Supporting Information

Design of non-steroidal anti-inflammatory drug-based ionic liquids with improved water solubility and drug delivery

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Table S1. Water content of ILs after drying in vacuum line.

	Water content (wt%)
[Ch][Ibu]	1.90 ± 0.11
[Ch][Ket]	2.12 ± 0.21
[Ch][Nap]	0.39 ± 0.08

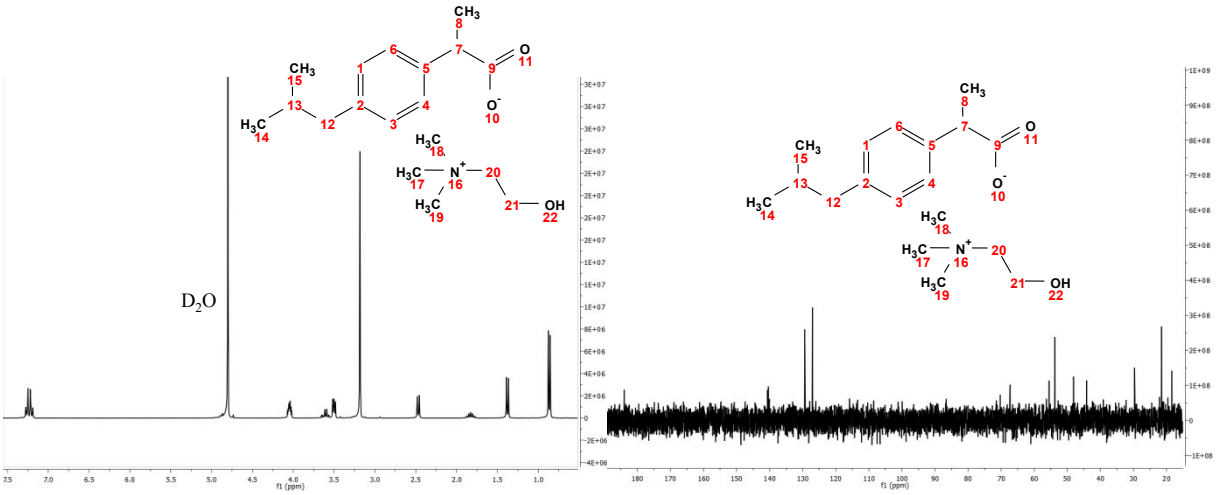

Figure S1. ^{1}H and ^{13}C NMR in D_2O of [Ch][Ibu].

^{1}H NMR (D_2O, 300 MHz, [ppm]): 0.86 (d, 6H, $\mathbf{H_{14,15}}$), 1.38 (d, 3H, $\mathbf{H_8}$), 1.83 (m, 1H, $\mathbf{H_{13}}$), 2.47 (d, 2H, $\mathbf{H_{12}}$), 3.18 (s, 9H, $\mathbf{H_{17,18,19}}$), 3.50 (q, 2H, $\mathbf{H_{20}}$), 3.60 (q, 1H, $\mathbf{H_7}$), 4.04 (m, 2H, $\mathbf{H_{21}}$), 7.23 (dd, 4H, $\mathbf{H_{1,3,4,6}}$).

^{13}C NMR (D_2O, 75 MHz, [ppm]): 18.23 (1C, $\mathbf{C_8}$), 21.52 (2C, $\mathbf{C_{14,15}}$), 29.42 (1C, $\mathbf{C_{13}}$), 44.04 (1C, $\mathbf{C_{12}}$), 48.00 (1C, $\mathbf{C_7}$), 53.73 (3C, $\mathbf{C_{17,18,19}}$), 55.45 (1C, $\mathbf{C_{21}}$), 67.46 (1C, $\mathbf{C_{20}}$), 127.06 (4C, $\mathbf{C_{1,3,4,6}}$), 129.38 (1C, $\mathbf{C_5}$), 140.19 (1C, $\mathbf{C_2}$), 183.74 (1C, $\mathbf{C_9}$).

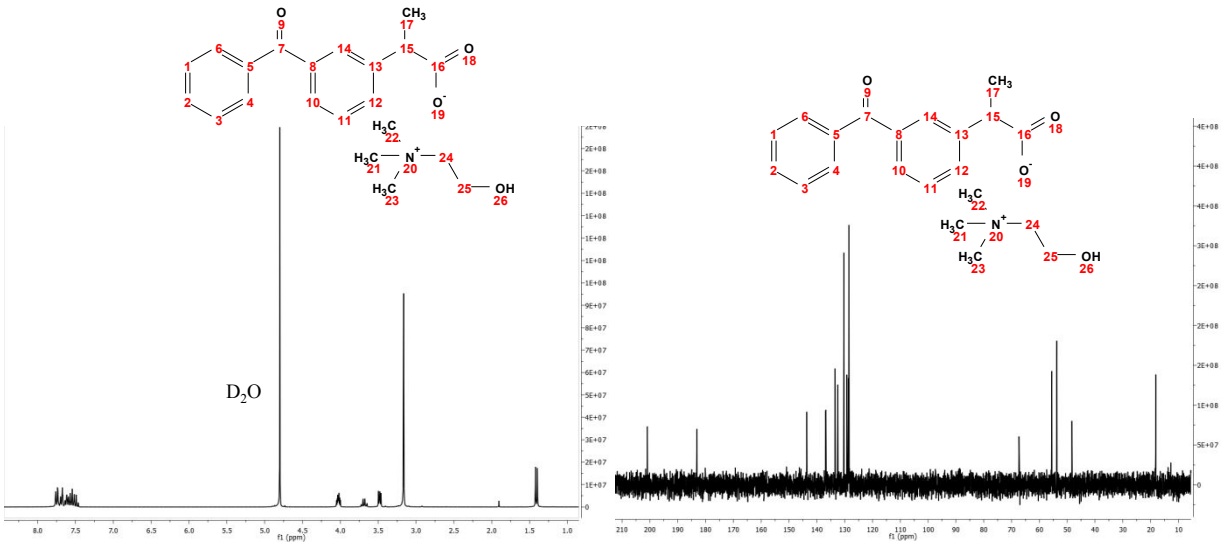

Figure S2. ^{1}H and ^{13}C NMR in D_2O of [Ch][Ket].

^{1}H NMR (D_2O, 300 MHz, [ppm]): 1.41 (d, 3H, $\mathbf{H_{17}}$), 3.16 (s, 9H, $\mathbf{H_{21,22,23}}$), 3.47 (q, 2H, $\mathbf{H_{24}}$), 3.69 (q, 1H, $\mathbf{H_{15}}$), 4.01 (m, 2H, $\mathbf{H_{25}}$), 7.46-7.76 (m, 9H, $\mathbf{H_{1,2,3,4,6,10,11,12,14}}$).

^{13}C NMR (D_2O, 75 MHz, [ppm]): 18.19 (1C, $\mathbf{C_{17}}$), 48.30 (1C, $\mathbf{C_{15}}$), 53.76 (3C, $\mathbf{C_{21,22,23}}$), 55.51 (1C, $\mathbf{C_{25}}$), 67.24 (1C, $\mathbf{C_{24}}$), 128.48-143.61 (12C, $\mathbf{C_{1,2,3,4,5,6,8,10,11,12,13,14}}$), 183.09 (1C, $\mathbf{C_{16}}$), 200.93 (1C, $\mathbf{C_7}$).

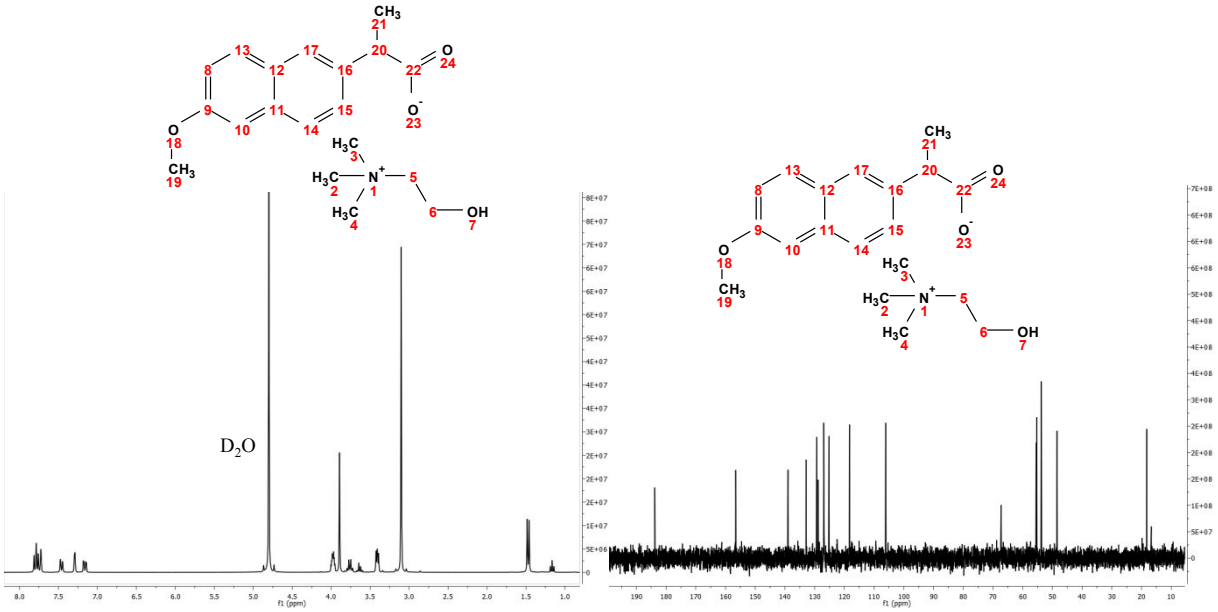

Figure S3. ^{1}H and ^{13}C NMR in D_2O of [Ch][Nap].

^{1}H NMR (D_2O, 300 MHz, [ppm]): 1.47 (d, 3H, $\mathbf{H_{21}}$), 3.10 (s, 9H, $\mathbf{H_{2,3,4}}$), 3.41 (q, 2H, $\mathbf{H_5}$), 3.60-3.83 (m, 1H, $\mathbf{H_{20}}$), 3.89 (s, 3H, $\mathbf{H_{19}}$), 3.97 (m, 2H, $\mathbf{H_6}$), 7.14-7.81 (m, 6H, $\mathbf{H_{8,10,13,14,15,17}}$).

^{13}C NMR (D_2O, 75 MHz, [ppm]): 18.24 (1C, $\mathbf{C_{21}}$), 48.42 (1C, $\mathbf{C_{20}}$), 53.70 (3C, $\mathbf{C_{2,3,4}}$), 55.46 (1C, $\mathbf{C_{19}}$), 67.27 (1C, $\mathbf{C_6}$), 106.10 (1C, $\mathbf{C_{10}}$), 118.27 (1C, $\mathbf{C_{18}}$), 125.20-129.33 (5C, $\mathbf{C_{12,13,14,15,17}}$), 132.90-138.95 (2C, $\mathbf{C_{11,16}}$), 156,57 (1C, $\mathbf{C_9}$), 183.79 (1C, $\mathbf{C_{22}}$).

Table S2. Cholinium:NSAID molar ratio calculated by ^{1}H NMR in D_2O.

	Ch:NSAID ratio
[Ch][Ibu]	1:0.88
[Ch][Ket]	1:1.00
[Ch][Nap]	1:1.02

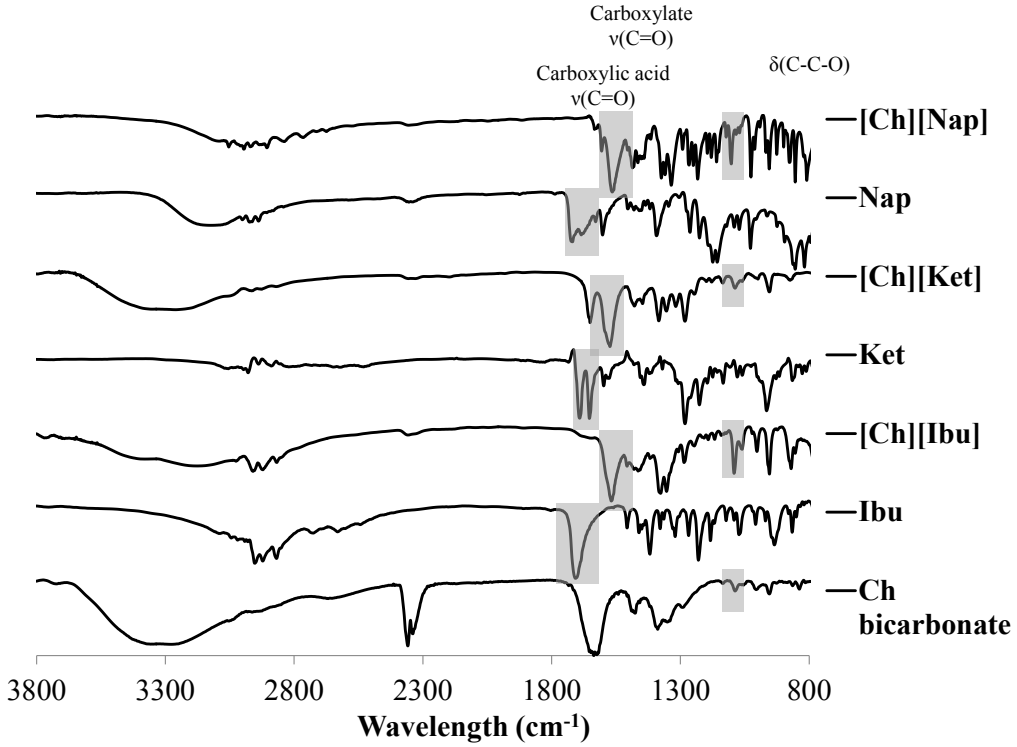

Figure S4. FTIR spectra of ILs and their respective precursors.

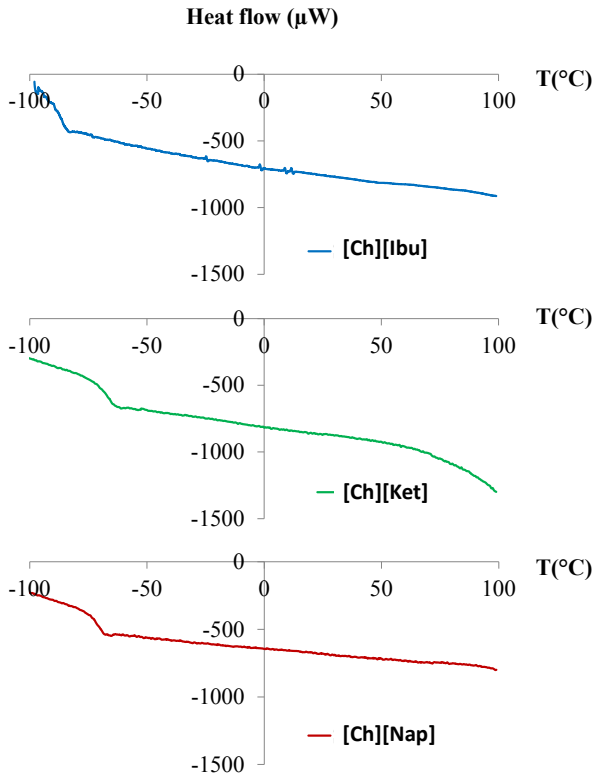

Figure S5. DSC curves of [Ch][NSAID] ILs.

Table S3. Incorporation of NSAIDs and respective ILs.

	Added compound ± uncertainty[1] (mg)	**Averaged retained compound ± S.D.[2] (mg)**	**Averaged ratio of compound incorporated + S.D.[2] (%)**
Ibu	10.00 ± 0.06	9.80 ± 0.16	98.0 ± 1.6
Ket	10.00 ± 0.06	9.30 ± 0.58	93.0 ± 5.8
Nap	10.00 ± 0.06	9.50 ± 0.35	95.0 ± 3.5
[Ch][Ibu]	15.00 ± 0.16	14.97 ± 0.07	99.8 ± 0.5
[Ch][Ket]	14.10 ± 0.15	13.84 ± 0.21	98.2 ± 1.5
[Ch][Nap]	14.50 ± 0.15	14.35 ± 0.21	99.0 ± 1.4

[1] Uncertainty of the mass of compound deposited in BC.

[2] Standard deviation determined from a set of 9 experiments.

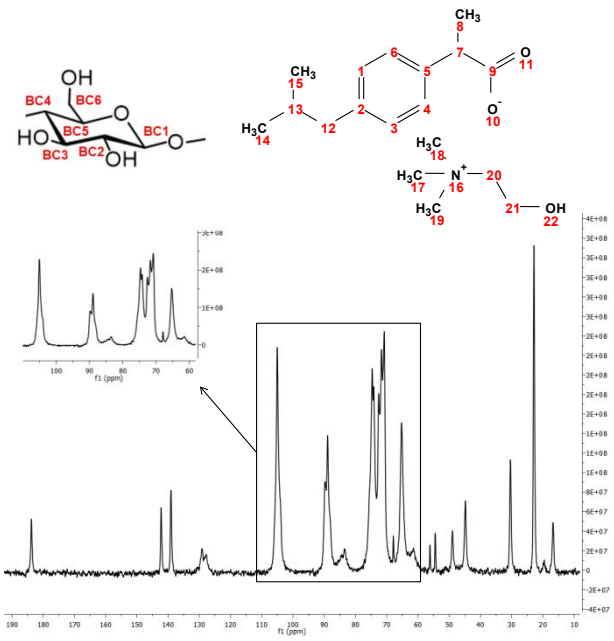

Figure S6. Solid ^{13}C NMR of BC-[Ch][Ibu].

16.78 (1C, $\mathbf{C_8}$), 22.86 (2C, $\mathbf{C_{14,15}}$), 30.39 (1C, $\mathbf{C_{13}}$), 44.80 (1C, $\mathbf{C_{12}}$), 48.96 (1C, $\mathbf{C_7}$), 54.47 (3C, $\mathbf{C_{17,18,19}}$), 56.15 (1C, $\mathbf{C_{21}}$), 65.26 (1C, **BC6**), 67.52 (1C, $\mathbf{C_{20}}$), 70.80-74.64 (3C, **BC2**, **BC3**, **BC5**), 88.91 (1C, **BC4**), 106.06 (1C, **BC1**), 127.73 (4C, $\mathbf{C_{1,3,4,6}}$), 129.06 (1C, $\mathbf{C_5}$), 139.08-142.22 (1C, $\mathbf{C_2}$), 183.77 (1C, $\mathbf{C_9}$).

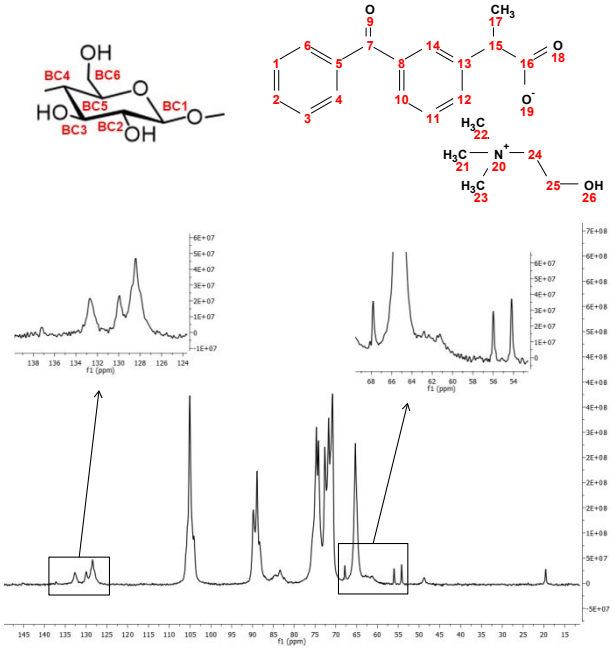

Figure S7. Solid ^{13}C NMR of BC-[Ch][Ket].

19.56 (1C, $\mathbf{C_{17}}$), 48.76 (1C, $\mathbf{C_{15}}$), 54.18 (3C, $\mathbf{C_{21,22,23}}$), 55.99 (1C, $\mathbf{C_{25}}$), 65.30 (1C, **BC6**), 67.82 (1C, $\mathbf{C_{24}}$), 70.80-74.64 (3C, **BC2, BC3, BC5**), 88.91 (1C, **BC4**), 105.08 (1C, **BC1**), 128.42-137.46 (12C, $\mathbf{C_{1,2,3,4,5,6,8,10,11,12,13,14}}$), 184.62 (1C, $\mathbf{C_{16}}$), 193.46 (1C, $\mathbf{C_7}$).

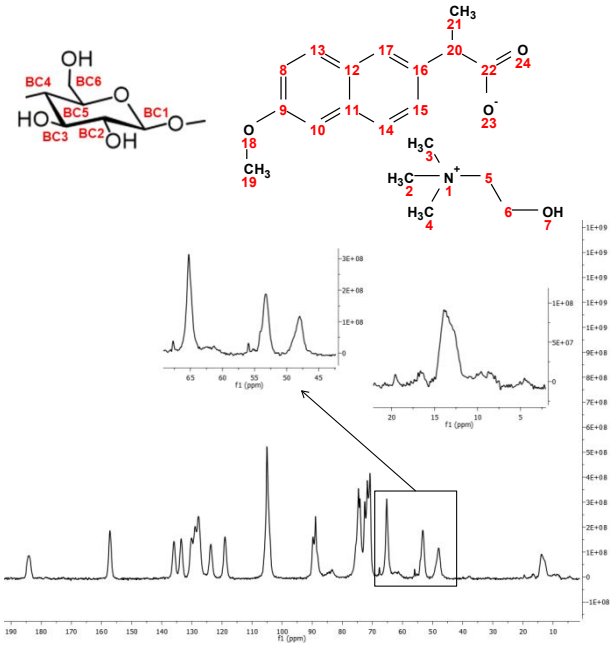

Figure S8. Solid ^{13}C NMR of BC-[Ch][Nap].

13.88 (1C, $\mathbf{C_{21}}$), 47.98 (1C, $\mathbf{C_{20}}$), 53.26 (3C, $\mathbf{C_{2,3,4}}$), 55.96 (1C, $\mathbf{C_{19}}$), 65.25 (1C, **BC6**), 67.69 (1C, $\mathbf{C_6}$), 70.78-74.60 (3C, **BC2**, **BC3**, **BC5**), 88.89 (1C, **BC4**), 106.03 (1C, **BC1**),118.98(1C, $\mathbf{C_{18}}$), 123.65-130.08 (5C, $\mathbf{C_{12,13,14,15,17}}$), 133.53-135.93 (2C, $\mathbf{C_{11,16}}$), 157.20 (1C, $\mathbf{C_9}$), 184.05 (1C, $\mathbf{C_{22}}$).

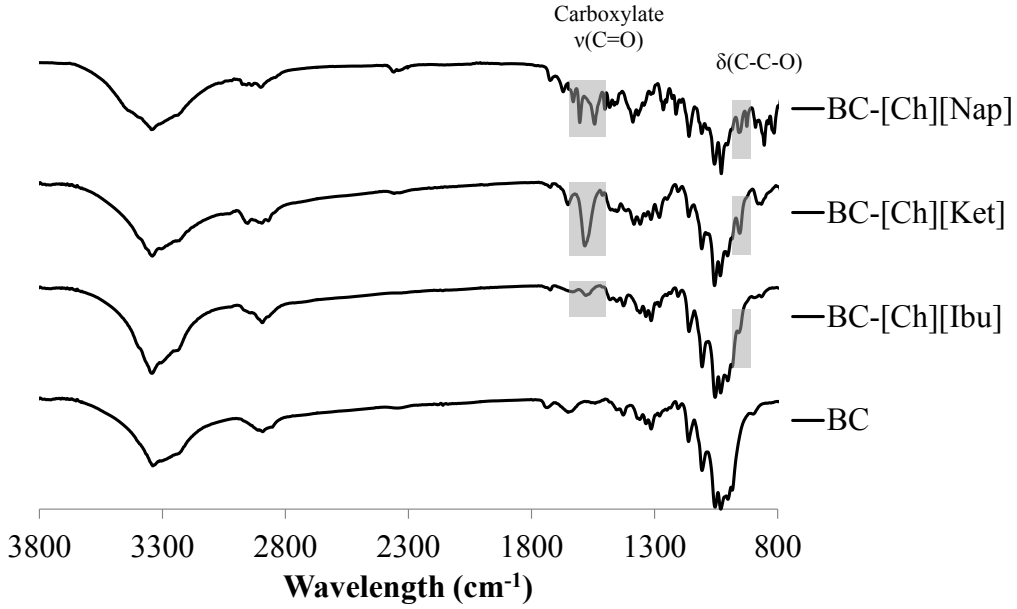

Figure S9. FTIR spectra of IL-incorporated BC membranes.

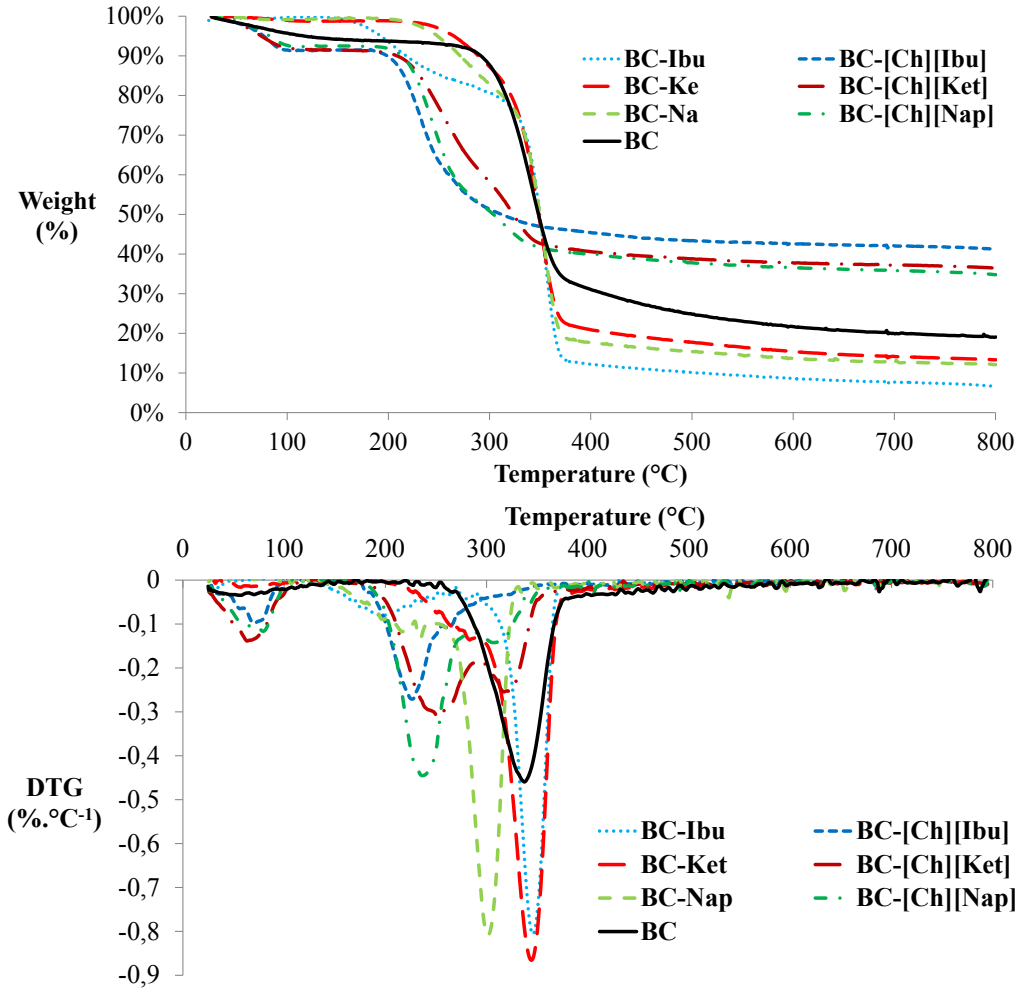

Figure S10. Thermogravimetrical curves (top) and associated derivative curves (down) of BC-NSAID and BC-IL membranes.

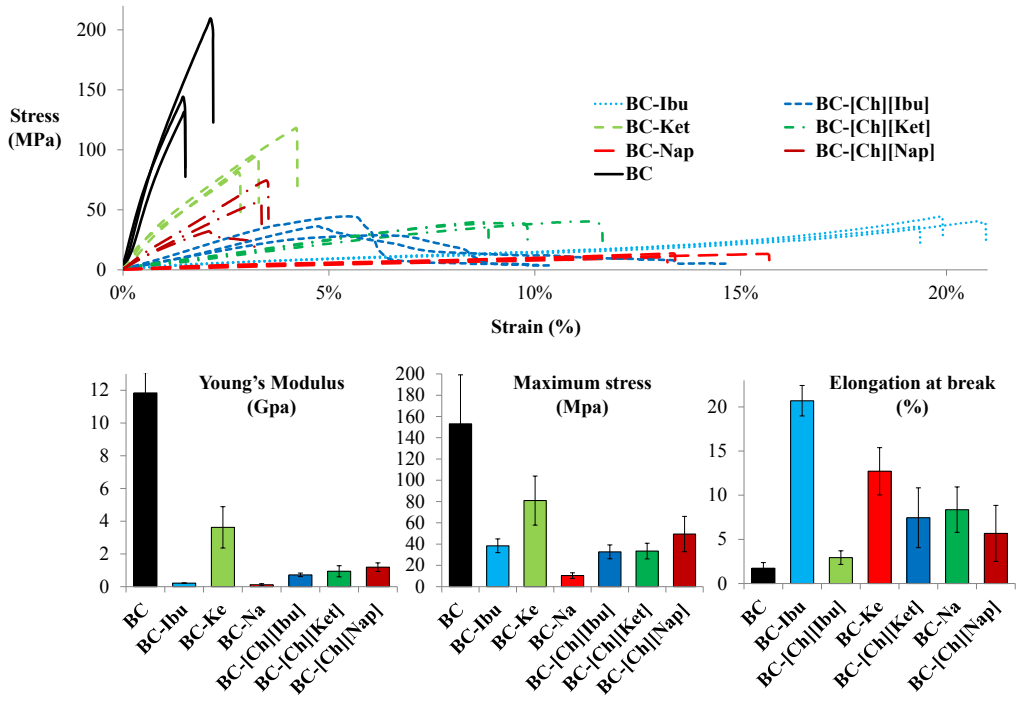

Figure S11. Top: Stress/strain curves of BC, BC-NSAID and BC-ILs membranes; bottom: tensile tests results on membranes with Young's modulus (left), maximum stress (middle) and elongation at break (right).

Table S4. *n* and *a* parameters and fitting factor between experimental data and the Weibull model described as: $\boldsymbol{log\,(-ln\,(Max\ release - Cumulative\ release))\ =\ n * log\,(t)\ - log\,(a)}$.

	n	***a***	***R²***
BC-Ibu	0.66	-0.42	0.94
BC-[Ch][Ibu]	0.30	0.68	0.95
BC-Ket	0.79	0.46	0.99
BC-[Ch][Ket]	0.56	0.82	0.99
BC-Nap	0.94	0.18	1.0
BC-[Ch][Nap]	0.20	0.53	0.99