

# Instantaneous degelling thermoresponsive hydrogel

Noam Y. Steinman <sup>1</sup> and Abraham J. Domb <sup>2,\*</sup>

<sup>1</sup> The Alex Grass Center for Drug Design and Synthesis and Center for Cannabis Research and the Institute of Drug Research, School of Pharmacy-Faculty of Medicine, The Hebrew University of Jerusalem, Jerusalem, 91120, Israel; noam.steinman@mail.huji.ac.il

<sup>2</sup> The Alex Grass Center for Drug Design and Synthesis and Center for Cannabis Research and the Institute of Drug Research, School of Pharmacy-Faculty of Medicine, The Hebrew University of Jerusalem, Jerusalem, 91120, Israel; avid@ekmd.huji.ac.il

\* Correspondence: avid@ekmd.huji.ac.il

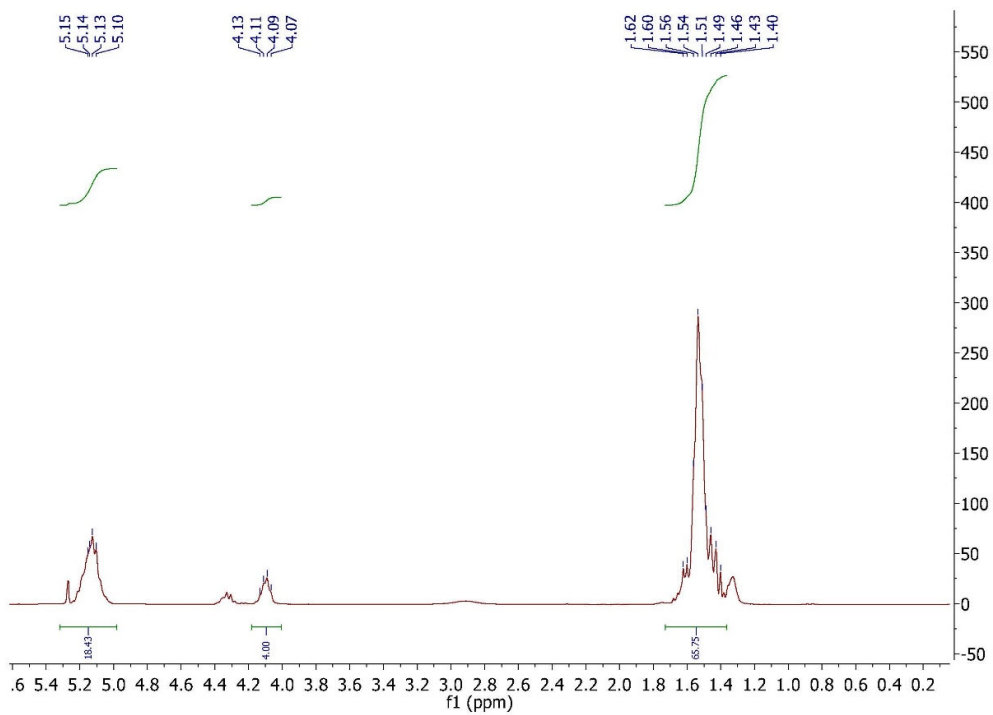
## Supporting Information

### *Synthesis of PEG-PLA-PEG analogue without disulfide bond*

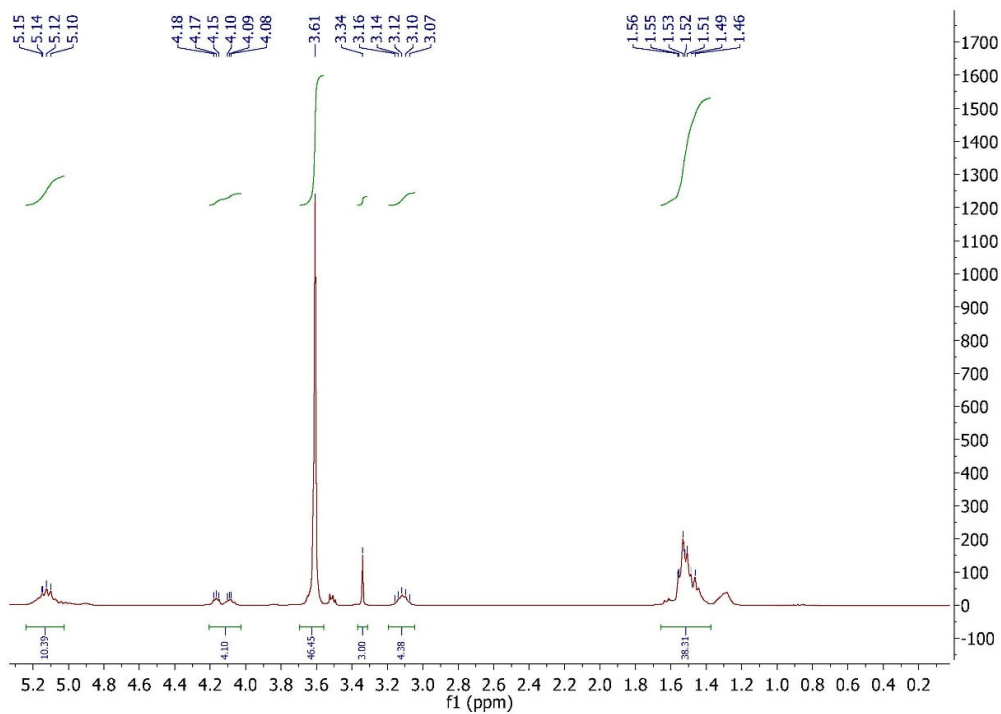
PEG-PLA-PEG analogue without disulfide bond was prepared in two steps. First, 50  $\mu\text{L}$  of a 10% solution of stannous octoate in dichloromethane (DCM) was added to a melt of 1,6-hexandiol (0.26 g, 2.2 mmol) and D,L-lactide (3.1 g, 21 mmol). Solvent was allowed to evaporate and the vial was purged with  $\text{N}_2$ . The mixture was stirred at  $120^\circ\text{C}$  for 2 h, followed by overnight stirring at  $150^\circ\text{C}$  to afford PLA as a pure substance. Proton nuclear magnetic resonance ( $^1\text{H}$  NMR) (300 MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 5.15-5.10 (m, LA), 4.13-4.07 (m,  $\text{CH}_2$   $\alpha$ -ester), 1.62-1.40 (m, LA).

In the next step, hexamethylene diisocyanate (0.59 mL, 3.7 mmol) was added to a melt of PLA (2.7 g, 1.8 mmol) and poly(ethylene glycol) methyl ether  $M_n = 550$  (1.9 mL, 3.1 mmol). One drop of stannous octoate was added, and the mixture was stirred at  $110^\circ\text{C}$  for one hour to afford PEG-PLA-PEG as a pure substance. Proton nuclear magnetic resonance ( $^1\text{H}$  NMR) (300 MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 5.15-5.10 (m, LA), 4.18-4.08 (m,  $\text{CH}_2$   $\alpha$ -ester,  $\alpha$ -urethane), 3.61 (s, PEG), 3.34 (s,  $\text{CH}_3$ ), 3.16-3.07 (m,  $\text{CH}_2$   $\alpha$ -urethane), 1.56-1.46 (m, LA).

*<sup>1</sup>H NMR of PEG-PLA-PEG analogue without disulfide bond*



**Figure S1. <sup>1</sup>H NMR spectrum of PLA analogue.**



**Figure S2. <sup>1</sup>H NMR spectrum of PEG-PLA-PEG analogue.**