Supplementary Information

Composite hydrogels of polyacrylamide and crosslinked pH-responsive micrometer-sized hollow particles

Kyriaki Pafiti, Zhengxing Cui, Louise Carney, Anthony J. Freemont, and Brian R. Saunders*

*Biomaterials Research Group, School of Materials, MSS Tower, The University of Manchester, Manchester, M13 9PL, U.K.

Division of Regenerative Medicine, School of Medicine, Stopford Building, The University of Manchester, Oxford Road, Manchester, M13 9PT

Regenerative Medicine, Developmental Biomedicine Research Group, School of Medicine, Stopford Building, University of Manchester, Oxford Road, Manchester, M13 9PT

Table of contents

I. Experimental details for copolymer synthesis 1
II. Copolymer characterisation 2
III. Figures 3
IV. References 5

I. Experimental details for copolymer synthesis

Synthesis of PMMA-MAA. The synthesis of poly(methyl methacrylate-co-methacrylic acid) (PMMA-MAA) involved the synthesis of the random copolymer, PMMA-\(t\)-BuMA (\(t\)-BMA is tert-butyl methacrylate), by free-radical polymerisation followed by the hydrolysis of \(t\)-BuMA units to MAA units. For the synthesis, 2,2\(^\prime\)-azobis(2-methylpropionitrile) (AIBN, 0.25 g, 1.52 mmol) was dissolved in THF (85 mL) and the solution was kept under an inert, water- and oxygen-free argon atmosphere for 30 min at 55 °C. Then a mixed solution of MMA (5.48 g, 54.7 mmol) and \(t\)-BuMA (4.52 g, 31.8 mmol) with AIBN (0.025 g, 0.152 mmol) was added dropwise to the flask over a period of 90 min. After 24 h the PMMA-\(t\)-BuMA
copolymer was recovered by precipitation in n-hexane and dried over a vacuum oven at room temperature (See Scheme S1, Step 1).

Scheme S1: Depiction of procedure for the synthesis of PMMA-MAA-GMA

Hydrolysis was performed using purified PMMA-t-BuMA (1.0 g) dissolved in anhydrous 1,4-dioxane (6.7 vol.%), followed by the addition of concentrated HCl (1.0 g) while stirring (Scheme S1, Step 2). The solution was heated at 80 °C overnight. After cooling, the solution was precipitated by addition to excess water and thoroughly rinsed with water and dried at 80 °C overnight to give 0.67 g of product with a yield of 67%.

Synthesis of PMMA-MAA-GMA. PMMA-MAA was vinyl-functionalised with GMA units after synthesis (Scheme S1, Step 3). PMMA-MAA (1.0 g) was diluted in DMF (2.90 mL). Then, triphenylphosphine (0.021 g, 0.080 mmol), DPPH (0.005 g, 0.013 mmol) and, finally, GMA (0.21 g, 1.47 mmol) were added to the reaction flask. The reaction mixture was left to react for 12 h at 90 °C. After completion of the reaction the product was purified by precipitation in diethyl ether (twice) and in acidic water (twice), and dried in a vacuum oven at room temperature for 48 h.

II. Copolymer characterisation

The hollow particles (HP_{XL} and HP_{VF}) used in this study differed to those reported in our earlier work\(^1\)\(^-\)\(^3\) because the pH-responsive copolymer contained vinyl functional groups from GMA. The number-average molecular weight, \(M_n\), of PMMA-t-BuMA was determined by GPC, and found to be \(8,300 \text{ g mol}^{-1}\) with a polydispersity of 1.9. PMMA-MAA and PMMA-
MAA-GMA were characterised by $^1$H NMR spectroscopy (Fig. S1). For the latter several new peaks appeared including the two characteristic peaks of vinyl protons at 6.1 and 5.4 ppm, confirming the successful incorporation of GMA groups. Based on the $^1$H NMR spectrum, the vinyl-functionalised copolymer contained MMA (68.2 mol.%), MAA (19.6 mol.%) and GMA (12.2% mol.%). Furthermore, PMMA-MAA contained MMA (64.5 mol.% and MAA (35.5 mol.%). The MMA contents for the two copolymers are within the experimental error for our $^1$H NMR data and are not considered significantly different.

**III. Figures**

![Fig. S1. $^1$H NMR spectra for the copolymers used to prepare hollow particles](image-url)
Figure S2. Potentiometric titration curves for HPVF and HP. These hollow particles comprised PMMA-MAA$_{0.20}$-GMA$_{0.12}$ and PMMA-MAA$_{0.35}$, respectively. The maximum at about 10 % neutralisation for the former is due to swelling of the particles and exposure of previously buried RCOOH groups.

Figure S3. Percolation model fitting. The graphs show data for the linearised form of equation (1) ($\Delta G' = A \Delta G_y$) obtained using selected values of $n$ (legends). The graphs are separated into two parts (a and b) to improve clarity. The equation for the line of best fit with highest $R^2$ is shown. If the $n$ value was too low or too high the data deviate increasingly above or below linear behaviour, respectively, with increasing $y$. 

\[ \Delta G^{1/2.6} = 0.418y - 1.838 \]

\[ R^2 = 0.97 \]
Figure S4. Establishing the best value for the scaling exponent. Variation of $R^2$ with $n$ from the lines of best fit to the data shown in Fig. S3. The maximum $R^2$ corresponds to $n = 2.6$.

References

