SUPPORTING INFORMATION

Glucose Regulation by Modified Boronic Acid-Sulfobetaine Zwitterionic Nanogels - A Non-Hormonal Strategy for the Potential Treatment of Hyperglycemia

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Experimental Section

Materials

N-(methacryloxypropyl)-N, N-dimethyl-N-(3-sulfopropyl) ammonium betaine (SBMA), glucose, tert-butyl lithium, 4-amino-3-fluorophenylboronic acid, trimethylborate, acryloyl chloride, N,N,N',N'-tetramethylethylenediamine (TMEDA), N-(3 dimethylaminoethyl)methacrylate, Sodium Bicarbonate ($NaHCO_3$), Methyl bromoacetate, N,N'-methylenebisacrylamide (MBA), poly(vinylpyrrolidone) (PVP), azobis(isobutyronitrile) (AIBN), and photoinitiator (Irgacure 2959) were purchased from Sigma-Aldrich (USA). USP-grade human recombinant insulin (27 U/mg) was purchased from Wisent (Quebec, Canada). All reagents were of analytical grade or higher and used without further purification.

In vitro Cytotoxicity Assay (Evaluation of Biocompatibility)

The *in vitro* cytotoxicity of used materials was measured by performing 3-(4,5)-dimethylthiahiazo(-z-y1)- 3,5-di phenytetrazoliumromide (MTT) assay on NIH3T3 fibroblast cells (from ATCC). Briefly, cells were seeded in 96-well plate at a density of 10000 cells per well. After 24 hours incubation in 200 µL of Dulbecco's Modified Eagle Medium (DMEM) with 10 % fetal bovine growth serum (FBS), samples were added into wells. The cells were incubated for 24 hours after treatment, and then 100 µL of MTT reagent were added to each of the treated wells and were incubated for 4 hours. In the next step, 100 µL of a solution of 10% SDS in 0.01

M HCl were added and incubated for an additional 4 hours. Finally, the absorbance of the plates was read at 550 nm using a BioRad UV-Vis plate reader. To determine the percent survival, the following equation was used and plotted on a semi-log scale.

$$\%\ survival = \frac{sample\ signal - background\ signal}{control\ signal - background\ signal} \times 100$$

Figures

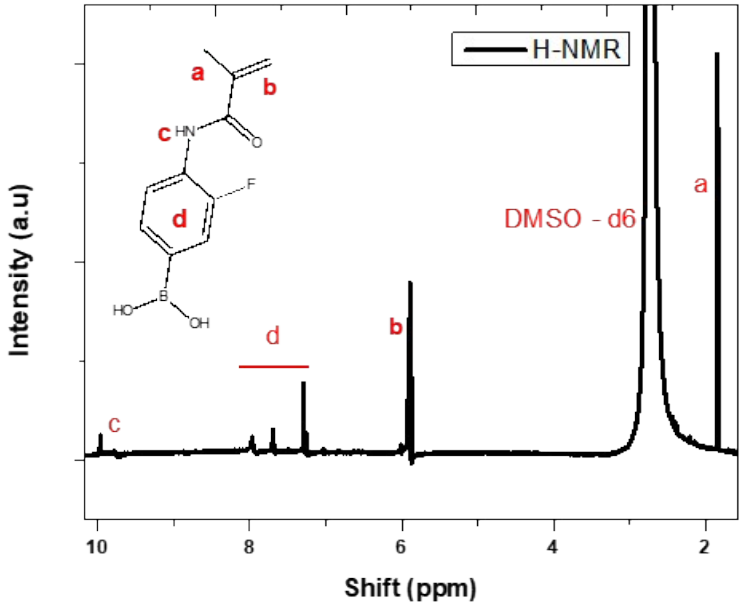

Figure SI1. [1]H-NMR spectrum of AFBA. Deuterated dimethyl sulfoxide (DMSO-d_6) was used as a good solvent for the pure monomer and its solvent peak was observable as a strong signal at 2.5 ppm.

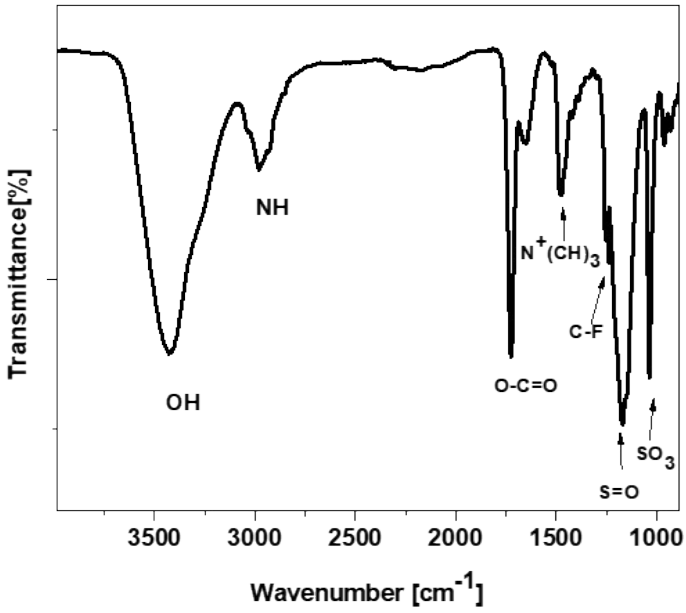

Figure SI2. FTIR result of the N-(methacryloxypropyl)-N, N-dimethyl-N-(3-sulfopropyl) ammonium betaine-co-4-acrylamido-3-fluorophenylboronic acid nanogels.

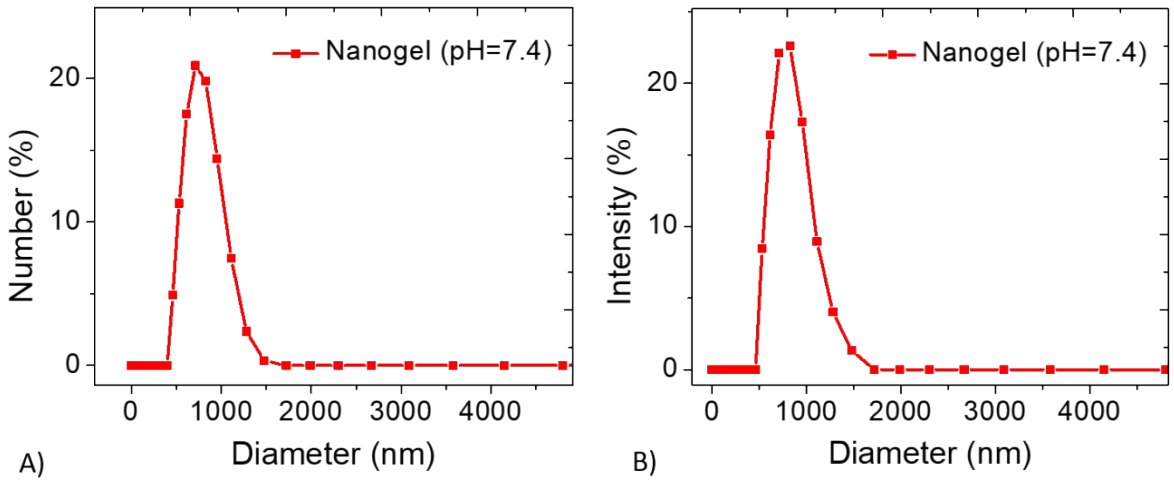

Figure SI3. A) Number and B) Intensity particle size distribution of nanogels at physiological pH determined by dynamic laser light scattering (PDI<0.2).

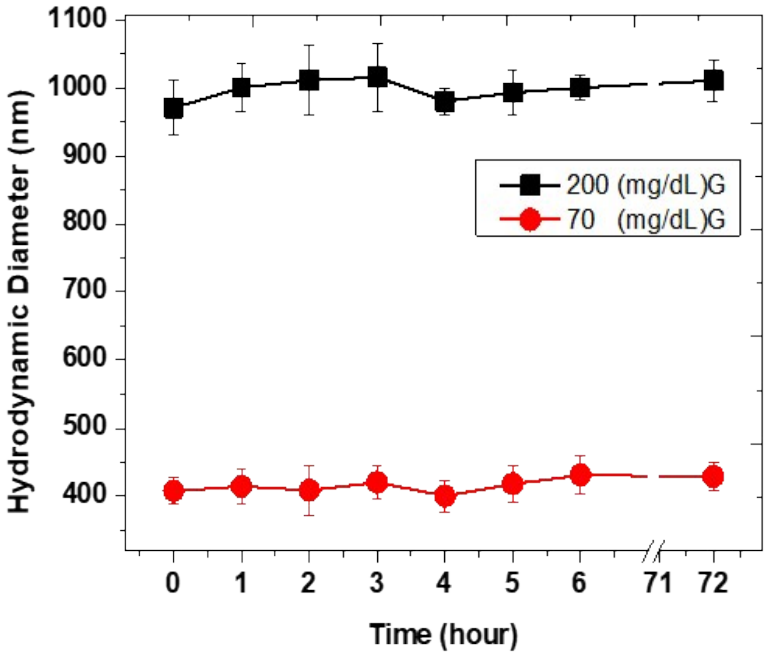

Figure SI4. Changes in the size of the nanogels as a function of immersion time in pH 7.4 PBS containing different glucose concentration.

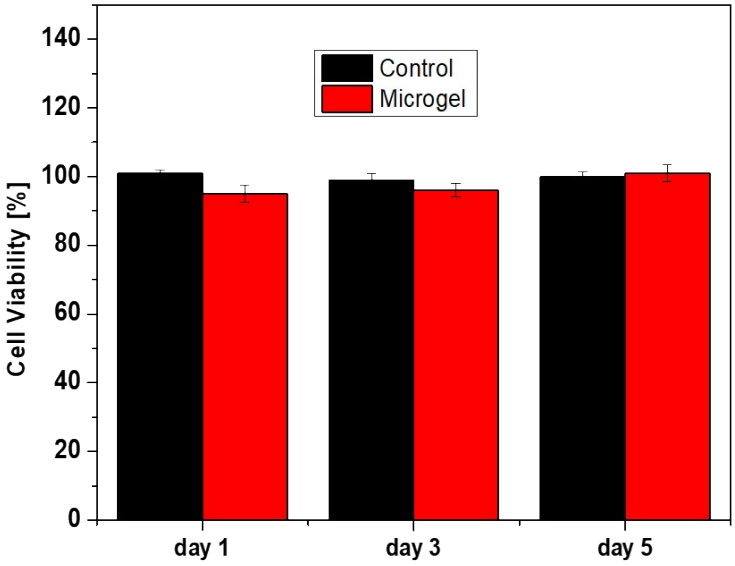

Figure SI5. Viability of NIH3T3 fibroblast cells incubated with the nanogels for up to 5 days determined by MTT assay.