Electronic Supplementary Material (ESI) for Journal of Materials Chemistry B.

Supporting Information:

Light-Degradable Nanocomposite Hydrogels for Antibacterial Wound Dressing Applications

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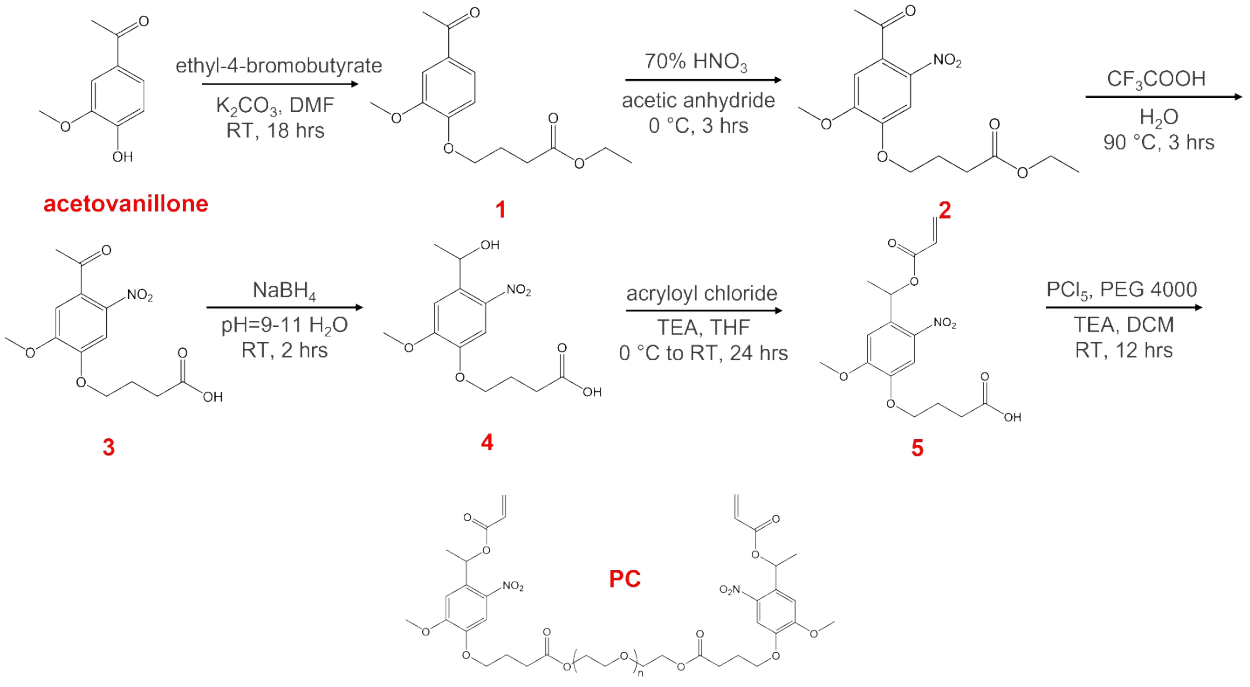
Materials and Methods

Materials

N, *N*-, dichloromethane (DCM), , acetovanillone (98%), acetic anhydride, trifluoracetic acid (CF_3COOH), sodium borohydride ($NaBH_4$), acryloyl chloride (98%), triethylamine (TEA), tetrahydrofuran (THF) and poly(ethylene glycol) 4000 were obtained from Sigma-Aldrich (Oakville, ON, Canada) and were used as received. Dimethylformamide (DMF), ethyl-4-bromobutyrate (97%) and phosphorus pentachloride (PCl_5) were purchased from Thermo Scientific Chemicals (Ottawa, ON, Canada) and were used as received.

S1. Synthesis of PEG-based light-degradable crosslinker (PC)

The PEG-based light-degradable crosslinker (PC) was synthesized via a multi-step reaction (Schematic S1) using acetovanillone as the starting material according to previous publications with some modifications [1]. The detailed synthesis procedure can be described as follows:



Schematic S1: Stepwise synthetic procedure for PEG-based light-degradable crosslinker (PC)

Ethyl 4-(4-Acetyl-2-methoxyphenoxy)butanoate (compound 1):

acetovanillone (4.98 g, 30 mmol) and ethyl-4-bromobutyrate (4.7 mL, 33 mmol) were dissolved in 25 mL dimethylformamide (DMF). The solution was stirred for 10 mins and K_2CO_3 (6.22 g, 45 mmol) was added into the solution. The resulting mixture was further stirred for 18 hours at room temperature. Afterward, the mixture was precipitated into 250 mL of water and further stirred for 2 hours before cooling at 4 ℃ for 2 hours. After cooling, the precipitate was collected via vacuum filtration, washed with cold water and dried under vacuum (white powder, yield=96%). 1H NMR (400 MHz, CDCl3): δ= 1.24 (t, 3H), 2.19 (pentet, 2H), 2.52 (t, 2H), 2.56 (s, 3H), 3.91 (s, 3H), 4.12-4.17 (m, 4H), 6.89 (d, 1H), 7.52-7.56 (m, 2H).

Ethyl 4-(4-acetyl-2-methoxy-5-nitrophenoxy)butanoate (compound 2):

Compound 1 (6.72 g, 20.65 mmol) was dissolved in 20 mL of acetic anhydride. Afterward, the resulting solution was slowly added into the solution of 70% HNO_3 (134 mL) and acetic anhydride (26 mL) cooled at 0 ℃. The reaction was stirred for 3 hours. Then, the reaction mixture was poured into ice-cooled water (350 mL). The precipitate was collected via vacuum filtration, washed with cooled water and dried under vacuum at 40 ℃ overnight (yellow powder, yield=64%). 1H NMR (400 MHz, CDCl3): δ= 1.24 (t, 3H), 2.10 (pentet, 2H), 2.52 (t, 2H), 2.53 (s, 3H), 3.96 (s, 3H), 4.17-4.20 (m, 4H), 6.78 (s, 1H), 7.60 (s, 1H).

4-(4-(1-hydroxyethyl) -2-methoxy-5-nitrophenoxy)butanoic acid (compound 3):

Compound 2 (6.35 g, 19.5 mmol) was ground to a fine powder and added into a solution of water (127 mL) and trifluoroacetic acid (12.7 mL). The mixture was stirred and heated to 90 ℃ on a hot plate. After 3 hours of reaction, the mixture was cooled to room temperature and further collected via vacuum filtration, washed with water and dried under vacuum at 40 ℃ overnight (yellow solid, yield=87%). 1H NMR (400 MHz, DMSO-d6): δ= 1.98 (pentet, 2H), 2.38 (t, 2H), 2.53 (s, 3H), 3.92 (s, 3H), 4.12 (t, 2H), 7.22 (s, 1H), 7.64 (s, 1H).

4-(4-(1-hydroxyethyl)-2-methoxy-5-nitrophenoxy)butanoic acid (compound 4):

Compound 3 (4.18 g) was dispersed in water (56 mL). Then, $NaHCO_3$ (2.34 g) was added in portions; ethanol (7.23 mL) was used to get rid of foams. $NaBH_4$ (1.09 g) was added over 1 hour and the pH of the reaction mixture was kept 9-11 by adding $NaHCO_3$ (1.86 g). After 2 hours, the suspension became transparent and acidified with 2N HCl. The precipitate was filtered, washed with water and dried under vacuum at 40 ℃ overnight (yellow solid, yield=94%). 1H NMR (400 MHz, DMSO-d6): δ= 1.35 (d, 3H), 2.00 (pentet, 2H), 2.38 (t, 2H), 3.89 (s, 3H), 4.04 (t, 2H), 5.22 (q, 1H), 7.35 (s, 1H), 7.52 (s, 1H).

4-(4-(1-(acryloyloxy)ethyl)-2-methoxy-5-nitrophenoxy) butanoic acid (compound 5):

Compound 4 (4.53 g, 15.14 mmol) and triethylamine (8.28 mL, 59.5 mmol) was dissolved in 50 mL of fresh tetrahydrofuran (THF). The solution was cooled to 0 ℃ and flushed with N_2. When the temperature reached 0 ℃, acryloyl chloride (2.82 mL, 52.0 mmol) in THF (10 mL) was added

dropwise. After the addition, the solution was warmed to room temperature and stirred for 24 hours. Afterwards, the solution was poured into water (1200 mL) and stirred at room temperature for 2 hours. The organic phase was extracted with chloroform (5x200 mL), dried with Na_2SO_4 and concentrated to dryness by rotary evaporation (yellow viscous liquid, yield=80%). 1H NMR (400 MHz, CDCl3): δ= 1.68 (d, 3H), 2.21 (pentet, 2H), 2.62 (t, 2H), 3.95 (s, 3H), 4.15 (t, 2H), 5.88-6.44 (m, 4H), 7.03 (s, 1H), 7.62 (s, 1H).

PEG 4000-bis(4-(4-(1-(acryloyloxy)ethyl)-2-methoxy-5-nitrophenoxy) butanoic acid) (PC):

Compound 5 (0.32 g, 0.90 mmol) was reacted with PCl_5 (0.32 g, 1.5 mmol) at room temperature for 60 minutes. Then, the resulting phosphorous oxychloride was removed using a vacuum oven. The mixture was dissolved in DCM (6.5 mL) and added dropwise to a solution of PEG 4000 (0. 90 g, 0.225 mmol) and TEA (126 µL, 0.905 mmol) in DCM (6.5 mL) on an ice bath. The solution was mixed overnight. Next, the solution was concentrated using a rotary evaporator and redissolved in a small amount of DCM (1 mL). The product was precipitated into cold diethyl ether (100 mL), filtered and dried under vacuum. 1H NMR (400 MHz, CDCl3): δ= 1.65 (d, 3H), 2.21 (m, 2H), 2.60 (t, 2H), 3.50-3.65 (m, many Hs), 3.90 (s, 3H), 4.15 (t, 2H), 5.85-6.70 (m, 4H), 7.00 (s, 1H), 7.58 (s, 1H)

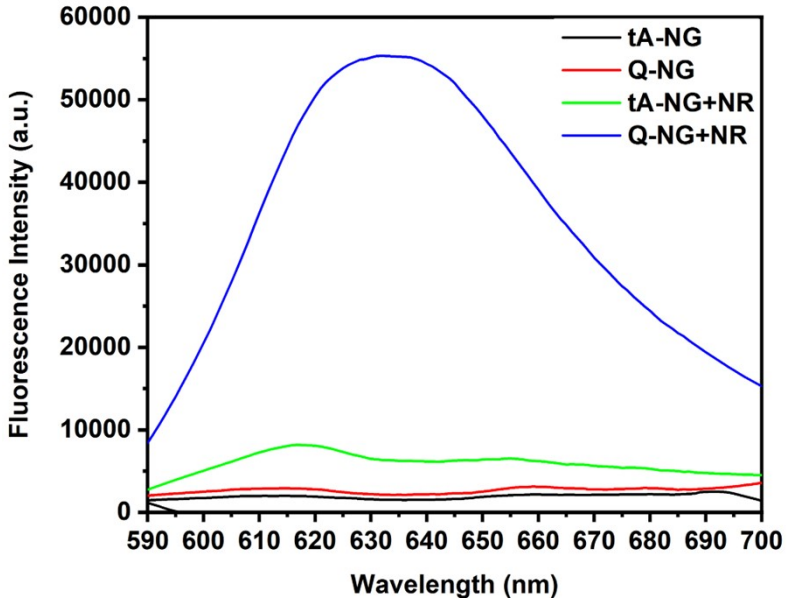


Figure S1: Fluorescence emission spectra of blank nanogels, as well as Nile Red loaded nanogels. Excitation wavelength = 540 nm.

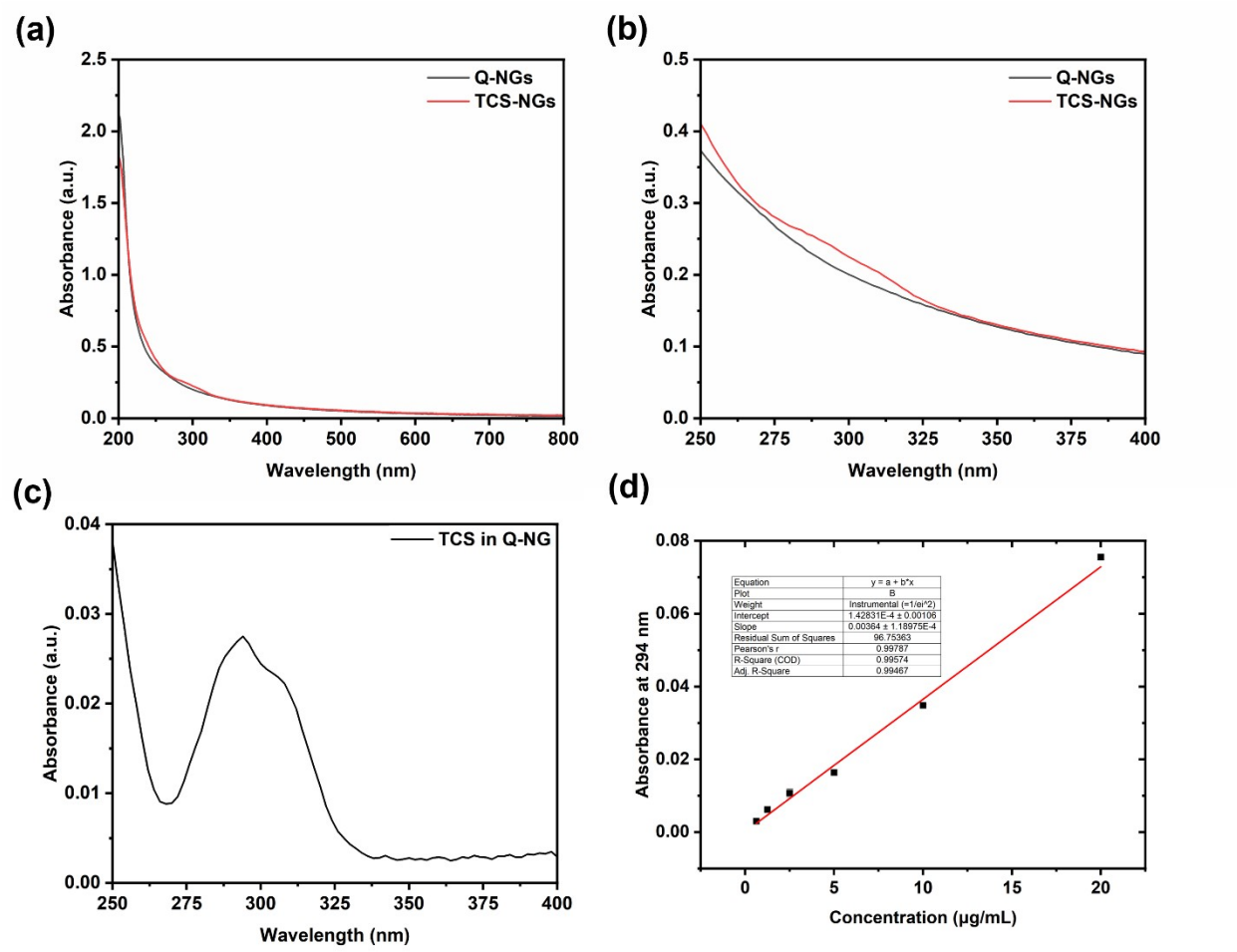


Figure S2: Determining loading of TCS in nanogels. (a): UV-Vis absorbance spectra of Q-NGs and TCS-NGs from 200 to 800 nm. (b): spectra of Q-NGs and TCS-NGs from 250 to 400 nm(c):spectrum of TCS in nanogels after subtraction of Q-NGs' spectrum. (d): calibration curve of TCS in DI H_2O. Concentration of nanogels = 0.05 mg/mL

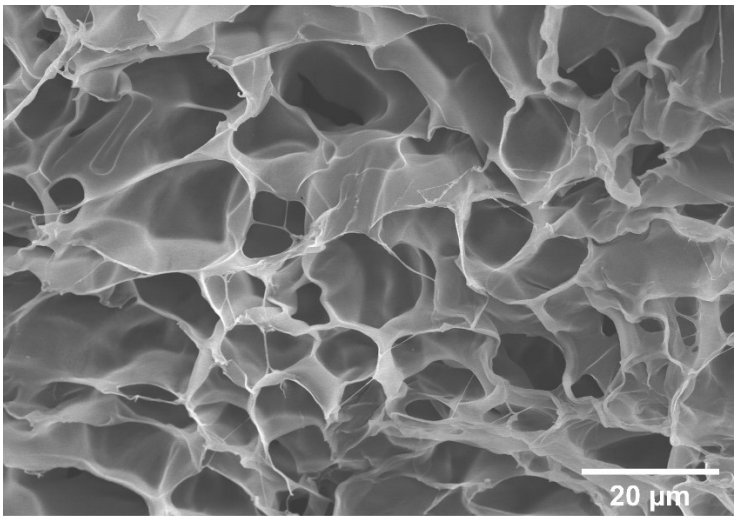


Figure S3: SEM image of hydrogels without incorporated nanogels.

[1] aA. M. Kloxin, A. M. Kasko, C. N. Salinas, K. S. Anseth, *Science* **2009**, *324*, 59-63; bD. R. Griffin, A. M. Kasko, *Journal of the American Chemical Society* **2012**, *134*, 13103-13107.