Electronic Supplementary Information

Recovery of an antidepressant from pharmaceutical wastes using ionic liquid-based aqueous biphasic systems

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Experimental

Merchuk equation:

$$[IL] = A \cdot \exp\left(B \cdot [Salt]^{0.5} - C \cdot [Salt]^{3}\right) \quad \textbf{eqn. S1}$$

where A, B, and C are the constants obtained through the regression of experimental data, while [IL] and [Salt] are, respectively, IL and salt weight percentage compositions.

Tie-lines determination:

$$[IL]_{Salt} = A \cdot \exp\left(B \cdot [Salt]_{Salt}^{0.5} - C \cdot [Salt]_{Salt}^{3}\right) \quad \textbf{eqn. S2}$$

$$[IL]_{IL} = A \cdot \exp\left(B \cdot [Salt]_{IL}^{0.5} - C \cdot [Salt]_{IL}^{3}\right) \quad \textbf{eqn. S3}$$

$$[IL]_{IL} = \frac{[IL]_{M}}{\alpha} - \frac{1-\alpha}{\alpha} \cdot [IL]_{Salt} \quad \textbf{eqn. S4}$$

$$[Salt]_{IL} = \frac{[Salt]_{M}}{\alpha} - \frac{1-\alpha}{\alpha} \cdot [Salt]_{Salt} \quad \textbf{eqn. S5}$$

where α is the ratio between the mass of the top phase and the overall system and subscripts *IL*, *Salt* and *M* correspond to IL-rich (top), Salt-rich (bottom) and mixture point, respectively.

Tie-line length (TLL) determination:

$$TLL = \sqrt{\left([IL]_{IL} - [IL]_{Salt}\right)^{2} + \left([Salt]_{IL} - [Salt]_{Salt}\right)^{2}} \quad \textbf{eqn. S6}$$

Table S1 Validation parameters for the HPLC method developed.

	Concentration regime	
	High	**Low**
Number of standards	10	7
Quantification range (ppm)	2 - 25	0.15- 3.5
Correlation coefficient	0.9992	0.9996
RSD (%)	1.8	6
Limit of Detection ***(taken as a + 3Sa)***	0.6	0.05
Limit of Quantification ***(taken as 3 times LOD)***	1.9	0.15
Intraday standard deviation (%)	1.7 - 4.8	
Interday standard deviation (%)	2.1 - 9.3	

Results and Discussion

Table S2 Weight fraction data for systems composed of $[N_{4444}]Br$ + K_2HPO_4 + water at 298 (± 1) K and atmospheric pressure.

$[N_{4444}]Br$ / (wt%)	water / (wt%)	K_2HPO_4 / (wt%)	$[N_{4444}]Br$ / (wt%)	water / (wt%)	K_2HPO_4 / (wt%)
57.27	40.88	1.859	15.96	72.14	11.91
44.16	53.95	1.886	15.80	72.23	11.97
40.64	56.22	3.142	15.57	72.29	12.14
37.88	58.81	3.308	15.41	72.39	12.20
37.08	59.36	3.562	15.28	72.47	12.25
34.89	60.66	4.447	15.08	72.52	12.40
33.01	62.39	4.592	14.96	72.58	12.46
32.37	62.79	4.838	14.81	72.68	12.51
31.04	63.66	5.300	14.63	72.71	12.67
30.11	64.44	5.455	14.50	72.79	12.71
29.64	64.67	5.682	14.19	72.93	12.89
29.14	64.98	5.881	14.00	72.97	13.02
27.96	65.67	6.371	13.82	73.02	13.15
27.04	66.29	6.666	13.61	73.16	13.23
26.47	66.75	6.785	13.46	73.21	13.34
26.09	66.97	6.940	13.25	73.22	13.53
25.73	67.17	7.100	13.14	73.29	13.57
25.41	67.35	7.237	12.99	73.38	13.63
25.06	67.53	7.405	12.85	73.41	13.74
24.68	67.78	7.547	12.69	73.46	13.85
24.33	67.97	7.705	12.59	73.54	13.87
24.08	68.06	7.852	12.35	73.62	14.03
23.81	68.20	7.996	11.60	73.86	14.54
23.47	68.42	8.114	10.99	74.04	14.96
23.24	68.55	8.215	10.22	74.32	15.46
22.92	68.75	8.329	9.597	74.50	15.90
22.60	68.96	8.441	8.925	74.65	16.43
22.19	69.06	8.754	8.334	74.77	16.89

21.87	69.24	8.890	7.557	74.90	17.54
21.58	69.41	9.012	6.845	74.94	18.21
21.12	69.66	9.215	6.281	74.98	18.74
20.64	69.92	9.439	5.695	74.94	19.37
20.38	70.08	9.534	5.334	74.67	20.00
20.14	70.22	9.639	5.118	74.80	20.08
19.77	70.33	9.895	4.411	74.63	20.96
19.56	70.46	9.981	4.381	74.66	20.96
19.19	70.59	10.22	3.854	74.42	21.72
18.94	70.75	10.31	3.709	74.24	22.05
18.65	70.93	10.43	3.185	73.91	22.90
18.45	71.05	10.51	2.728	73.52	23.75
18.09	71.16	10.75	2.354	73.15	24.50
17.88	71.28	10.83	1.960	72.59	25.45
17.57	71.38	11.05	1.601	71.89	26.51
17.37	71.50	11.13	1.284	71.32	27.40
17.17	71.65	11.19	0.955	70.19	28.85
16.90	71.73	11.36	0.660	68.86	30.48
16.67	71.82	11.51	0.426	67.29	32.29
16.48	71.95	11.57	0.277	65.77	33.96
16.22	72.04	11.75			

Table S3 Weight fraction data for systems composed of $[N_{4444}]Br$ + K_3PO_4 + water at 298 (± 1) K and atmospheric pressure.

$[N_{4444}]Br$ / (wt%)	**water / (wt%)**	**K_3PO_4 / (wt%)**	**$[N_{4444}]Br$ / (wt%)**	**water / (wt%)**	**K_3PO_4 / (wt%)**
34.40	61.45	4.149	9.801	75.35	14.85
33.28	62.20	4.525	9.058	75.60	15.34
32.39	62.91	4.706	8.278	75.83	15.89
31.51	63.41	5.074	7.557	75.39	17.05
30.51	64.02	5.470	7.428	76.01	16.56
29.22	64.95	5.832	6.707	76.15	17.14
28.32	65.61	6.070	6.532	76.13	17.34
27.01	66.41	6.574	5.899	76.21	17.89
25.75	67.20	7.055	5.465	75.94	18.60
24.09	68.21	7.703	5.236	76.23	18.54
22.67	69.04	8.285	4.699	75.85	19.45
21.79	69.51	8.696	3.903	75.79	20.30
20.38	70.35	9.279	3.052	75.33	21.62
19.11	71.07	9.818	2.525	74.99	22.48
17.91	71.69	10.40	1.958	74.47	23.57
16.81	72.29	10.90	1.508	73.80	24.69
15.81	72.75	11.44	1.134	73.02	25.85
14.98	73.15	11.87	0.8591	72.19	26.95
14.14	73.57	12.29	0.6813	71.48	27.84
13.29	73.95	12.76	0.5457	70.81	28.65
12.45	74.32	13.23	0.3715	69.64	29.99
11.57	74.71	13.73	0.3140	69.15	30.54
10.62	75.02	14.37			

Table S4 Weight fraction data for the systems composed of $[N_{4444}]Cl$ + K_2HPO_4 + water at 298 (± 1) K and atmospheric pressure.

$[N_{4444}]Cl$ / (wt%)	**water / (wt%)**	**K_2HPO_4 / (wt%)**	**$[N_{4444}]Cl$ / (wt%)**	**water / (wt%)**	**K_2HPO_4 / (wt%)**
55.68	43.53	0.7904	13.79	71.68	14.52
42.79	55.31	1.894	12.42	71.88	15.71
40.77	57.02	2.201	11.22	72.02	16.76
39.12	58.23	2.644	10.03	72.15	17.82
37.40	59.77	2.821	8.915	72.21	18.88
35.34	61.10	3.565	8.450	71.86	19.69
33.80	62.23	3.966	7.867	72.20	19.93
32.46	63.20	4.342	7.014	72.16	20.82
30.94	64.21	4.852	6.840	72.06	21.10
29.62	65.07	5.306	6.349	72.10	21.55
27.46	66.37	6.171	5.523	71.87	22.60
26.15	67.20	6.654	4.674	71.62	23.71
24.24	68.01	7.752	3.814	71.25	24.93
22.91	68.77	8.322	3.299	71.05	25.66
21.48	69.34	9.181	2.741	70.67	26.59
20.27	69.87	9.860	2.165	70.11	27.72
18.77	70.38	10.84	1.508	69.18	29.32
17.25	70.85	11.91	1.083	68.27	30.65
15.88	71.23	12.89	0.7603	67.28	31.96
14.98	71.45	13.57	0.5341	66.27	33.20

Table S5 Parameters of Merchuk equation for the different IL + salt + H_2O systems determined in this work.

IL	**Salt**	***A***	***B***	$\boldsymbol{C \cdot 10^4}$
$[N_{4444}]Br$	**K_2HPO_4**	94.4 ± 4.7	-0.473 ± 0.022	0.93 ± 0.14
	K_3PO_4	86.2 ± 3.1	-0.440 ± 0.015	1.384 ± 0.072
$[N_{4444}]Cl$	**K_2HPO_4**	77.0 ± 1.9	-0.410 ± 0.012	0.585 ± 0.61

Table S6 Compositions (weight fraction) for the IL + phosphate-based salts + H_2O ternary systems at 298 (± 1) K and corresponding values of TLL at 298 (±1) K and atmospheric pressure.

IL	Salt	$[IL]_{IL}$ / (wt%)	$[Salt]_{IL}$ / (wt%)	$[IL]_{M}$ / (wt%)	$[Salt]_{M}$ / (wt%)	$[IL]_{Salt}$ / (wt%)	$[Salt]_{Salt}$ / (wt%)	TLL
$[P_{4444}]Br$	**K_2HPO_4/KH_2PO_4**	66.80	0.84	29.92	15.06	0.85	26.27	70.69
$[N_{4444}]Br$	**K_2HPO_4/KH_2PO_4**	53.09	1.45	29.99	15.39	0.78	33.01	61.10[22]
$[N_{4444}]Cl$	**K_2HPO_4/KH_2PO_4**	39.02	2.50	27.52	13.86	0.13	40.89	54.64
$[N_{4444}]Br$	**K_2HPO_4**	60.61	0.58	30.01	15.03	0.57	28.94	66.41
$[N_{4444}]Br$	**K_3PO_4**	65.20	0.63	29.99	15.04	0.72	27.02	69.66
$[N_{4444}]Cl$	**K_3PO_4**	53.95	0.70	29.88	15.13	0.22	32.91	62.65
$[P_{i(444)1}][Tos]$	**K_2HPO_4/KH_2PO_4**	61.91	3.77	30.06	15.00	0.92	25.27	64.67
$[P_{4441}][MeSO_4]$	**K_2HPO_4/KH_2PO_4**	51.77	1.60	29.54	14.79	1.25	31.57	58.74
$[N_{4444}]Cl$	**K_2HPO_4**	49.53	1.01	30.02	15.04	0.31	36.40	60.63

Table S7 Weight fraction and extraction efficiency data obtained during the assessment of the maximum concentration of amitriptyline hydrochloride able to be processed by IL-based ABS (considering the ternary system composed of $[N_{4444}]Br$ + K_3PO_4 + H_2O): mass of amitriptyline initially added in the ABS (m_{Ami}^{ABS}), concentration of amitriptyline IL-rich phase (C_{Ami}^{IL}), concentration of amitriptyline in salt-rich phase (C_{Ami}^{Salt}), extraction efficiencies (EE_{Ami}) and logarithmic partition coefficients ($\log K_{Ami}$) with corresponding standard deviations (σ).

$[N_{4444}]Br]_M$ / (wt%)	$[K_3PO_4]_M$ / (wt%)	$[water]_M$ / (wt%)	m_{Ami}^{ABS} / (mg)	C_{Ami}^{IL} / ($mg.g^{-1}$)	C_{Ami}^{Salt} / ($\mu g.g^{-1}$)	$EE_{Ami} \pm \sigma$ / (%)	$\log K_{Ami} \pm \sigma$
10.01	24.78	65.21	2.53	3.2	0.52	89.3 ± 0.6	>2.5
9.97	24.78	65.25	5.12	6.0	0.31	83 ± 2	>2.5
10.02	24.76	65.22	10.2	12.1	0.37	84 ± 2	>2.5
10.00	24.76	65.24	13.8	16.3	0.70	87.0 ± 0.5	>2.5
10.13	24.86	65.01	29.9	37.4	1.52	88.5 ± 0.7	>2.5
10.13	24.98	64.89	49.8	67.9	3.18	97 ± 3	>2.5
10.16	25.21	64.63	75.4	93.5	2.04	90 ± 3	>2.5
10.24	25.22	64.54	100.6	88.2	3.46	66 ± 1	>2.5

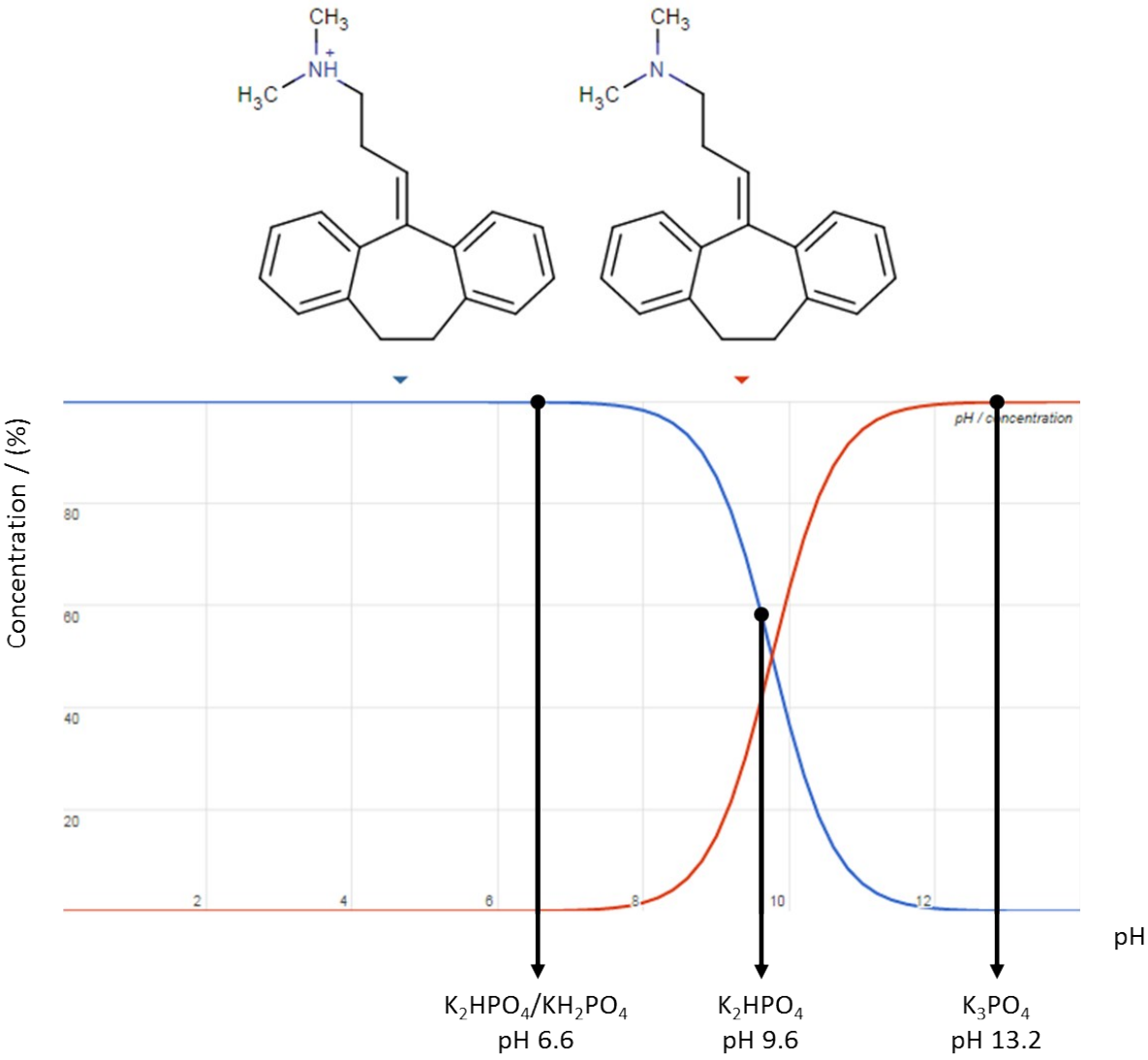

Fig. S1 Speciation curves of amitriptyline hydrochloride for the different values of pH investigated in this work (adapted from the content acquired in the chemical free database Chemspider – www.chemspider.com) – accessed on 24th November 2015.