Supplementary Information for

Self-Healing Injectable Gelatin Hydrogels for Localized Therapeutic Cell Delivery

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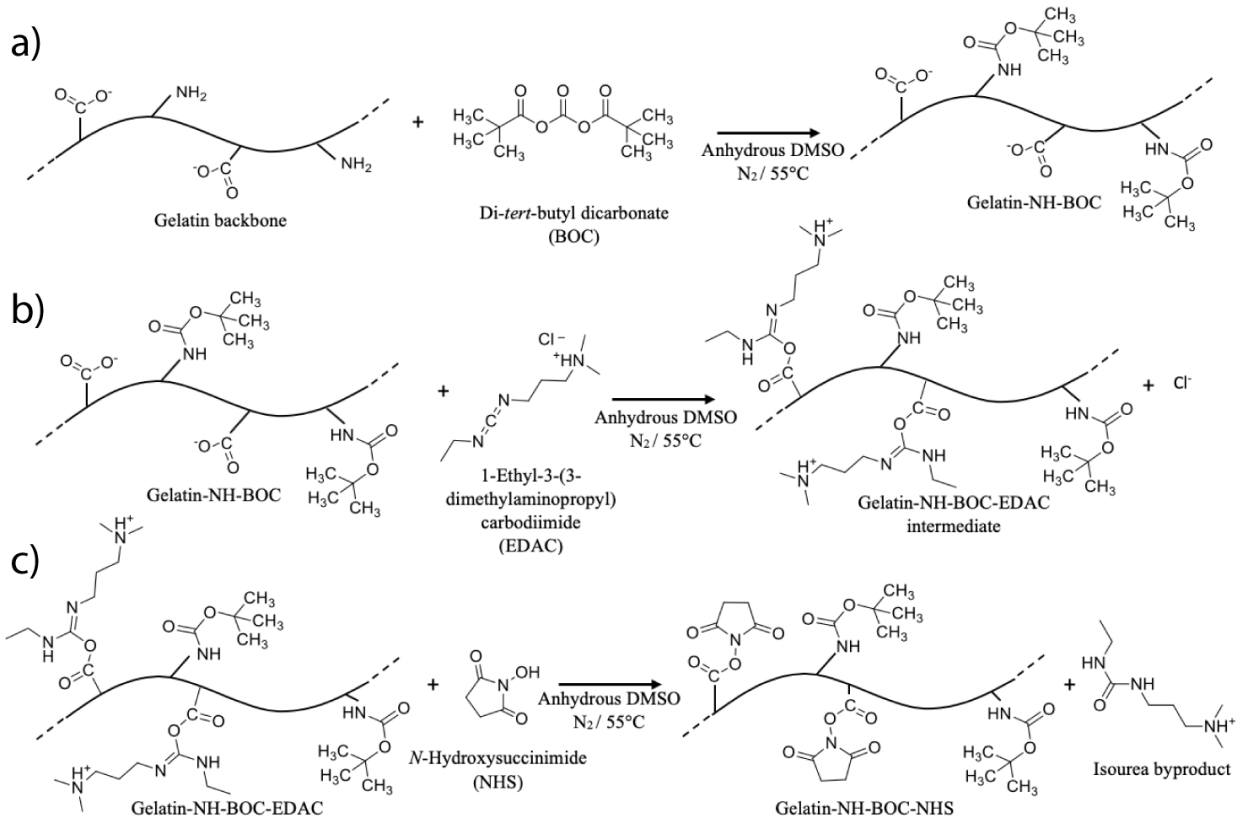

Figure S1. Synthesis of Gel-NHS-Boc. (a) A schematic representation of gelatin is presented by a backbone line with the amine and carboxylic acid side chains. Initial step is protection of primary amines *via* Boc protecting group for the prevention of chemical crosslinking of the gelatin. (b) Second, EDAC is introduced to form an active intermediate. (c) Then, NHS is added to replace the highly active EDAC and form a more stable reactive intermediate. The NHS-modified gelatin can be readily reacted with primary amine-containing compounds to form stable amine linkages.

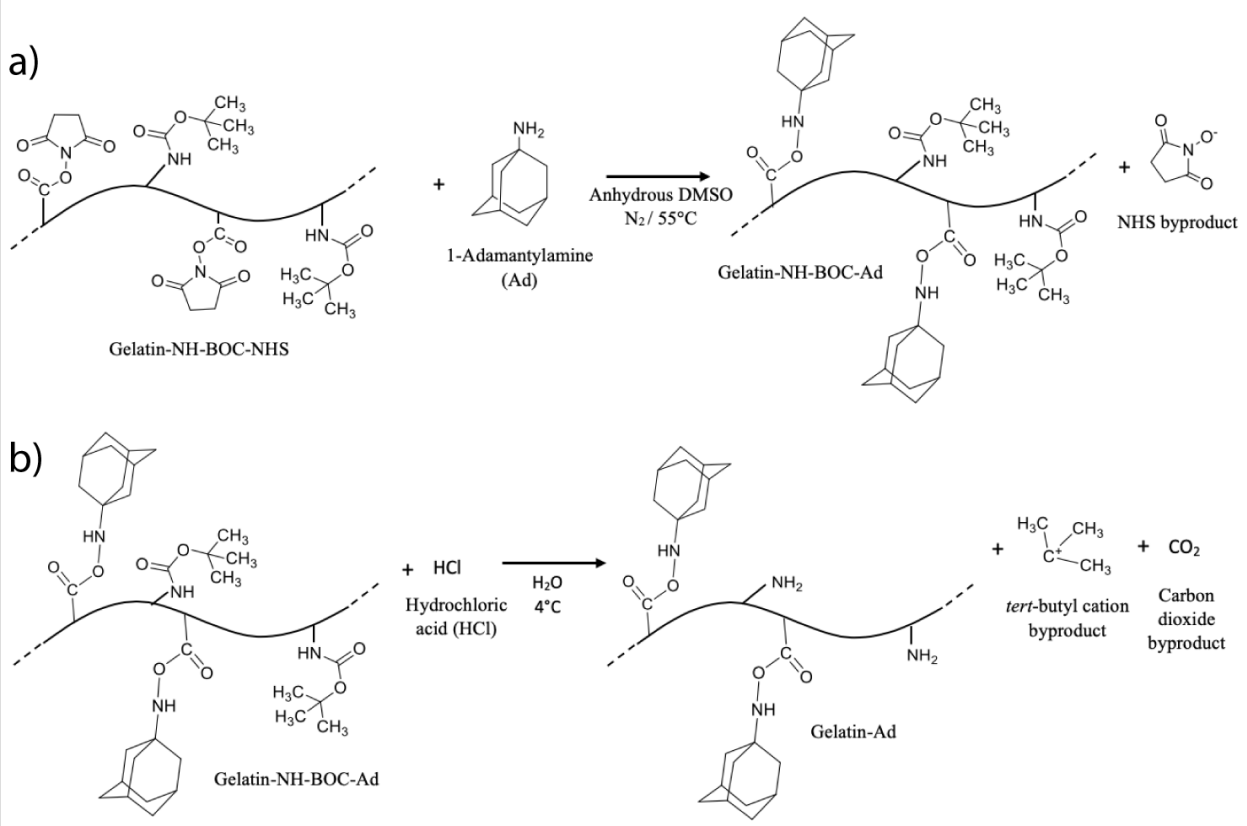

Figure S2. Synthesis of Gel-AD. Gel-NHS-Boc is reacted with 1-adamantylamine (AD) under dry DMSO and N_2 conditions. An amide bond is formed between the activated carboxylic acid on the gelatin backbone and the primary amine of AD. Boc deprotection with mild acid yields the final Gel-AD species.

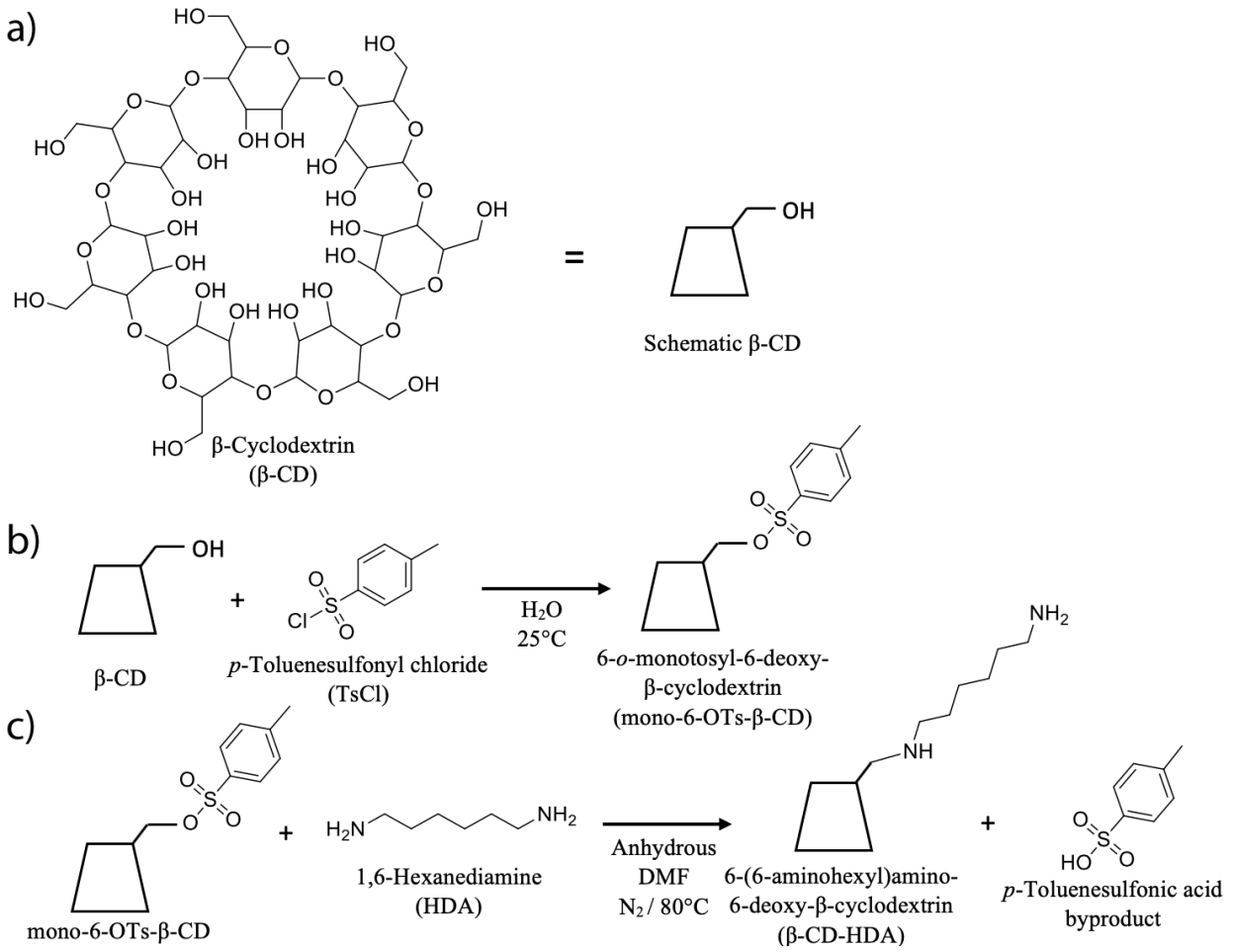

Figure S3. Synthesis of CD-HDA. (a) Schematic representation of β-Cyclodextrin (CD). (b) First step of alcohol activation using TsCl. Single tosylation was achieved by dropwise addition of TsCl to a basic aqueous solution containing CD. (c) Excess of HDA was introduced to the dry mono-6-OTs-β-CD under anhydrous conditions for overnight reaction at 80 °C. Final product CD-HDA was achieved as a white powder.

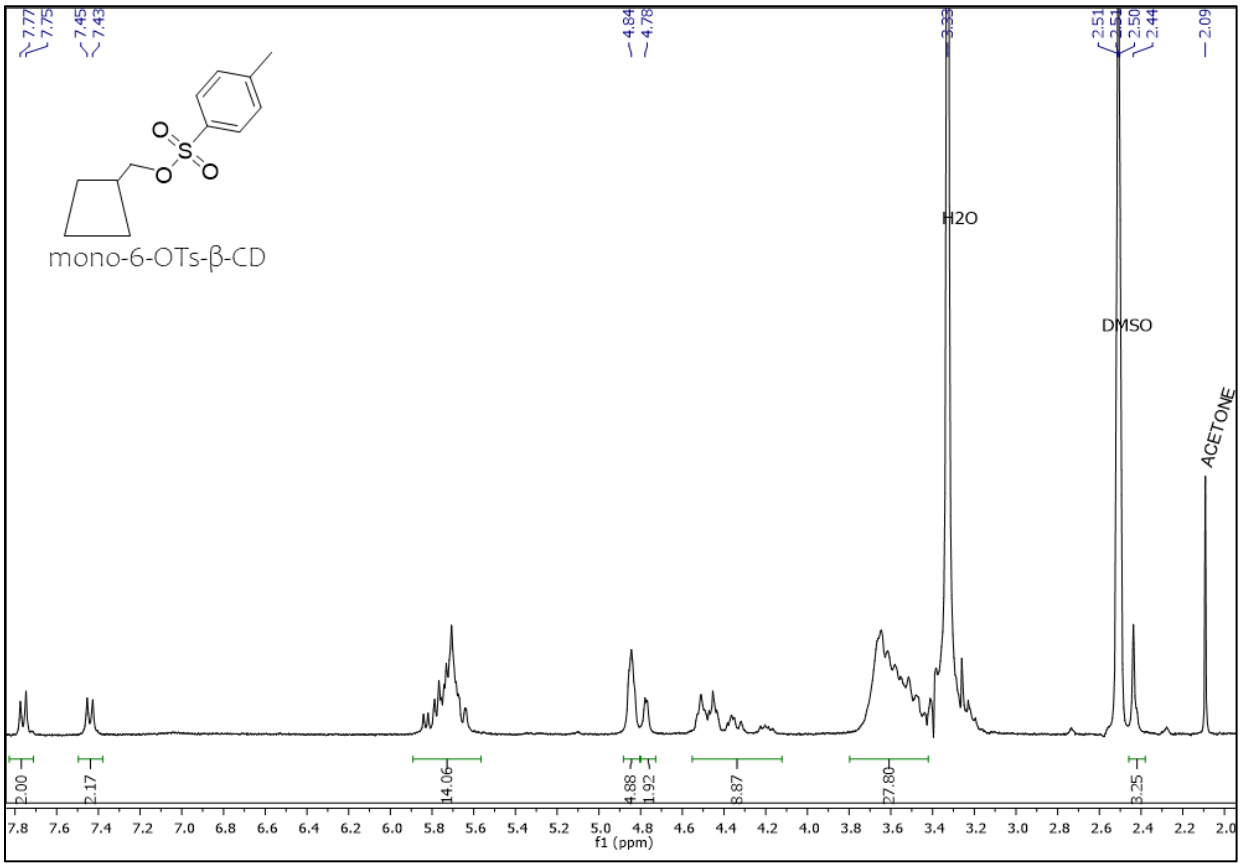

Figure S4. ^{1}H NMR of mono-6-OTs-β-CD. Mono-6-OTs-β-CD chemical structure was verified using ^{1}H NMR in DMSO-d6. δ = 7.76 (d, 2H), 7.44 (d, 2H), 5.89-5.56 (m, 14H), 4.84 (s, 5H), 4.78 (s, 2H), 4.12-4.55 (m, 9H), 3.8-3.42 (m, 28H), 3.41-3.06 (m, overlaps with H2O), 2.42 (s, 3H). Other peaks are a result of solvents used during reaction or DMSO-d6 and are noted on the spectrum.

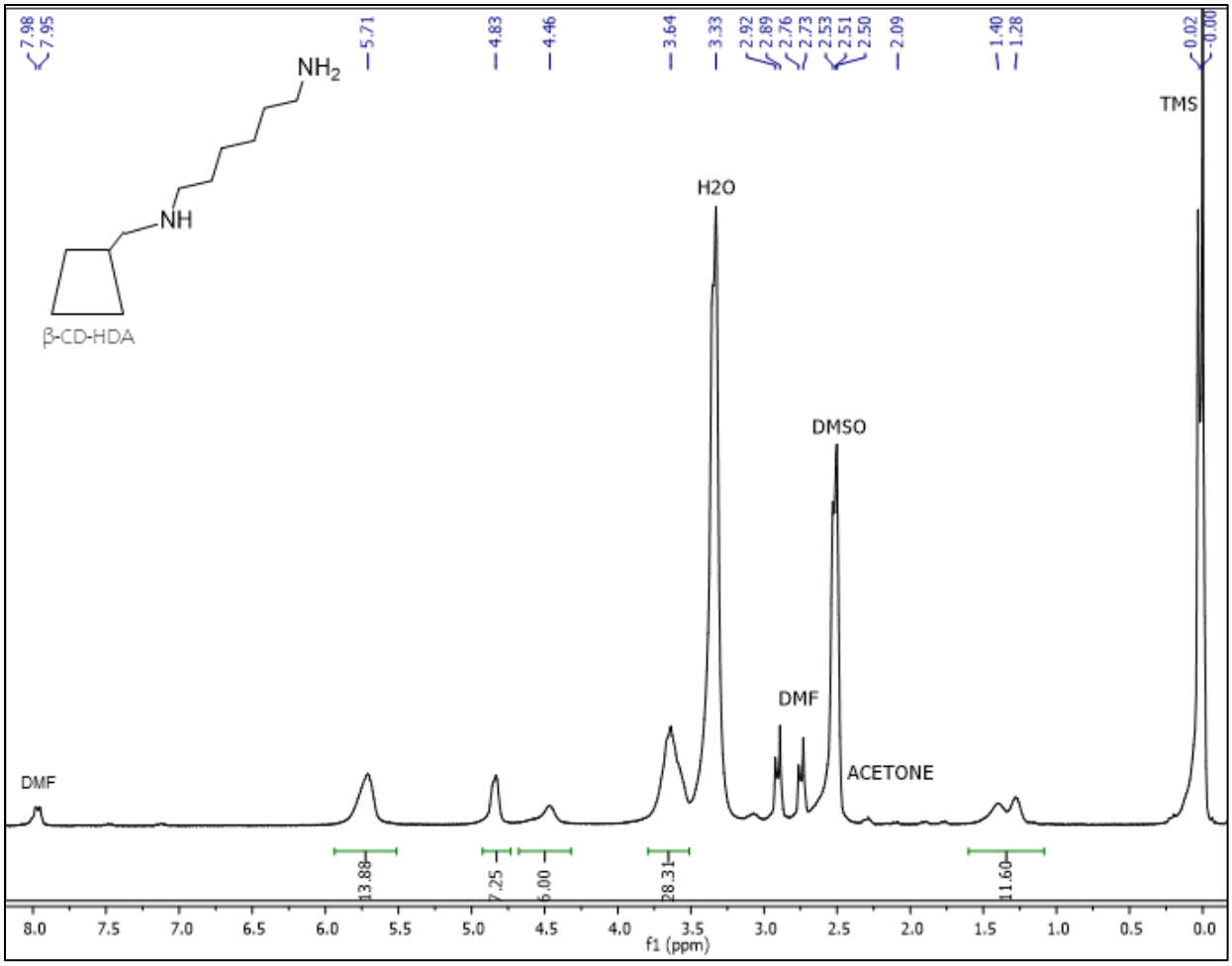

Figure S5. ^{1}H NMR of CD-HDA. CD-HDA chemical structure was verified using ^{1}H NMR in DMSO-d6. δ = 5.71 (br s, 14H), 4.83 (br s, 7H), 4.46 (br s, 6H), 3.79-3.5 (m, 28H), 3.5-3.17 (m, overlaps with H_2O), 1.6-1.08 (m, 12H). Other peaks are a result of solvents used during reaction or DMSO-d6 and are noted on the spectrum.

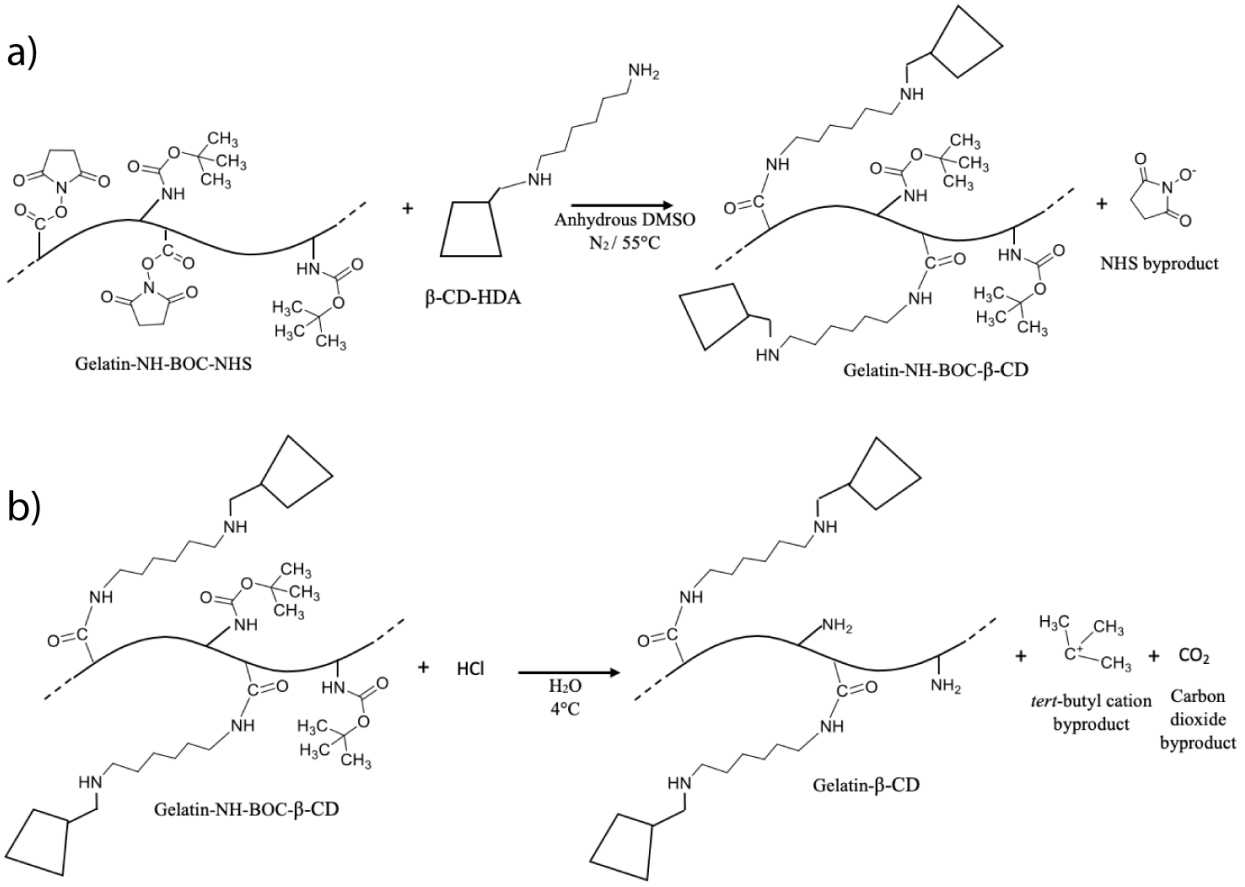

Figure S6. Synthesis of Gel-CD. Gel-NHS-Boc is reacted with CD-HDA under dry DMSO and N_2 conditions. An amide bond is formed between the activated carboxylic acid on the gelatin backbone and the primary amine of CD-HDA. Boc deprotection with mild acid yields the final Gel-CD species.

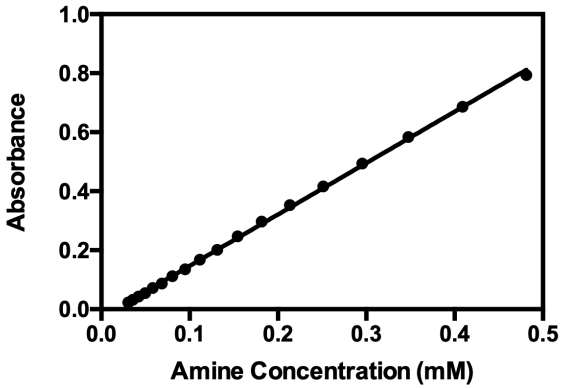

Figure S7. Calibration curve for primary amine concentration. Calibration curve to determine amine concentration in modified and unmodified gelatin was prepared using glycine standards in increasing concentrations and under identical conditions and OPA stock solution. A linear correlation with $R^2 = 0.9993$ was observed, following the Beer-Lambert law.

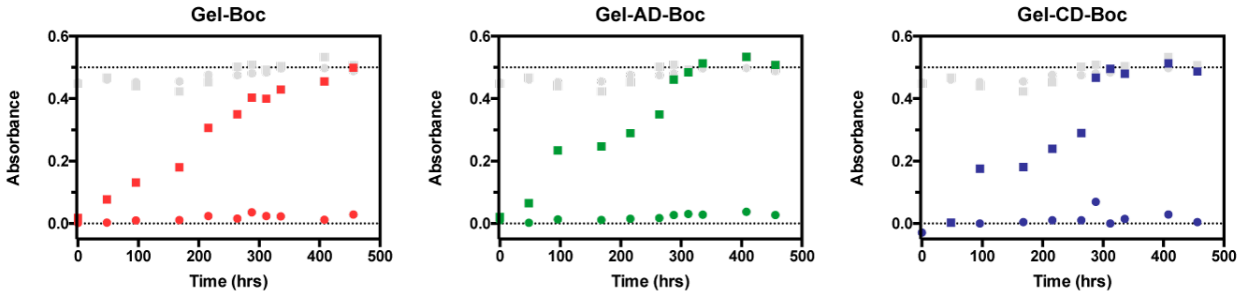

Figure S8. Deprotection of modified gelatin. Amine content of unmodified gelatin (grey), Gel-Boc (red), Gel-AD-Boc (green), and Gel-CD-Boc (blue) was determined a function of time for untreated samples (circles) and those treated with 0.5% v/v HCl 12M (squares), as measured using the OPA reagent with an assay absorbance of 340 nm.