1. Experimental Section

1.1 General methods

All chemicals unless otherwise stated were purchased from Aldrich Chemical Company (Dorset, UK) in reagent grade ≥98% and used without further purification.

Nuclear Magnetic Resonance Spectroscopy (NMR). $^1$H and $^{13}$C NMR spectra were collected utilizing a Bruker spectrometer 500 MHz Bruker Avance Spectrometer Bruker/Magnex UltraShield 500 MHz magnet operating at 500 MHz for $^1$H and 125 MHz for $^{13}$C spectra, respectively.

Thermogravimetrical Analysis (TGA). Thermogravimetric analysis was performed on a Mettler Toledo Stare TGA/DSC unit (Leicester, UK) under nitrogen. Samples between 5 and 10 mg were placed in open alumina pans and were heated from 25 °C to 800 °C with a heating rate of 5 °C/min. Decomposition temperatures (T$_{5\%\text{dec}}$) were reported from onset to 5 wt% mass loss.

Differential Scanning Calorimetry (DSC). Differential scanning calorimetry was performed on a Mettler Toledo Star DSC unit (Leicester, UK) under nitrogen. Samples were placed in closed aluminum pan perforated with a pin-hole to equilibrate pressure from potential expansion of evolved gases or residual solvents. An empty closed pan was used as a reference. For standard DSC experiments, samples between 5 and 10 mg were heated from 25 °C to 110 °C at a heating rate of 5 °C/min followed by a 5 min isotherm. A cooling rate of 5 °C/min to -70 °C was followed by a 5 min isotherm at -70 °C, and the cycle was repeated twice. Second and third cycles proved to be identical and only the third heating run was used for data collection. For DSC analysis of SILP-materials, samples between 5 and 10 mg were heated from -80 °C to 200 °C at a heating rate of 5 °C/min.

Fourier Transform Infra Red Spectroscopy (FTIR). Infrared spectra were recorded on neat samples from 650 - 4000 cm$^{-1}$ on a Perkin-Elmer (Dublin, Ireland) Spectrum 100 FT-IR spectrometer fitted with a Universal ATR Sampling Accessory.
UV-VIS. The UV-VIS spectra used for development of calibration curves and in the determination of the release of the active ingredient from the supported phases were performed on a Varian CARY 3 UV-Visible Spectrophotometer.

1.2. Synthesis

Synthesis of ibuprofenic acid

Ibuprofenic acid was synthesized from sodium ibuprofenate dihydrate by the treating sodium ibuprofenate with an excess of 2 N HCl. Diethyl ether was added to obtain two clear layers, and the aqueous layer was extracted with diethyl ether. The combined organic layers were repeatedly washed with deionized H2O, dried over Na2SO4, and the solvent was removed under reduced pressure. Any remaining volatiles were removed under high vacuum (0.01 mbar, 24 h) to yield ibuprofenic acid as a colorless solid. Analytical data were in accordance with literature values.

Synthesis of tetrabutylphosphonium ibuprofenate ([P4444][Ibu]) 1

Ibuprofenic acid (1.032 g, 5 mmol) and tetrabutylphosphonium hydroxide (~40% sol. in H2O) (3.414 g, 5 mmol) were dissolved in 20 mL of acetone and stirred for 15 min at room temperature. The solvent was evaporated and the remaining viscous liquid was dried at 0.1 mbar with stirring for 24 h to obtain [P4444][Ibu] in quantitative yield as a colorless viscous liquid.

1H-NMR (300 MHz, d6-DMSO) δ (ppm) = 7.13 (d, J = 8.08 Hz, 2H), 6.94 (d, 8.08 Hz, 2H), 3.21 (q, 7.74 Hz, 1H), 2.48 (m, 2H), 2.36 (d, 7.28 Hz, 2H), 2.14 (m, 8H), 1.77 (sept, 6.15 Hz, 1H), 1.40 (m, 16 H), 1.18 (d, J = 7.03 Hz, 3H), 0.91 (t, 7.02 Hz, 12H), 0.84 (d, J = 7.02 Hz, 6H).

13C-NMR (75 MHz, d6-DMSO) δ (ppm) = 174.8, 144.2, 136.9, 127.8, 127.2, 49.3, 44.4, 29.7, 23.4 (d, J = 15.8 Hz), 22.7 (d, J = 4.7 Hz), 22.2, 20.5, 17.3 (d, J = 48.1 Hz), 13.3.

IR (neat) ν = 2957, 2929, 2870, 1588, 1459, 1371, 1341, 860, 721 cm⁻1.

HRMS (ES+) [m/z] = 259.2550; (ES-) [m/z] = 205.1237.

Tg -43 °C (DSC), T5%onset 237 °C (TGA).
Synthesis of lidocainium ibuprofenate ([Lid][Ibu]) 2

Ibuprofenic acid (3.09 g, 15.0 mmol) and lidocaine free base (3.51 g, 15.0 mmol) were melted with stirring until a free-flowing clear liquid was obtained. The mixture was cooled to room temperature to obtain 2 as a yellow liquid. The identity and purity of the obtained product were confirmed via $^1$H NMR.

$^1$H-NMR (300 MHz, d6-DMSO) $\delta$ (ppm) = 9.19 (s, 1H), 7.19 (d, $J = 8.03$ Hz, 2H), 7.08 (m, 5H), 3.63 (q, $J = 7.07$ Hz, 1H), 2.63 (q, $J = 6.87$ Hz, 4H), 2.42 (d, $J = 7.47$ Hz, 2H), 2.15 (s, 6H), 1.81 (m, 1H), 1.35 (d, $J = 7.38$ Hz, 2H), 1.08 (t, $J = 7.16$ Hz, 6H), 0.86 (d, 6.74 Hz, 2H).

$^{13}$C-NMR (75 MHz, d6-DMSO) $\delta$ (ppm) = 175.5, 169.4, 139.5, 138.6, 153.2, 135.1, 129.0, 127.6, 127.1, 126.2, 56.8, 48.1, 44.4, 44.3, 29.7, 22.2, 18.6, 18.2, 12.1.

IR (neat) $\nu$ = 3268, 2964, 2931, 2871, 1680, 1501, 1461, 1379, 1209, 1065, 768 cm$^{-1}$.

HRMS (ES$^+$) [m/z] = 235.1799; (ES$^-$) [m/z] = 205.1249.

$T_g$ -27 °C (DSC); $T_{5\%onset}$ 177 °C (TGA)

Figure S1. TGA profiles of SiO$_2$-90 (black), neat [Lid][Ibu] 2 (red), and 20% loading of 2 on the silica (blue).
1.3 General procedure for the synthesis of supported phases.

Preparation of the solid carrier:

Non pre-calcined silica: Silica (pore size 90 Å) was dried under heating (70 °C) and vacuum (0.01 mbar).

Pre-calcined silica: Calcination of silica (pore size 90 Å) was done at 450 °C, for 24 h in air.

Loading procedure:

The IL used was dried under vacuum and heated to remove volatiles or water and then 0.01 g of IL was dissolved in ~20 mL of dry ethanol. The solid carrier (appropriate to the wt% target loading: 0.09 g solid carrier for 10 wt% loading; 0.04 g solid carrier for 20 wt% loading; 0.01 g solid carrier for 50 wt% loading) was suspended in the IL solution and stirred for 2 h at room temperature. The solvent was evaporated and the sample kept under high vacuum (0.01 mbar) overnight.

1.4 General procedure for the pore size measurements.

Surface area and pore volume were determined by nitrogen adsorption and desorption measurements at liquid nitrogen temperature with a Micromeritics ASAP 2020 instrument. The samples were outgassed in vacuum at 300 °C for 16 h prior to the measurements. The total surface area was calculated according to the Brunauer-Emmett-Teller (BET) method, the micropore volume was determined by the t-plot method, and the mesopore volume was determined by the Barrett-Joyner-Halenda (BJH) method.

Figure S2. Nitrogen Adsorption/desorption: Comparison of silica-supported [P_{4444}][Ibu] 1, and the starting material SiO_{2-90}.
1.5 Controlled release of the active ingredient from the supported phases.

100 mg of SILP was suspended in 100 mL of preheated aqueous medium (phosphate buffered saline, simulated gastric fluid, or simulated intestinal fluid according to USP standards)\textsuperscript{5} and placed in a thermostated shaker at 37 °C at 150 rpm. In intervals, a 250 µL sample was taken and diluted to 2.5 mL, filtered over a syringe filter to stop the leaching, and measured via UV-visible spectrometry. 250 µL of fresh media was immediately added to the leaching experiment to replace the missing volume.

**Figure S3.** Effect of precalcination of silica on the leaching kinetics in PBS of a 20% loading of [P\textsubscript{4444}][Ibu] 1: non pre-calcined silica (blue) and pre-calcined silica (red).
**Calibration curves**

**General procedure:**
Aqueous stock solutions of [P₄₄₄₄][Ibu] 1 and [Lid][Ibu] 2 were first prepared, with a concentration 500 ppm (for 1) and 100 ppm (for 2), respectively. Several standard dilutions in the concentration range of 0-100 ppm (for 1) and 0-50 ppm (for 2) were prepared by dilution. For a more accurate calculation of the final concentration, all dilutions were made by weight. The standard samples were run on a Varian CARY 3 UV-visible spectrophotometer, and the absorbance at 221 nm was recorded. The plots of concentration against absorbance at 221 nm were fit to a straight line in the selected concentration range, with good correlation coefficients being obtained (R² ≥ 0.999). The linear regression obtained was used to calculate “a” and “b” coefficients for the corresponding equation:

\[ A = a \times C + b \]  

(where A – absorbance and C – concentration)

The “a” and “b” coefficients and the absorbance values recorded by UV were further used in the same linear equation to calculate the concentration of the leached compounds.

**Figure S4.** Calibration Curves.

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<th>Concentration (ppm)</th>
<th>Absorbance @ 221 nm (a.u.)</th>
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**Calibration curve for [P₄₄₄₄][Ibu] 1**

\[ A = 0.019 \times C + 0.007 \]

**R² = 0.999** (R – linearity)

<table>
<thead>
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<th>Absorbance @ 221 nm (a.u.)</th>
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**Calibration curve for [Lid][Ibu] 2**

\[ A = 0.032 \times C + 0.014 \]

**R² = 0.999** (R – linearity)