

## Supporting Information

### Dual-stimuli responsive injectable microgel/solid drug nanoparticle nanocomposites for release of poorly soluble drugs

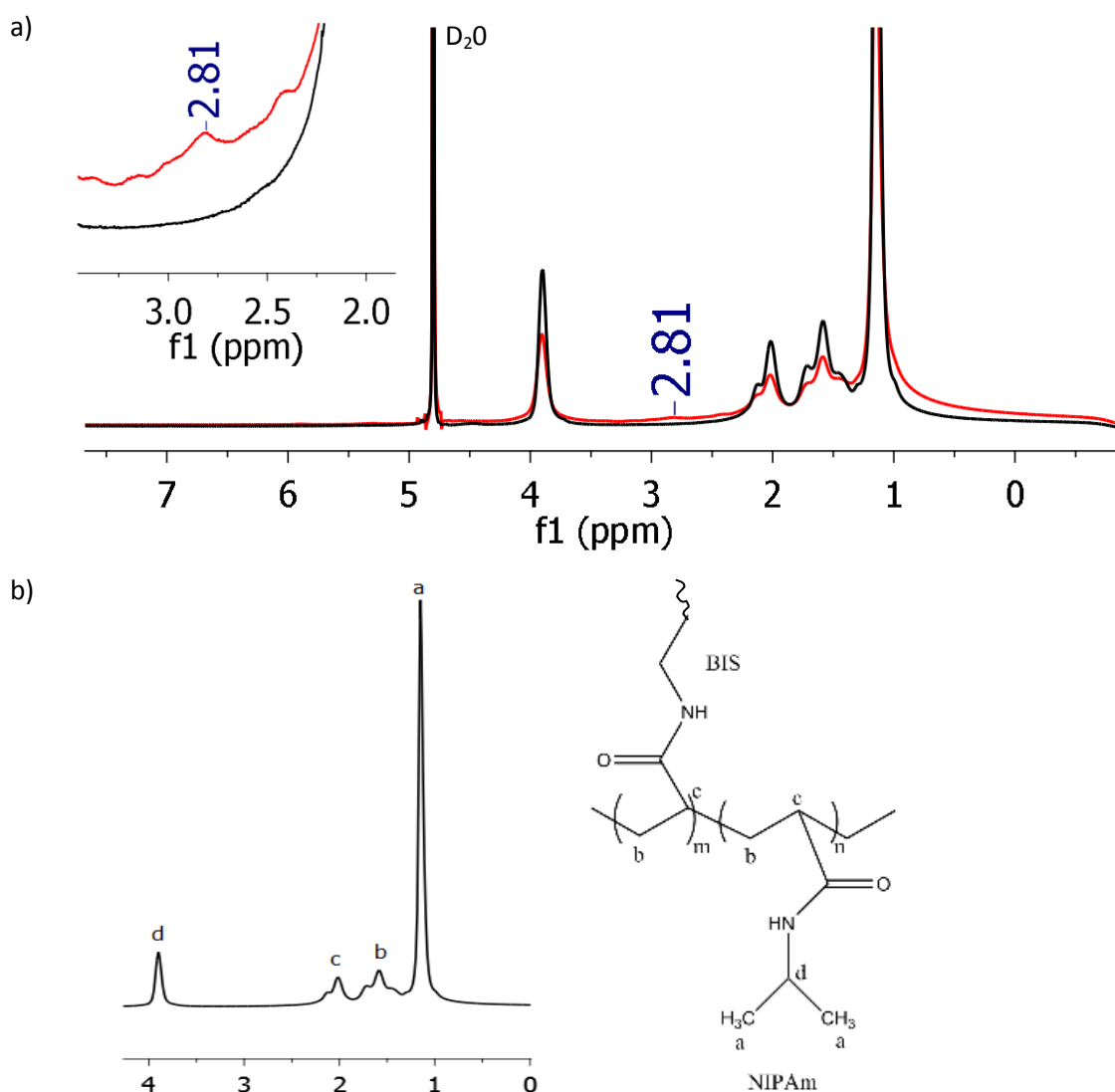
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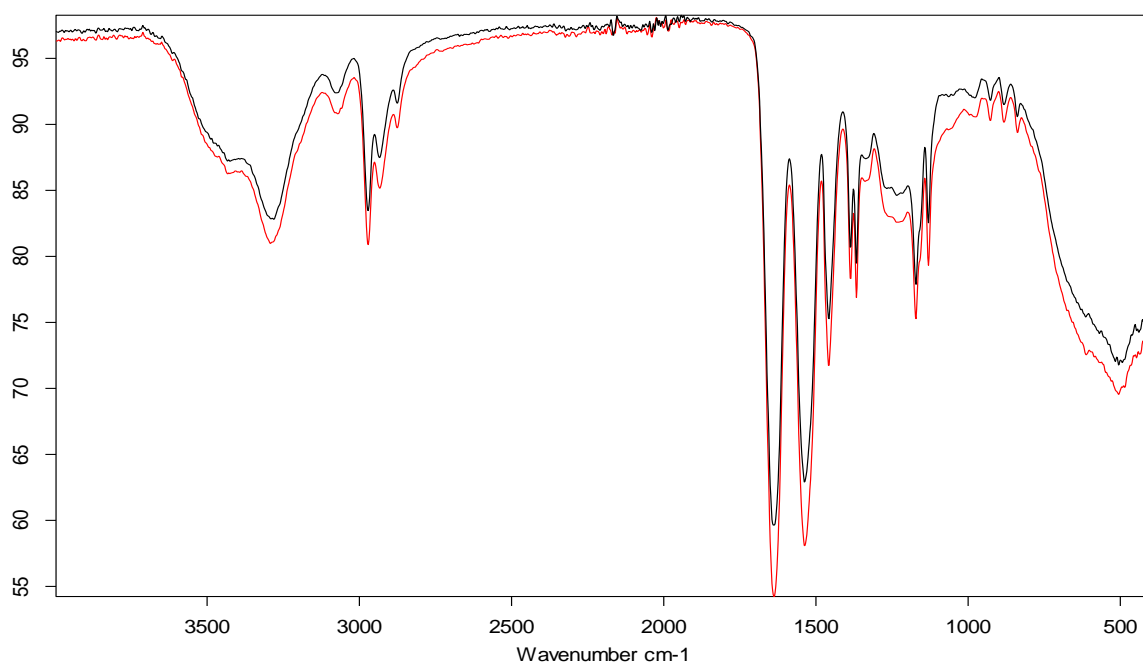
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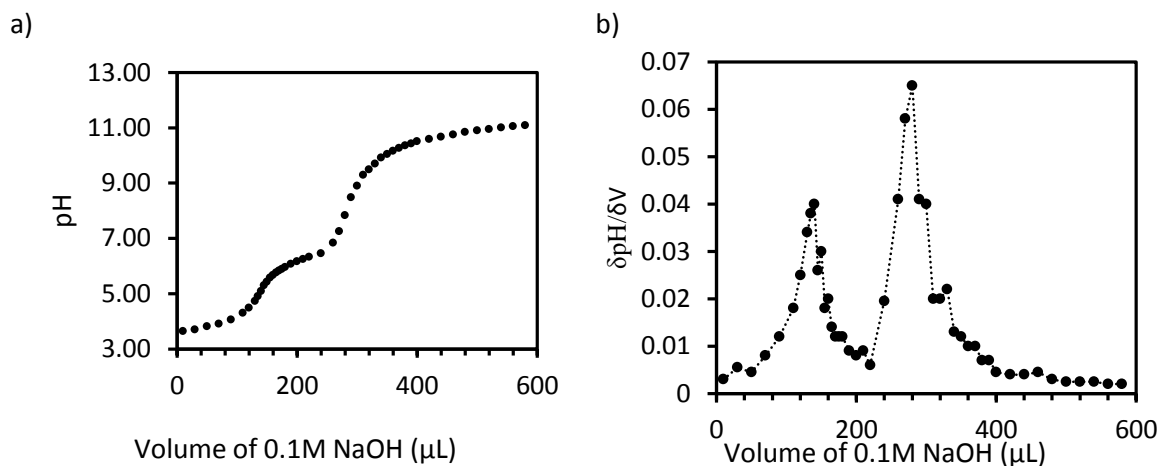
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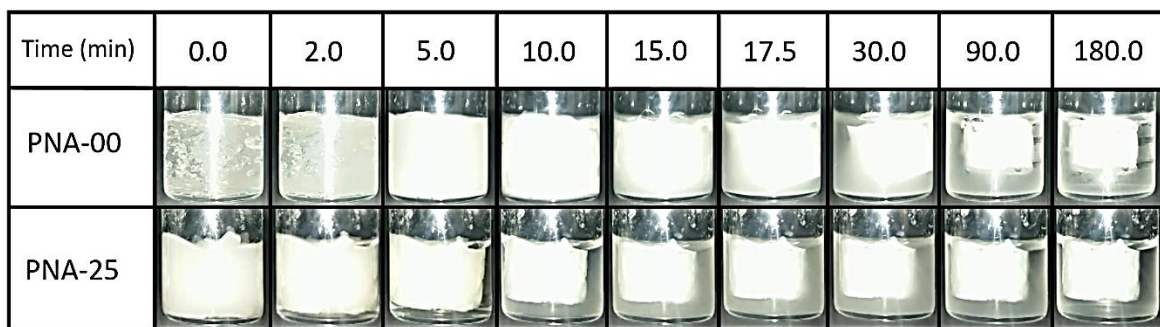
**Figure S1.** <sup>1</sup>H NMR Spectra of microgels a) comparison of PNA-00 (black) and PNA-25 (red). Peak at 2.81 ppm indicates presence of AIA comonomer due to NH<sub>2</sub> protons. b) identification of PNIPAm peaks.



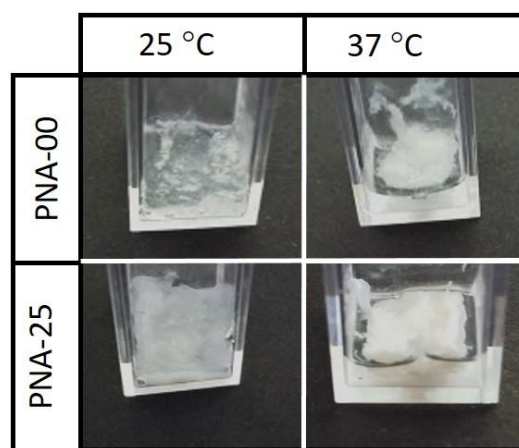
**Figure S2.** FTIR Spectra of microgels. PNA-00 (black) and PNA-25 (red). 910–665 (s, b) N–H wag 1°, 2° amines, 3400–3250 (m) N–H stretch 1°, 2° amines, amides, 1650–1580 (m) N–H bend 1° amines, 1250–1020 (m) C–N stretch aliphatic amine.



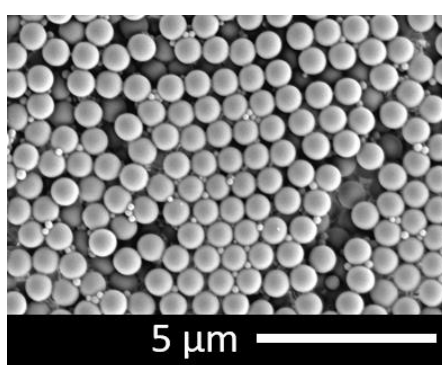
**Figure S3.** a) Potentiometric titration curve of PNA-25. Sample solution prepared by dissolving 50 mg of lyophilized microgel into 50 mL of distilled water, followed by lowering sample pH to <math>pH4</math> with HCl. Sample titrated with 0.1M NaOH at 25 °C  $\pm$  0.5 °C under a nitrogen atmosphere. b) Differential of titration curve, difference between two equivalence points used to calculate AIA content in microgel.



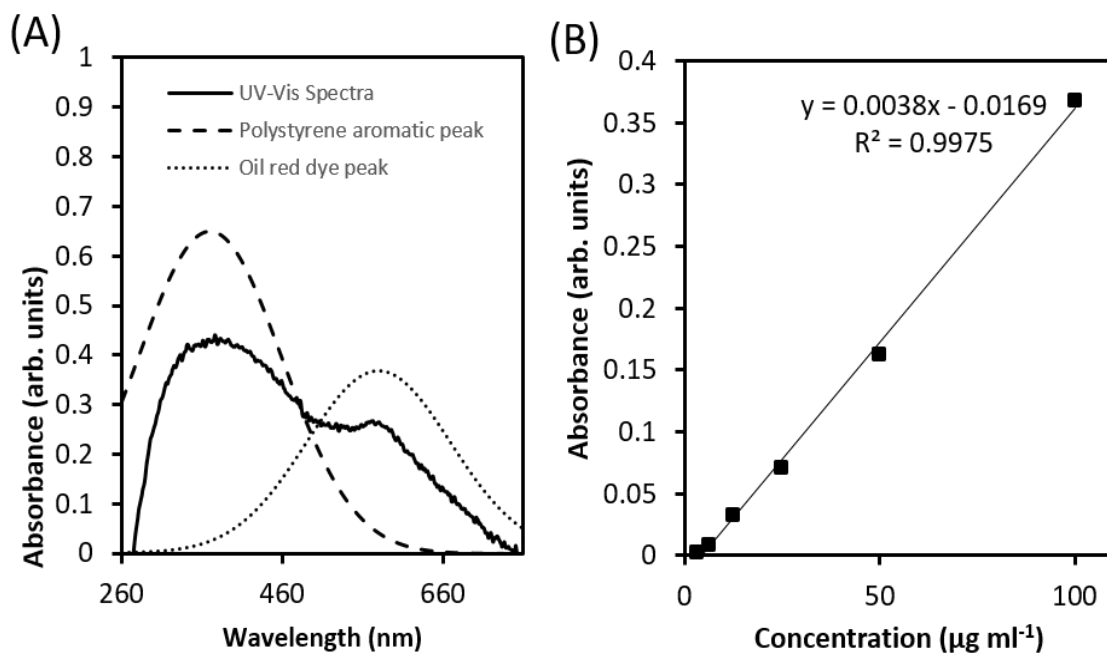
**Figure S4.** Images of microgel aggregate formation from swollen gel over time. The swollen gel was formed in PBS and placed in an incubator at 37 °C



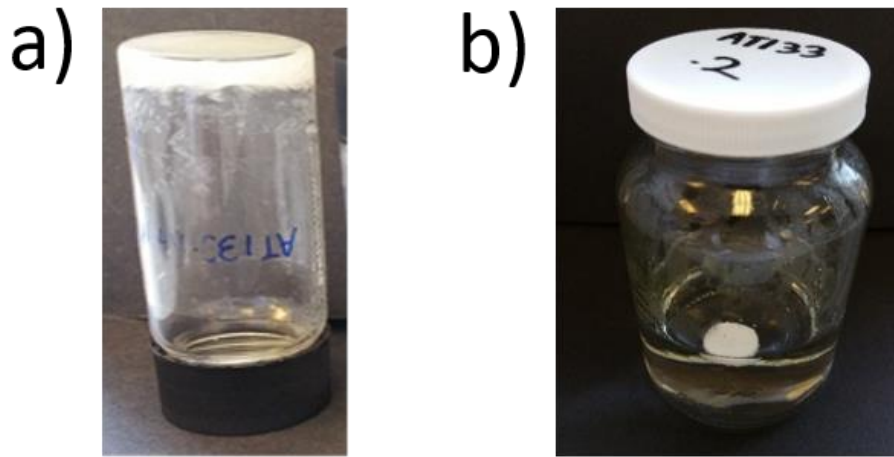
**Figure S5.** Images of dual-responsive transition of the microgels in HBSS; from swollen self-supporting gels to bulk aggregates. Microgel samples as swollen gel (left) and bulk aggregate (right). PNA-00, 14.90% (w/w), (top) and PNA-25, 6.24% (w/w), (bottom).



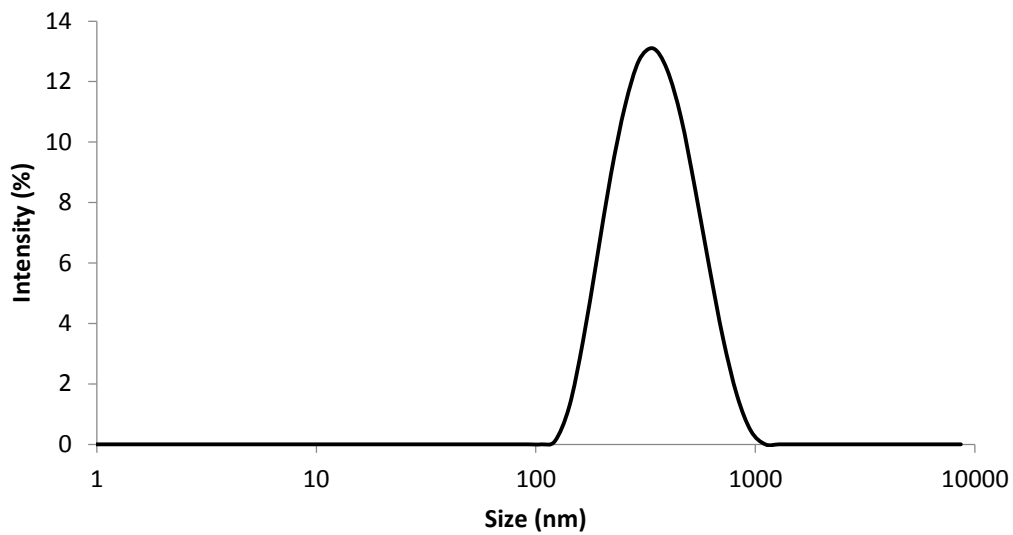
**Figure S6.** SEM image of Polystyrene Particles. Sample diluted to 0.01 mg mL<sup>-1</sup> in distilled water. Sputter coated with gold (EMITECH K550X) with a deposition current of 25 mA for 100 seconds before imaging. SEM images were then obtained using a Hitachi S-4800 FE-SEM at 3 kV.



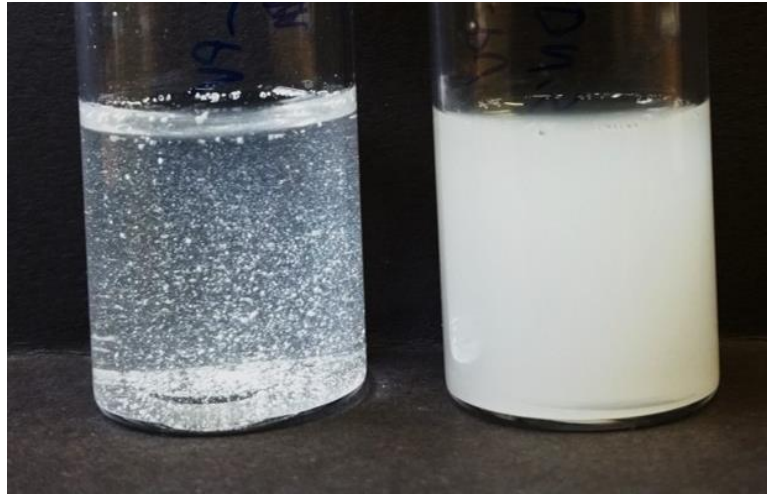
**Figure S7.** (A) UV-vis absorbance spectrum of oil red dyed polystyrene nanoparticles, deconvoluted into two component peaks using Gaussian amplitude peak fitting with a Gaussian response width of 2 standard deviations. (B) UV-Vis calibration data using absorbance of deconvoluted oil red dye peak, linear relationship between absorbance and concentration from 0-1000  $\mu\text{g mL}^{-1}$ .



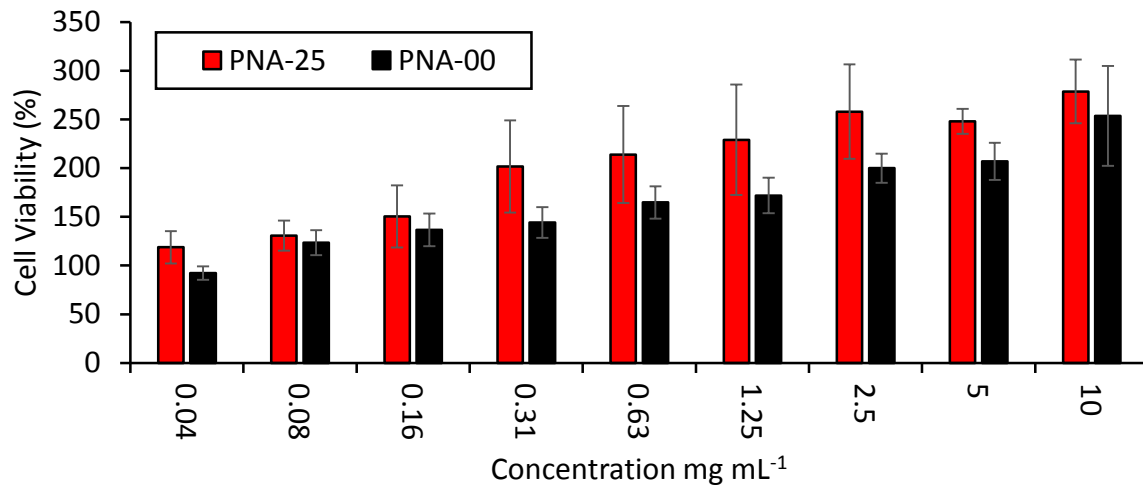
**Figure S9.** Lopinavir release experiment a) example of formulation of microgel and lopinavir solid drug nanoparticles at room temperature b) formulation in shrunken disk form after heating to 37 °C and transferring to 100 mL of release medium (PBS).



**Figure S8.** DLS analysis of lopinavir solid drug nanoparticles. Size distribution by intensity at 25 °C. Z-average diameter = 330 nm, Pdl = 0.18.



**Figure S10.** (left) Lopinavir drug particulates and (right) Lopinavir SDN's. Both dispersed in water at  $1\text{ mg ml}^{-1}$ .



**Figure S11.** Cytotoxicity of microgels towards cells in MTP Assay.