Electronic Supporting Information for Soft Matter

A Vegetable Oil-Based Organogel for use in pH-Mediated Drug Delivery

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NCA Synthesis

An established procedure was adopted for the synthesis of the n-carboxyanhydride of serine *O*-benzyl-L-serine.[1]

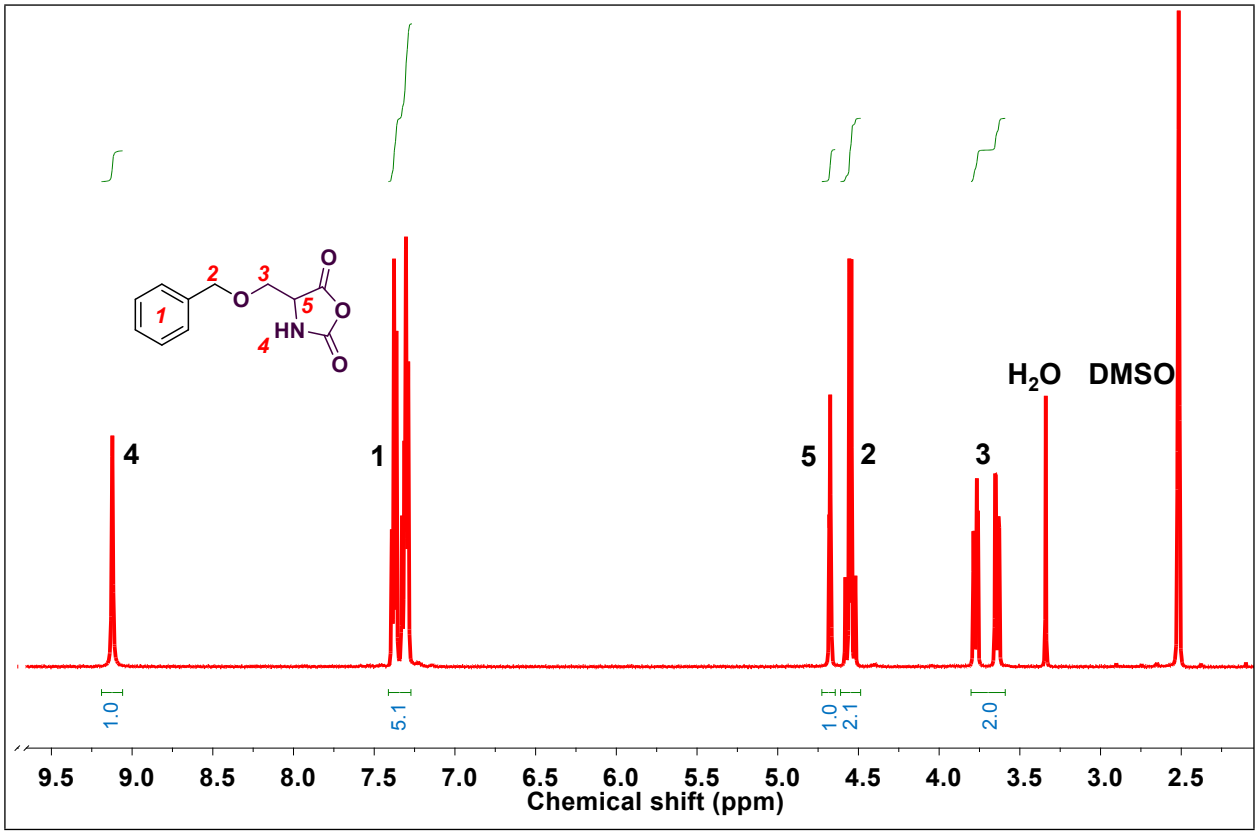

Figure S1. 500MHz ^{1}H NMR spectrum of the *n*-carboxyanhydride of *O*-benzyl-l-serine in DMSO-d_6, at 25°C.

Elemental analysis was employed to determine the purity of the monomer (Table S1).

Table S1. Atomic composition of the n-carboxyanhydride of O-benzyl-l-serine.

	Theoretical (%)	Found (%)
Carbon	59.7	59.8
Nitrogen	6.3	6.6
Hydrogen	5.0	5.1

Poly(serine) (PS) Synthesis

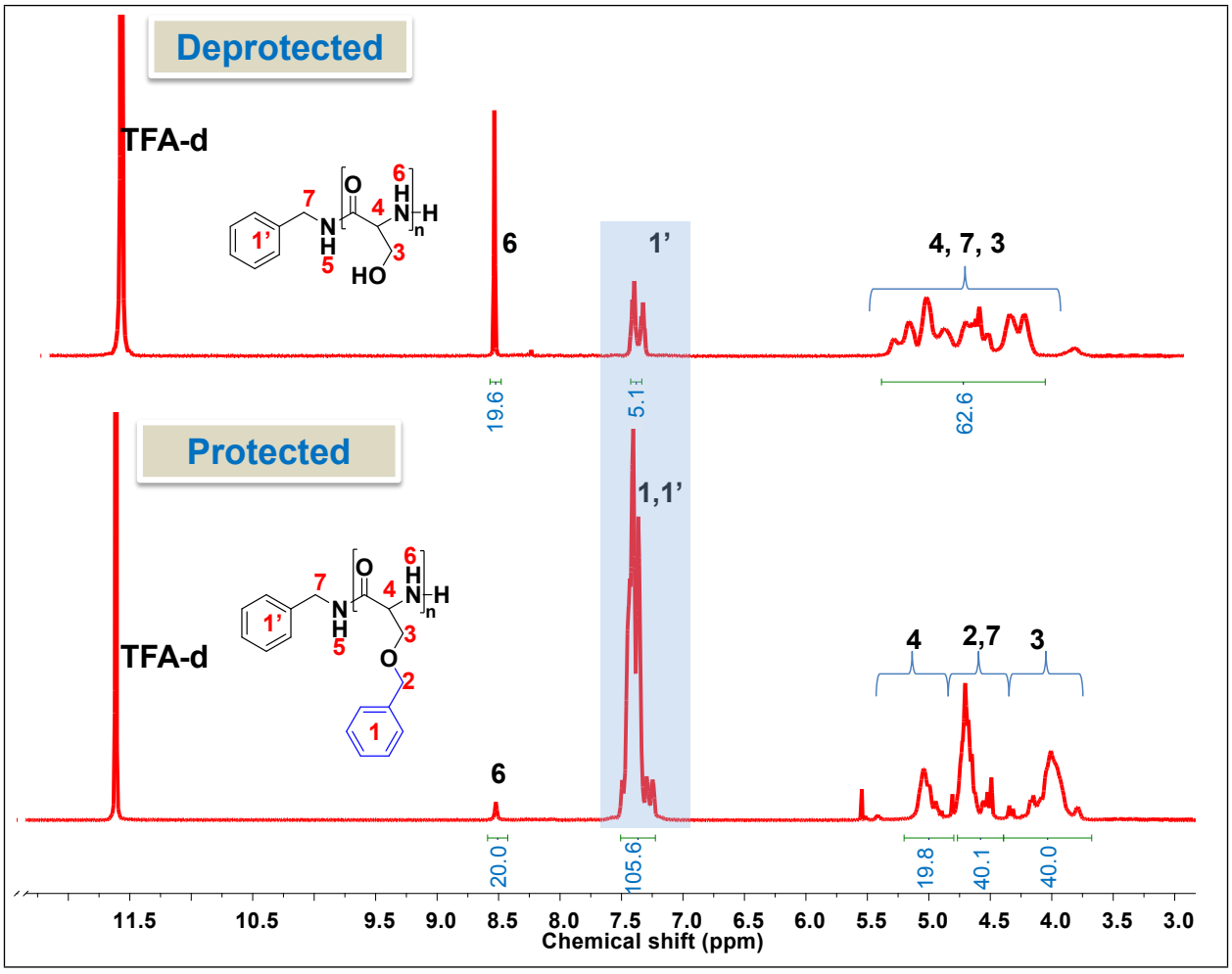

Figure S2. ^{1}H NMR spectra of poly(serine) before deprotection and after deprotection of the serine side group to expose the hydroxyl groups.

GPC Analysis of PS

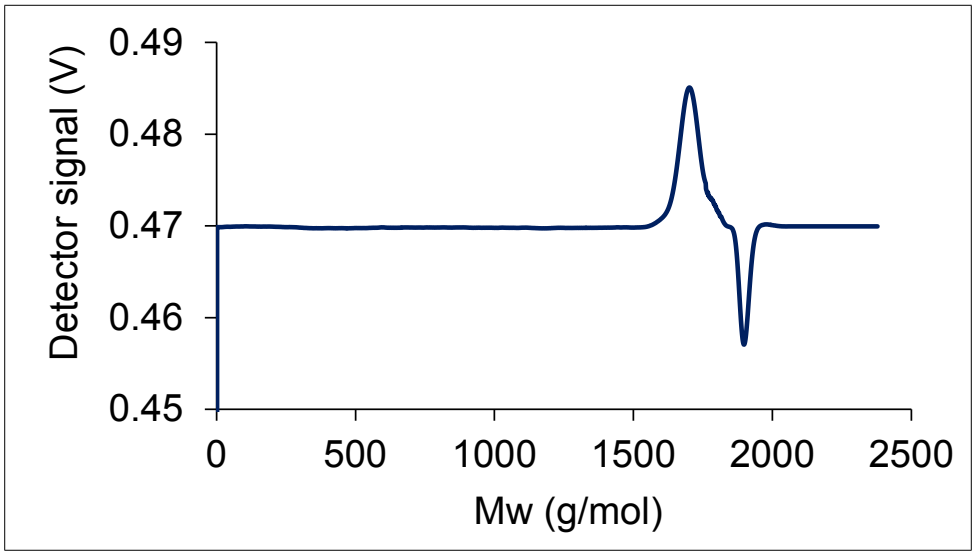

Figure S3. GPC trace of poly(serine) in DMF + 1 g/L LiBr, at 0.6 mL/min, at 50°C. Molecular weight was obtained by using methyl methacrylate standard for instrument calibration. The negative peak is indicative of the solvent used (DMF). M_n = 1862, M_w = 1959 g/mol, PDI = 1.05.

Mass Spectrometry Analysis of PS

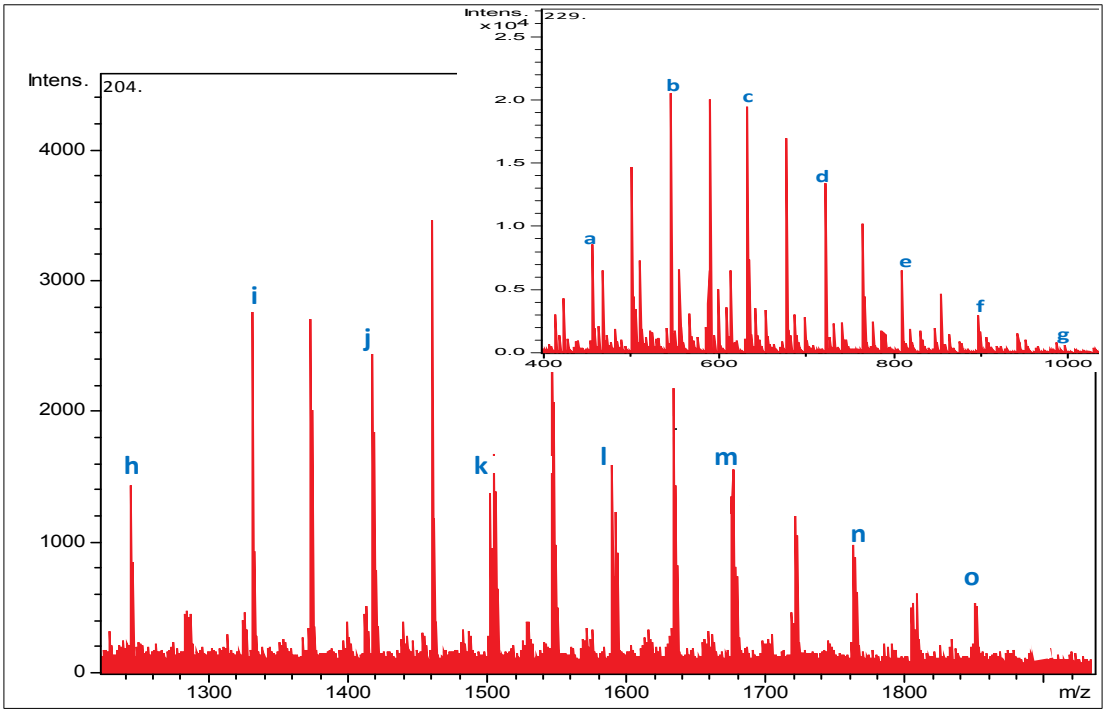

Figure S4. ESI-MS fragmentation pattern obtained from the poly(serine) backbone. The lettered peaks may be assigned to the various fragments of the macromolecule; **a**: Benzylamine-(Serine)$_4$, **b:** Benzylamine-(Serine)$_5$, **c:** Benzylamine-(Serine)$_6$, **d:** Benzylamine-(Serine)$_7$, **e:** Benzylamine-(Serine)$_8$, **f:** Benzylamine-(Serine)$_9$, **g:** Benzylamine-(Serine)$_{10}$, **h:** Benzylamine-(Serine)$_{13}$, **i:** Benzylamine-(Serine)$_{14}$, **j:** Benzylamine-(Serine)$_{15}$, **k:** Benzylamine-(Serine)$_{16}$, **l:** Benzylamine-(Serine)$_{17}$, **m:** Benzylamine-(Serine)$_{18}$, **n:** Benzylamine-(Serine)$_{19}$, **o:** Benzylamine-(Serine)$_{20}$.

^{1}H NMR Spectrum of PSSA

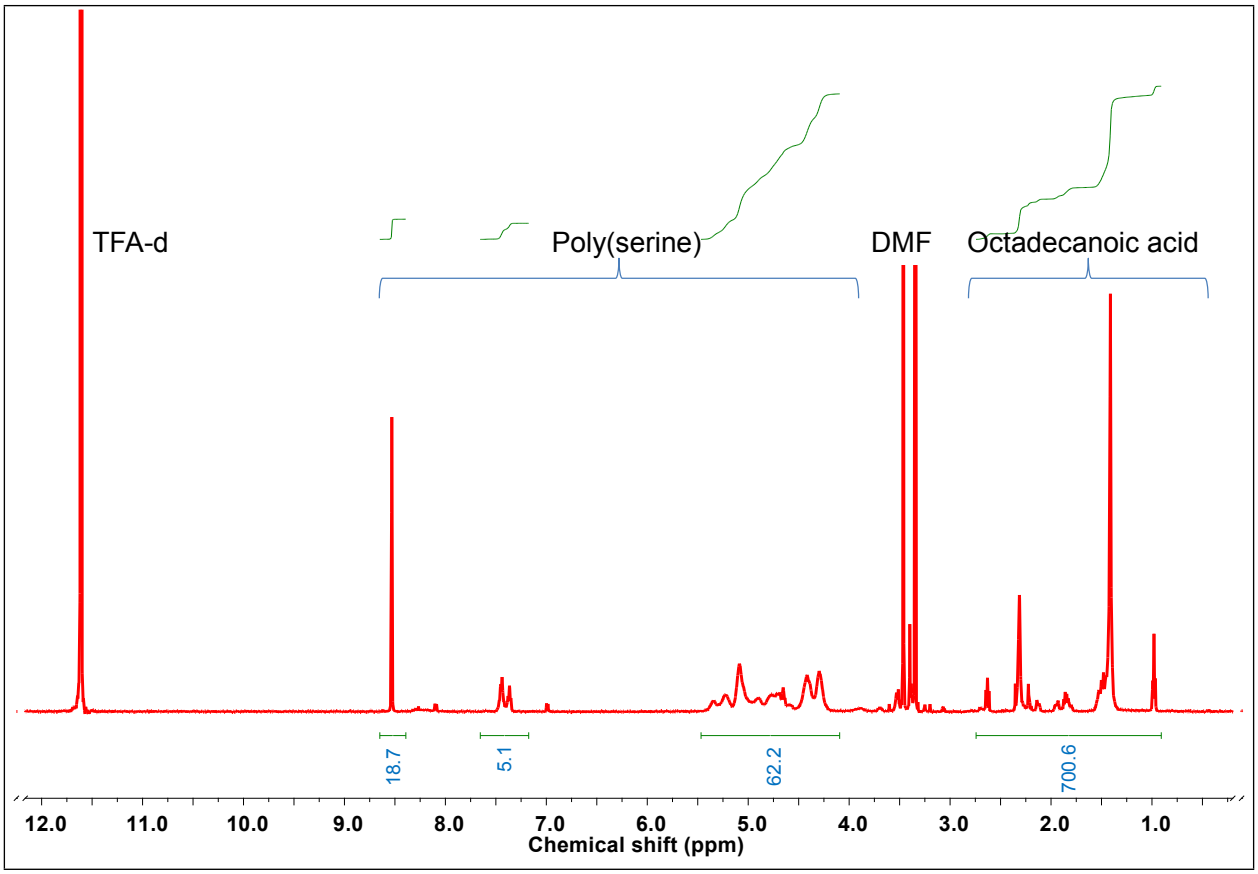

Figure S5. ^{1}H NMR of PSSA gelator showing new peaks to have emerged in the region 0.97 ppm – 2.64 ppm, emanating from the grafted octadecanoic acid.

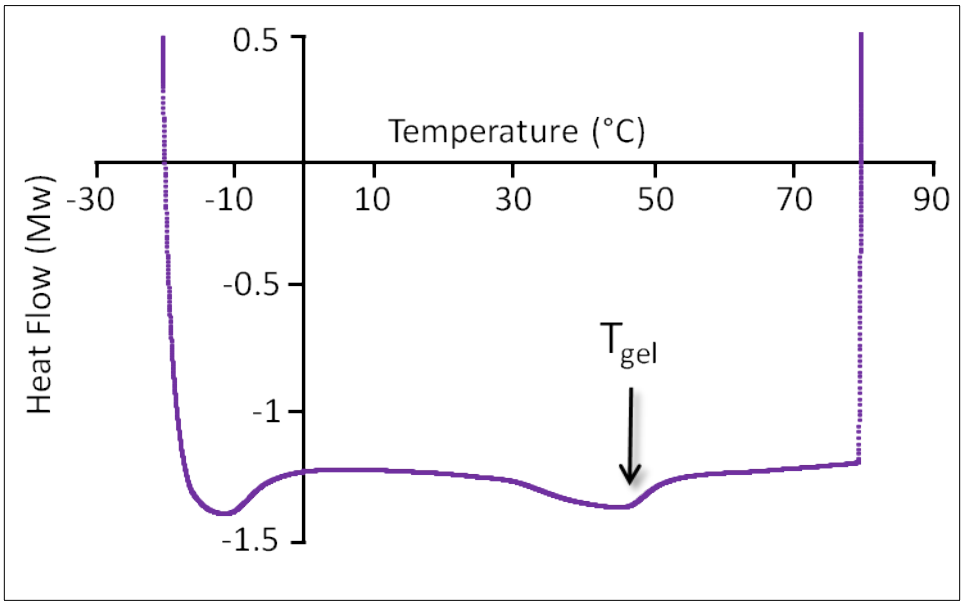

Figure S6. The DSC thermogram obtained from 2 wt.% PSSA-safflower oil organogel showing the gel/sol transition (T_{gel}) at 45.9 °C.

Differential Scanning Calorimetry

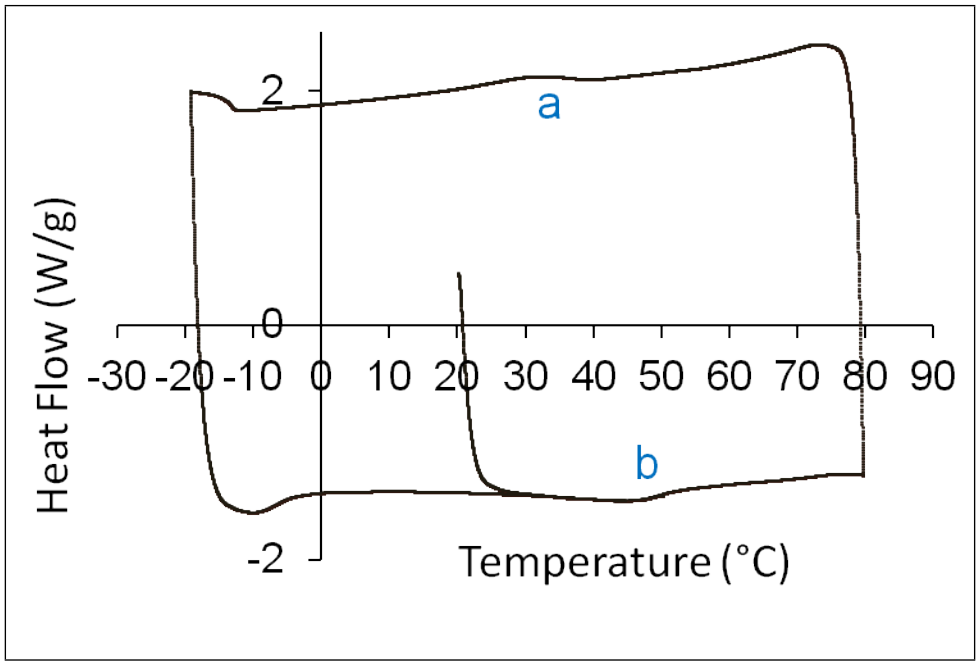

Figure S7. Fig 2. The DSC thermogram of the 2 wt.% organogel subjected to six heat-cool cycles.

Thermogravimetric Analysis

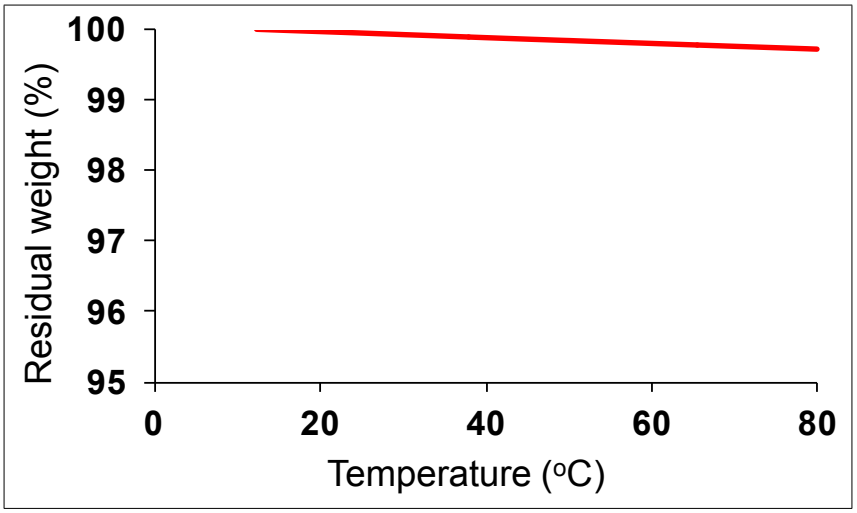

Figure S8. TGA thermogram of a PSSA-safflower oil organogel heated up to 80 °C. Only 0.29 % of the gel's initial weight was lost, emphasising the thermal stability of the gel system.

Elemental Analysis

Table S2. Atomic composition of poly(serine) and PSSA gelator.

	% Carbon	% Nitrogen	% Hydrogen
Poly(serine)	36.5	12.1	5.4
Poly(serine)-*g*-stearic acid (PSSA)	69.4	5.1	10.7

The atomic composition was used to estimate the grafting efficiency. The theoretical carbon content of PSSA, assuming 100 % grafting of the alkyl chains onto the poly(serine) backbone, was calculated to be 71.3 %. Assumingly, and as would be expected that the increase in the overall carbon content of PSSA is due to the grafted alkyl chains, then the grafting efficiency can be estimated as;

$$Grafting\ efficiency = \left(\frac{carbon\ content\ measured\ after\ grafting}{theoretical\ carbon\ content\ after\ grafting}\right) * 100\ \%$$

= (69.4/71.3)*100 %

= 97.3 %

Cell Culturing and Passaging

C3H mouse dermal fibroblasts were plated in 75 cm^2 Nunclon Δ™ plastic cell culture flasks (T75) in 20 mL Dulbecco's Modified Eagle Medium (DMEM) supplemented with 10 % (v/v) foetal bovine serum (FBS), 1 mM L-glutamine and 100 $U.ml^{-1}$ penicillin-100 $\mu g.ml^{-1}$ streptomycin cocktail. The flasks were then incubated in a humidified incubator at 37 ^oC and 5 % (v/v) CO_2 in air. Culture medium was changed every 2-3 days. Upon reaching 90 % confluence, the cells were passaged using trypsin/EDTA solution (2 mL) for 5 minutes at 37 ^oC. To neutralise the trypsin, an equal volume of culture medium was added followed by washing at 240 g for 10 min. Cells needed for subsequent studies were counted on a Marienfeld-Superior Neubauer-improved haemocytometer using an Olympus CK40 light microscope. Excess cells were cryopreserved in cryogenic-medium (DMEM supplemented with 20 % (v/v) FBS, 1mM L-glutamine and 100 $U.ml^{-1}$penicillin-100 $\mu g.ml^{-1}$ streptomycin cocktail) and frozen down in an isopropanol bath at a rate of 1 ^oC/ minute in a -80 ^oC freezer and subsequently stored in liquid nitrogen.

Plate Coating and Cell Seeding Plan for ATPlite Assays

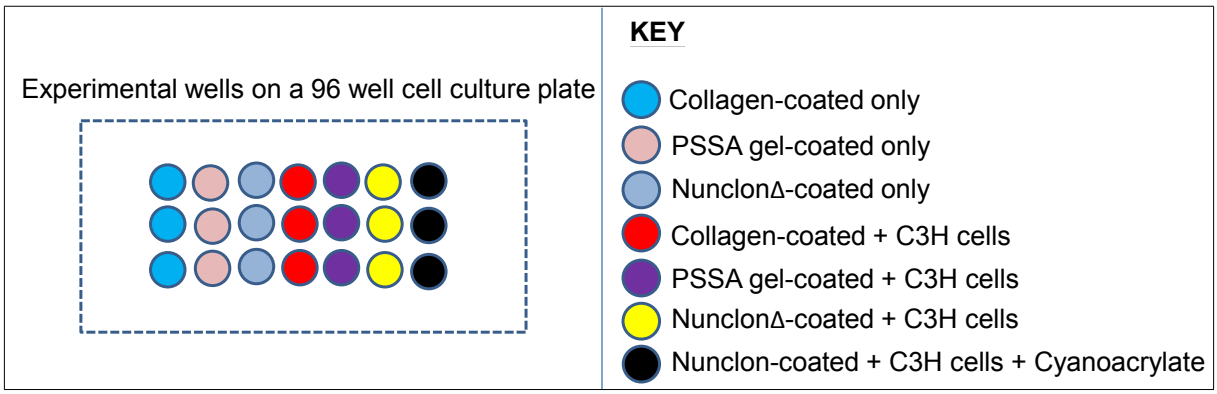

Figure S9. General illustration of the plate-coating and seeding plan for the ATP assays. The plan shows only the experimental wells in a 96 well cell culture plate. Empty peripheral wells were filled with sterilised Dulbecco's phosphate buffered saline so as to keep the environment damp and prevent the evaporation of culture medium from the seeded wells.

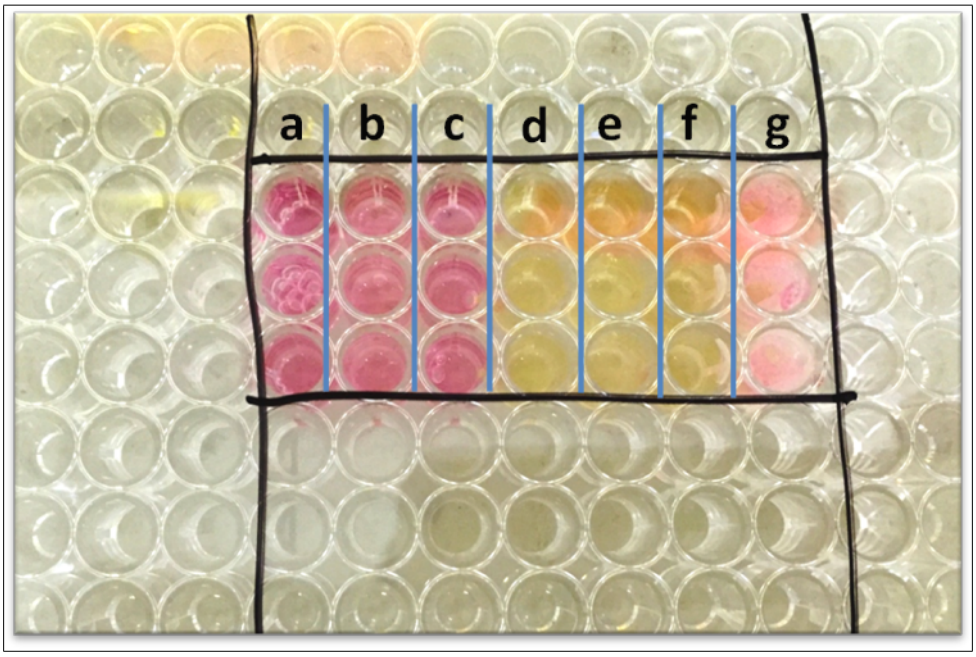

Figure S10. The plate seeding plan showing the appearance of the culture medium after 120 hours. a: collagen coated (unseeded); b: PSSA-safflower gel coated (unseeded); c: Nunclon Δ™ surface (unseeded); d: collagen coated + cells; e: PSSA-safflower gel coated + cells; f: Nunclon Δ™ surface + cells; g: Cyanoacrylate coated +cells. The culture medium in the seeded coated wells (with the exception of cyanoacrylate) turned from pink (unseeded control) to yellow (seeded) after 120 hours which is indicative of cellular metabolism (i.e., lactic acid accumulation lowers the pH).

UV-Vis Spectrophotometry Studies

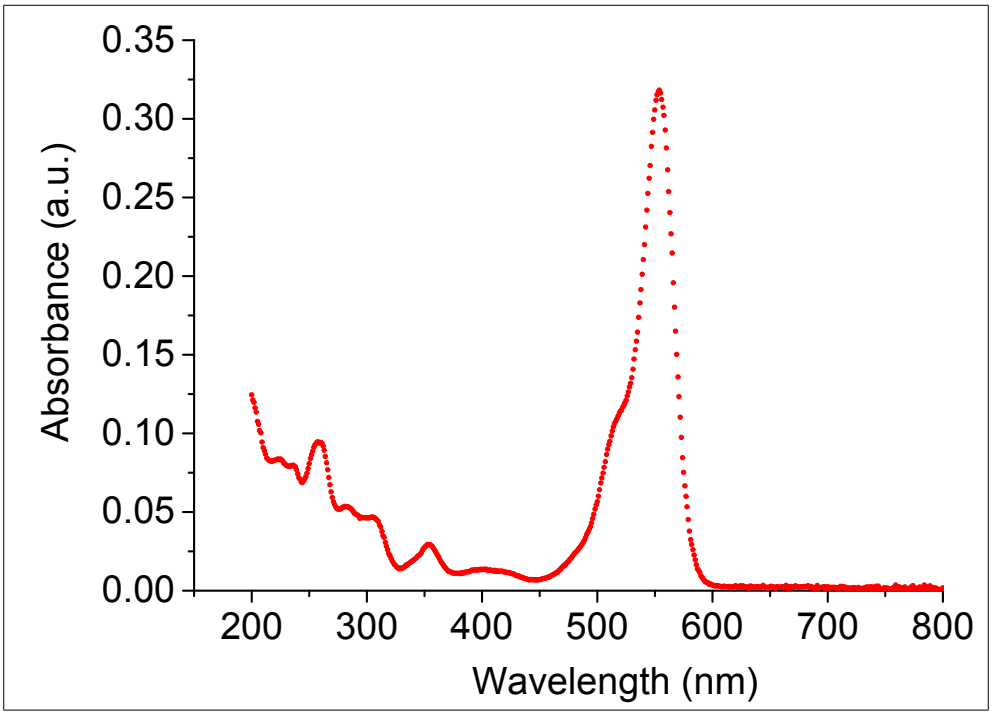

Figure S11. The UV-Vis spectrum of rhodamine B showing the λ_{max} at 554 nm.

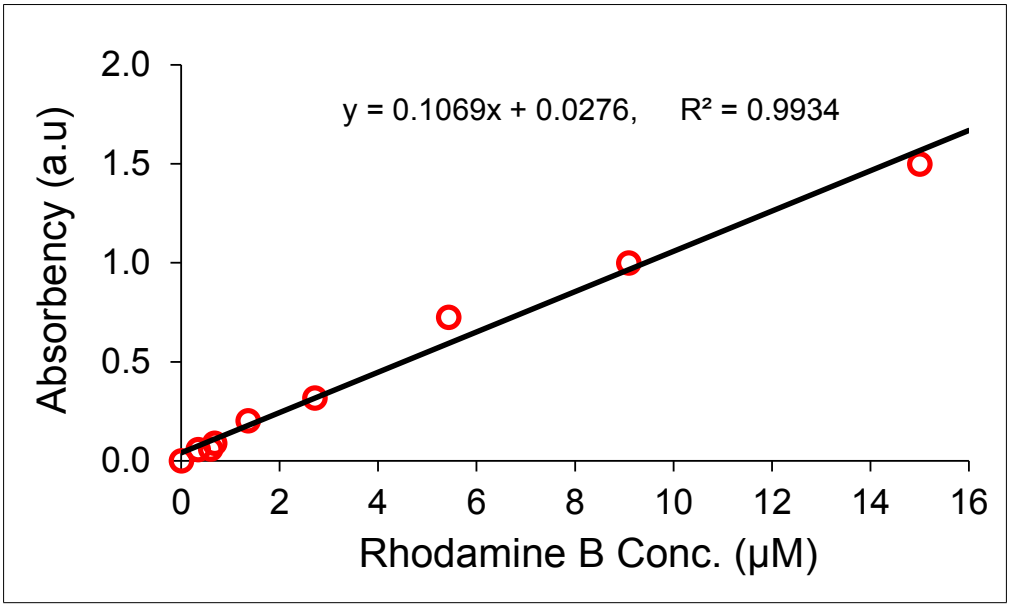

Figure S12. The calibration (linear) graph used to determine the quantity of Rhodamine B released from the PSSA-safflower oil organogels. The determined equation of the straight line was applied to calculate the release ratios from the raw data.

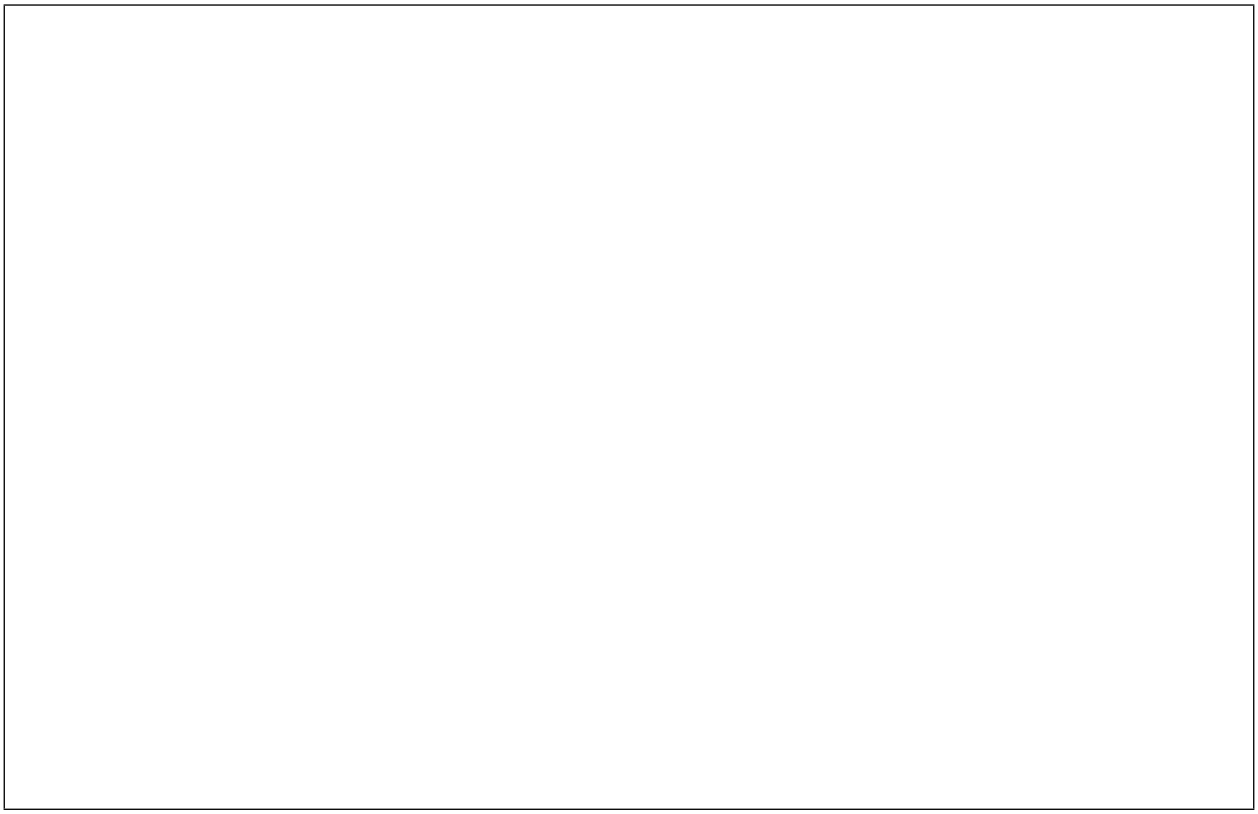

Figure S13. UV-vis spectra for the time-dependent release of rhodamine B from the 2 wt.% organogel into PBS buffer medium maintained at pH 4.2 (a) and at pH 7.4 (b). A greater extent of dye release was observed in response to acidic pH (greater absorbance values) than was the case at physiological pH.

Table S3. The release exponents (n) and correlation coefficients (r^2) obtained from the Korsmeyer–Peppas (KP) model.

pH	PSSA loading	0 – 5 hours		6 – 78 hours	
		n	r^2	n	r^2
4.2	2 wt.%	0.75	0.94	0.16	0.98
4.2	4 wt.%	0.52	0.93	0.11	0.96
7.4	2 wt.%	0.25	0.72	0.28	0.91

Reference

1. G. J. M. Habraken, C. E. Koning and A. Heise, *J. Polym. Sci. A Polym. Chem*. 2009, **47**, 6883.