

Development of a biocompatible and biodegradable hybrid hydrogel platform for sustained release of ionic drugs

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Supporting Information

Measurements

The physicochemical properties of the monomers, polymers and hydrogels were characterized by various standard methods. For Fourier transform infrared (FTIR) characterization, the dried samples were ground into powders and mixed with KBr at a sample/KBr ratio of 1:10 (w/w). FTIR spectra were then obtained with a PerkinElmer (Madison, WI) Nicolet Magana 560 FTIR spectrometer with Omnic software for data acquisition and analysis. ¹H NMR spectra were recorded with a Varian Unity Inova 400-MHz spectrometer (Palo Alto, CA). Deuterated water (D₂O-d₂) or deuterated dimethyl sulfoxide (DMSO-d₆) (Cambridge Isotope Laboratories, Andover, MA) with tetramethylsilane as an internal standard was used as the solvent. MestReNova software was used for the data analysis. Elemental analyses of the polymers/hydrogels were performed with a PE 2400 CHN elemental analyzer by Atlantic Microlab (Norcross, GA). The thermal property of the synthesized precursors (Arg-UPEAs and Pluronic) was characterized with a DSC 2920 (TA Instruments, New Castle, DE). The measurements were carried out from -10 to 200 °C at a heating rate of 10 °C/min and at a nitrogen gas flow rate of 25 mL/min. TA Universal Analysis software was used for thermal data analysis. For the MW measurement, Arg-UPEAs were prepared at a concentration of 1 mg/mL in a 0.1 % (w/v) LiCl in DMAc solution. The sample MWs were determined from a standard curve generated from polystyrene standards with MWs ranging from 841.7 kDa to 2.93 kDa that were chromatographed under the same conditions as the samples. The standard curve was generated from a 3rd order polynomial fit of the polystyrene standard MWs.

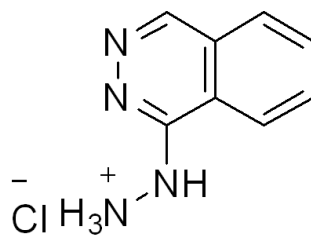


Figure S1, chemical structure of hydralazine salt

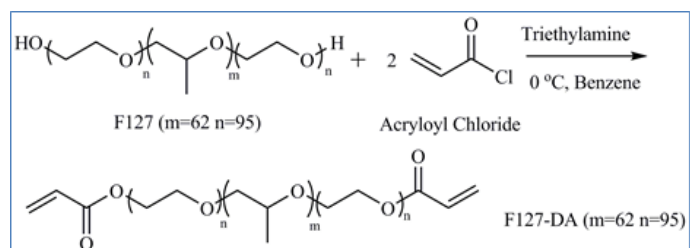


Figure S2, Synthesis of Pluronic-DA

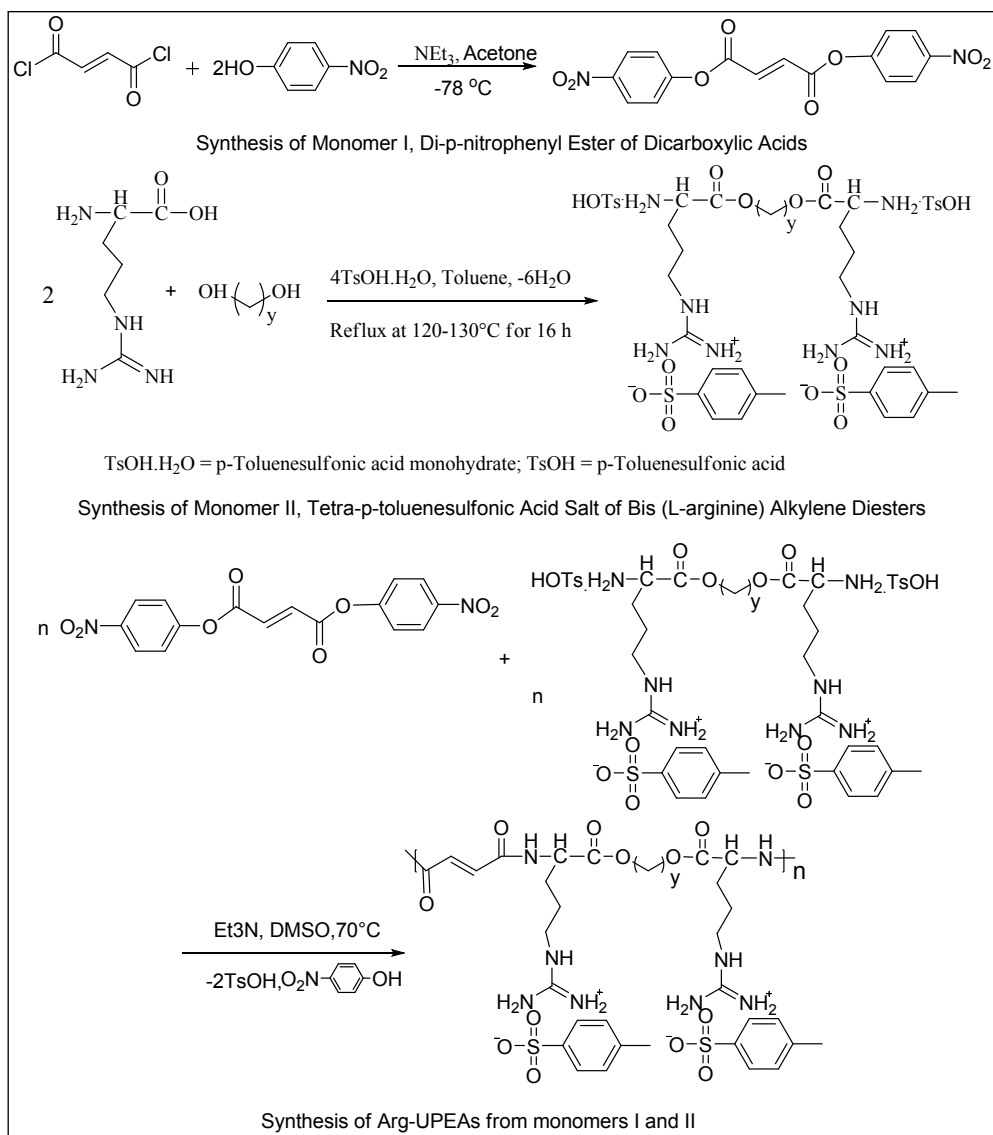


Figure S3, Synthesis of Arg-UPEAs

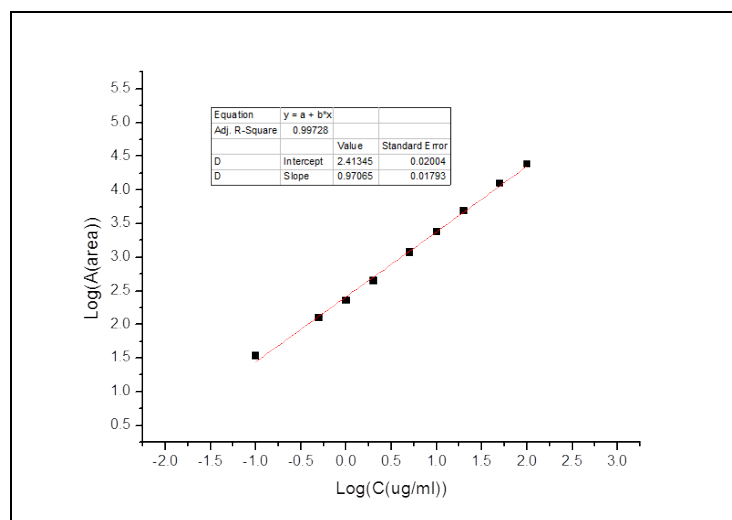


Figure S4, Standard calibration curve for hydralazine (HPLC)

Table S1, LC-MS Test of Released Hydralazine

| m/z | Relative abundance | Structure |
|-----|--------------------|------------------|
| 161 | 100% | M ⁺ . |

Cell Culture

Bovine endothelial aorta cells (BAECs) were purchased from VEC Technologies, kindly offered by Professor Cynthia Reinhart-King at Department of Biomedical Engineering of Cornell University. BAECs were cultured at 37 °C in 5 % CO₂ in Medium 199 (Invitrogen, Carlsbad, CA) supplemented with 10 % Fetal Clone III (HyClone, Logan, UT), and 1 % each of penicillin–streptomycin, MEM amino acids (Invitrogen, Carlsbad, CA), and MEM vitamins (Mediatech, Manassas, VA). BAECs were used from passages 8–12. Media was changed every 2 days. BAECs were grown to 70 % confluence before splitting or harvesting. Cell culture plates were coated with 2 wt% gelatin aqueous solution before using.

Statistics

Where appropriate, the data are presented as mean \pm standard error of the mean calculated over at least three data points. Significant differences compared to control groups were evaluated by unpaired Student's t-test or Dunnet test at p 0.05, and between more than two groups by

Tukey's test with or without one-way ANOVA analysis of variance. JMP software (version 8.0, from SAS Company) was used for data analysis.