185	20.9598			4.9278	18.7223
9.6313	20.6266			4.9013	18.1438
9.6153	20.1128			4.8410	17.3434
9.6970	19.8417			4.8630	16.8107
9.7262	19.2090			4.6159	15.5470
9.6881	18.7221				
9.6738	17.9102				
9.6428	17.3854				
9.6317	16.7796				
9.6235	16.5724				

Table. S4. Extraction yield (Y, $mg_{PAR}/ g_{biomass}$) of PAR in the monophasic region obtained at 25 ºC and partition coefficient (K) obtained in the biphasic regime at 35 ºC

IL	Y ± SD, $mg_{PAR}/g_{biomass}$	K
[Ch]Cl	2.40 ± 0.10	6.73
[Ch][Bit]	2.42 ± 0.10	7.12
[Ch][Lac]	2.79 ± 0.13	9.76
[Ch][Tos]	1.26 ± 0.06	6.78
[Ch][Ac]	2.12 ± 0.02	9.35
[Ch][DHCit]	1.91 ± 0.09	6.02
[Ch][DHP]	1.32 ±0.06	14.19