Electric Supplementary Information (ESI)

ESI 1. Materials

L-aspartic acid (Sigma), mesitylene (Aldrich), tetramethylene sulfone (Aldrich), phosphoric acid (Junsei), dimethyl sulfoxide (DMSO; Junsei), hexamethylenediamine (HMD; Aldrich), sodium hydroxide (NaOH; Junsei), *N*,*N*-dimethylformamide (DMF; Aldrich), and phosphate buffered saline tablets (Sigma) were used as received. mPEG-succinimidyl succinate (MW = 30 kDa) was purchased from Sunbio, Korea. Recombinant human-insulin (rh-insulin) was provided by Shemyakin-Ovchinnikov of Bioorganic Chemistry Russian Academy Sciences (Moscow, Russia)

ESI 2. Elemental analysis

The degree of cross-linking can be evaluated by the increment of N atoms after the cross-linking reaction and measured by EA. Since two N atoms increase after the cross-linking reaction of one HMD, the total increment of N atoms represents the actual degree of cross-linking. After the cross-linking reaction with HMD, part of the sample was collected before reacting with NaOH in order to measure the degree of cross-linking.

Table 1S. Elemental analysis results

	PEG-*b*-PSI	Nanogel-5	Nanogel-50	Nanogel-100
N (%)	3.99	4.23	5.07	6.35
C (%)	51.81	50.35	50.27	50.52
H (%)	7.53	7.56	7.81	7.95
Degree of cross-linking		2.7	26	66

ESI 3. Contribution of $I_{particle}(q)$ and $I_{fluct}(q)$

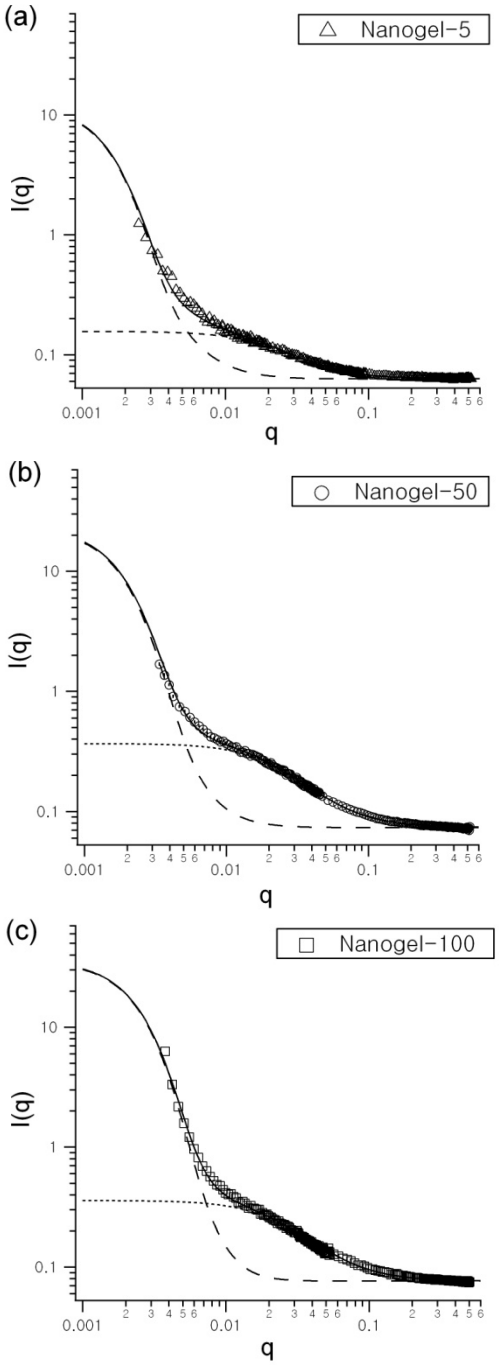

Figure 1S. SANS scattering profile of (a) Nanogel-5, (b) Nanogel-50 and (c) Nanogel-100 at concentration of 0.6 wt%. The solid lines represent fitting results according to the Eq (1). And dashed line and dotted line represent the contribution $I_{particle}(q)$ and $I_{fluct}(q)$, respectively.

ESI 4. Volume swelling ratio of nanogel core

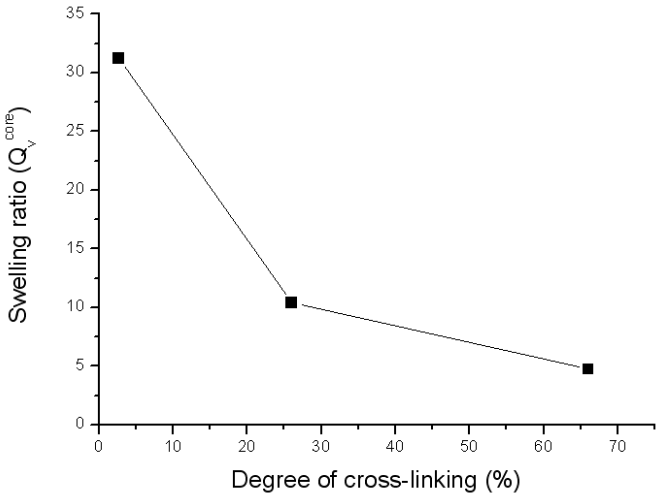

Figure 2S. Plot of volume swelling ratio of nanogel core as a function of degrees of cross-linking.

ESI 5. hERG K+ channel activity assay

hERG K+ channel activity assay was measured using hERG-HEK293 cells which is a recombinant cell line expressing human ERG (Ether-a-go-go Related Gene) potassium channel, and inhibition of hERG by various concentration of Nanogel-50 was measured by automated planar patch clamp (PatchXpress 7000A)

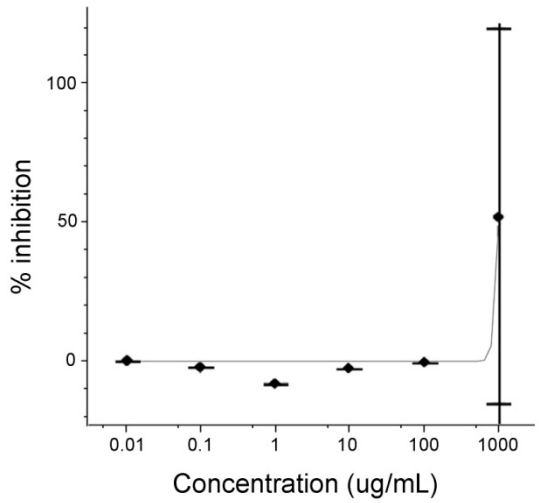

Figure 3S. hERG K+ channel inhibition by Nanogel-50

ESI 6. rh-insulin loading and release experiment.

The particle size of insulin loaded nanogels was 119.7 ± 29 nm, and smaller size of free insulin was not observed.

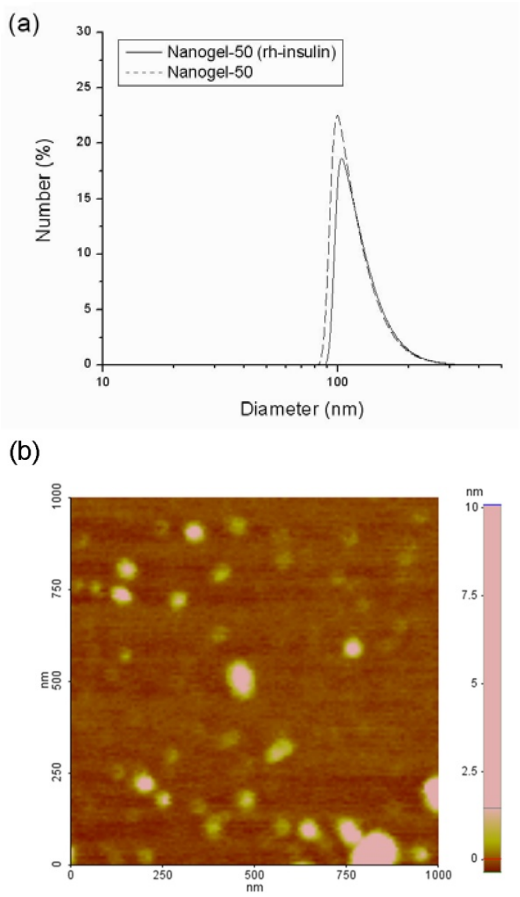

Figure 4S. (a) Size distribution of Nanogel-50 and rh-insulin loaded Nanogel-50. (b) AFM image of rh-insulin loaded Nanogel-50

ESI 7. Kinetic of drug release from PEG-PAsp nanogels

The rh-insulin release from Nanogel-50 at pH 7.4 and 2 were analyzed with a power law equation:

$$\frac{M_t}{M_\infty} = kt^n$$

where k is the release constant, exponent n describes the kinetic and physical mechanism for release, and M_t and M_∞ are the amount of drug released at a given time (t) and infinite time, respectively.

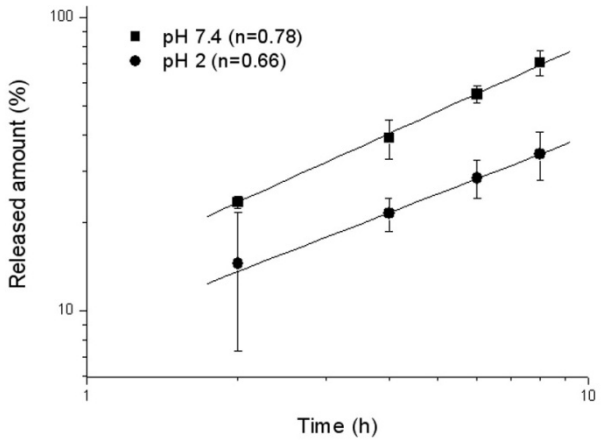

Figure 5S. The calculated diffusional exponents (n) based on the power law model for rh-insulin release from Nanogel-50 at pH 7.4 and 2.