Supplementary information

Rapid in situ forming PEG hydrogels for mucosal drug delivery

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Table S1. Gelation and degradation times of rapid forming PEG gels.

4-arm PEG-SH (%w/v)	4-arm PEG-SH (%w/v)	Gelation time	
		10kD PEG	20 kD PEG
0.5	0.5	~4 min	~1.5 min
0.5	1	~1.5 min	~50 s
1	0.5	~2 days	~5 min
1	1	~30 s	~30 s
1.5	1	~30 s	~25 s
1.5	1.5	~10 s	~15 s
2	1	>2 hr.	~20s

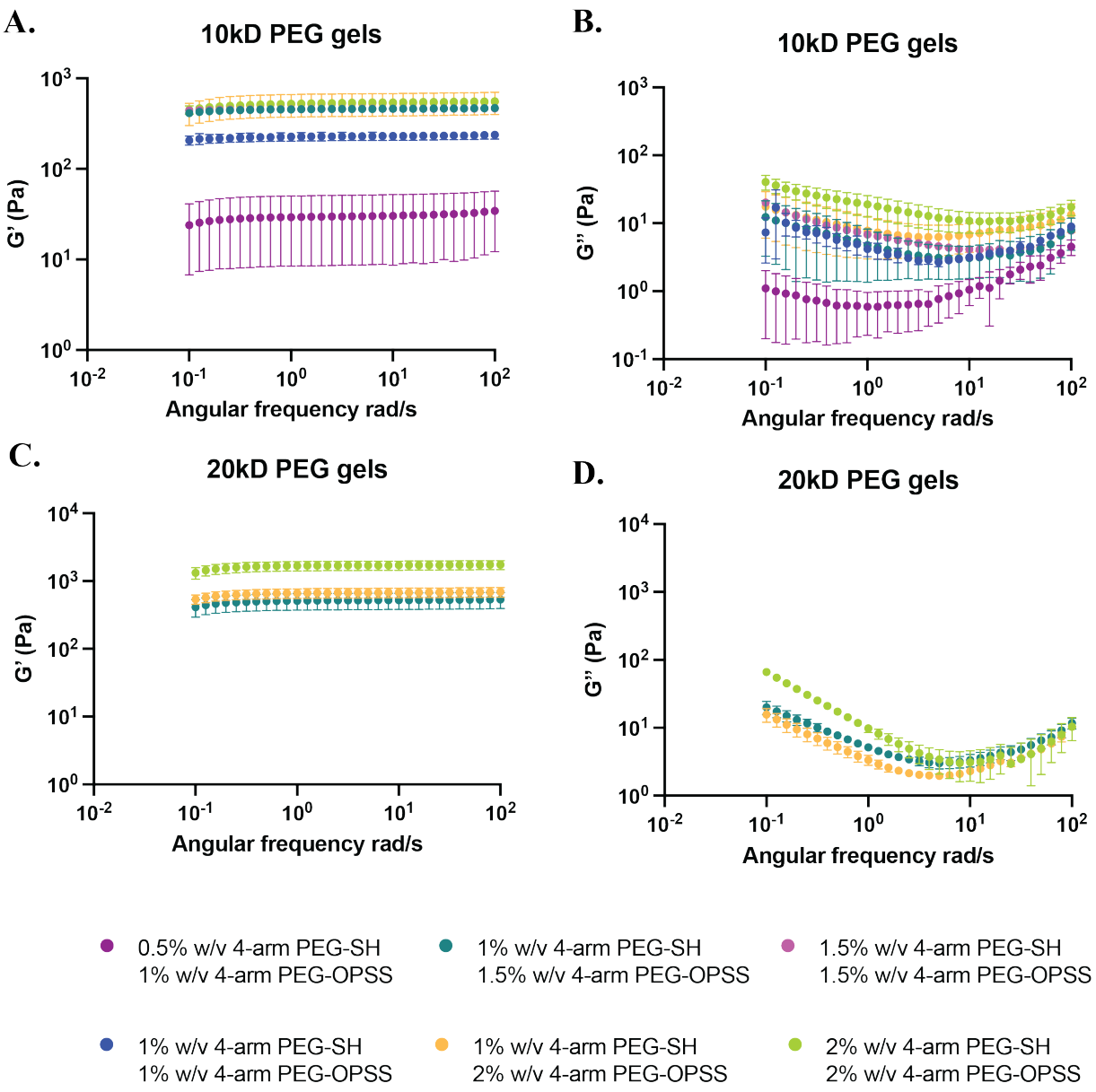

Figure S1. Bulk rheological properties of rapid in situ forming PEG gels. (A), (B) Storage modulus (G') and (C), (D) Loss modulus (G") as a function of frequency at 10% strain (n=3).

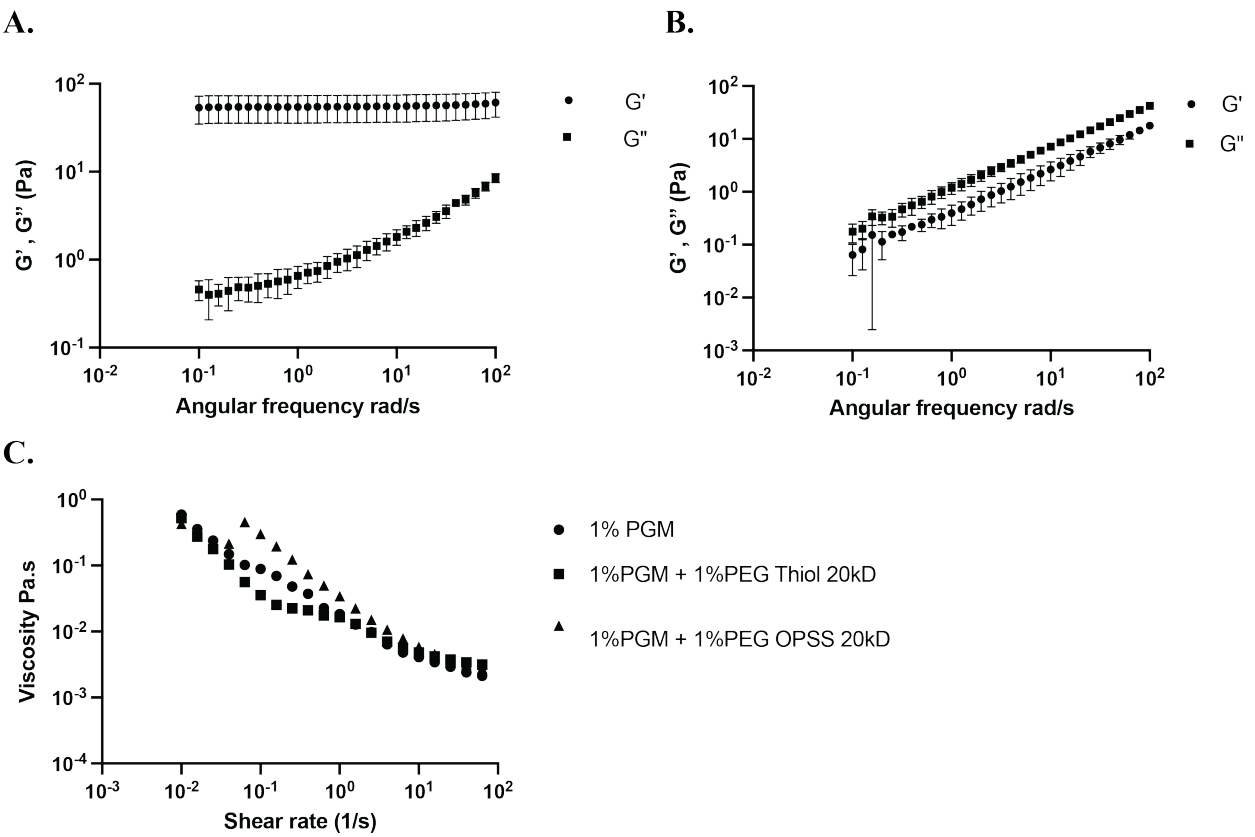

Figure S2. Bulk rheological properties of control gels used for mucoadhesion. Storage modulus (G') and Loss modulus (G") as a function of frequency at 10% strain of (A) 2% w/v 4-arm PEG-DBCO 10kD crosslinked with 2%w/v 4-arm PEG-Azide 10kD (n=3), (B) 4% w/v chitosan (n=3). (C) Flow sweep (n=1) showing no instant crosslinking between mucin chains and PEG-Thiol or PEG-OPSS indicating mucoadhesion at 0 hr. is driven by polymer-mucin chain entanglement and hydrogen bonding.

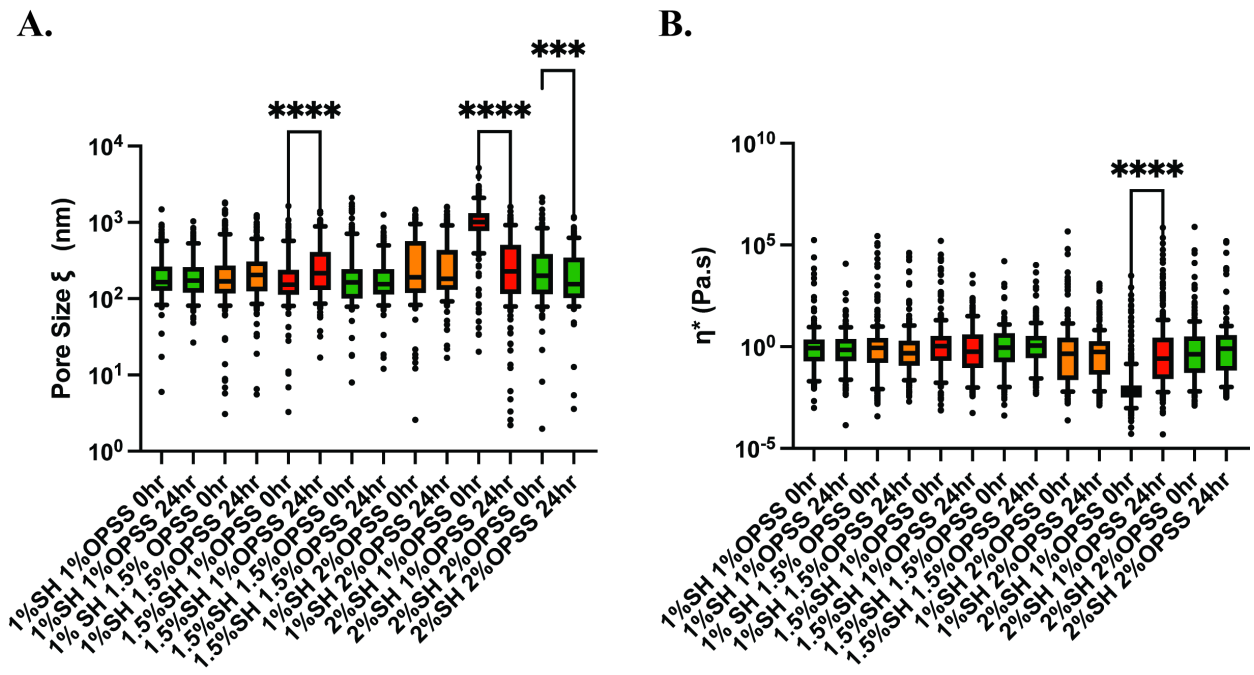

Figure S3. Micro rheological properties of 10kD PEG gels at 0 hr. and 24 hr. after mixing PEG-SH and PEG-OPSS solutions. (A) Estimated pore size based on analysis of mean square displacement (MSD) at τ=1s. (B) Complex microviscosity (η^*) at a frequency $\omega = 1$ Hz calculated from measured MSD. * p <0.05, **p <0.01, ***p <0.001, ****p <0.0001 for Kruskal-Wallis test.

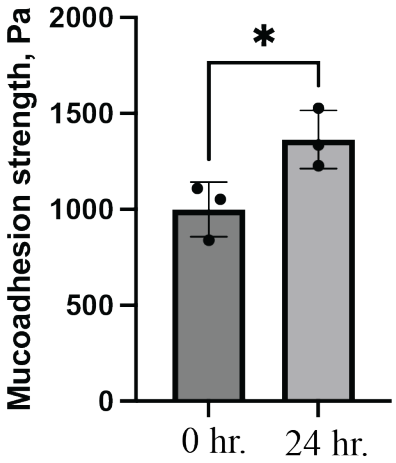

Figure S4. Mucoadhesive properties of 0.5% w/v 4-arm PEG-SH 10kD and 1% w/v 4-arm PEG-OPSS 10kD gels at 0 hr. and 24hr. after application to porcine intestinal tissue (n=3). * p <0.05 for Welch's t test.

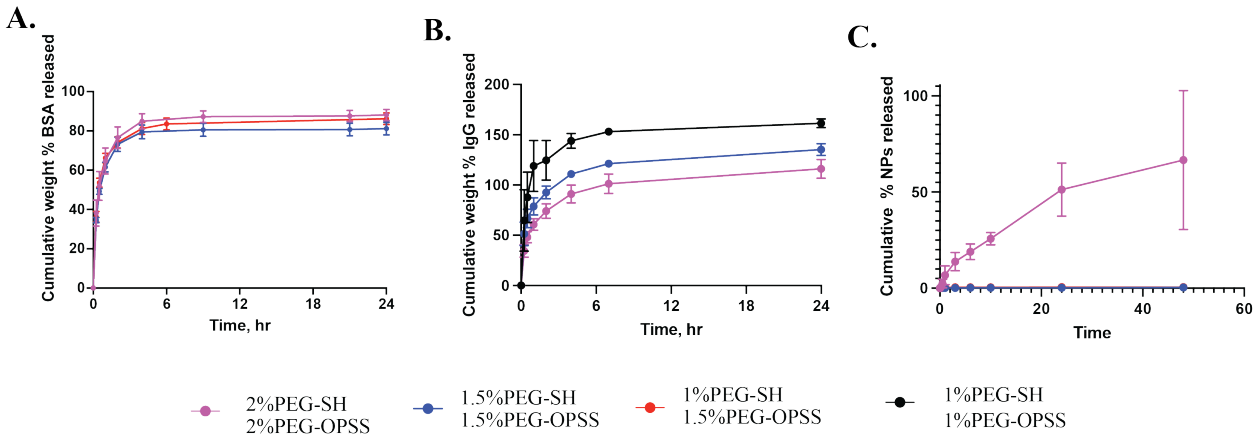

Figure S5. Release kinetics of model therapeutic cargo from different formulations of rapid forming PEG hydrogels. Cumulative release profile of (A) BSA from 10kD PEG gels (n=3), (B) IgG from 10kD PEG gels (n=3), and (C) 20nm nanoparticles (NP) from 20kD PEG gels (n=3) over 24 hours.

FITC labeled IgG was used for these release experiments. More than 100% release was observed likely due to fluorescence dequenching following IgG hydrolysis over time.[1]

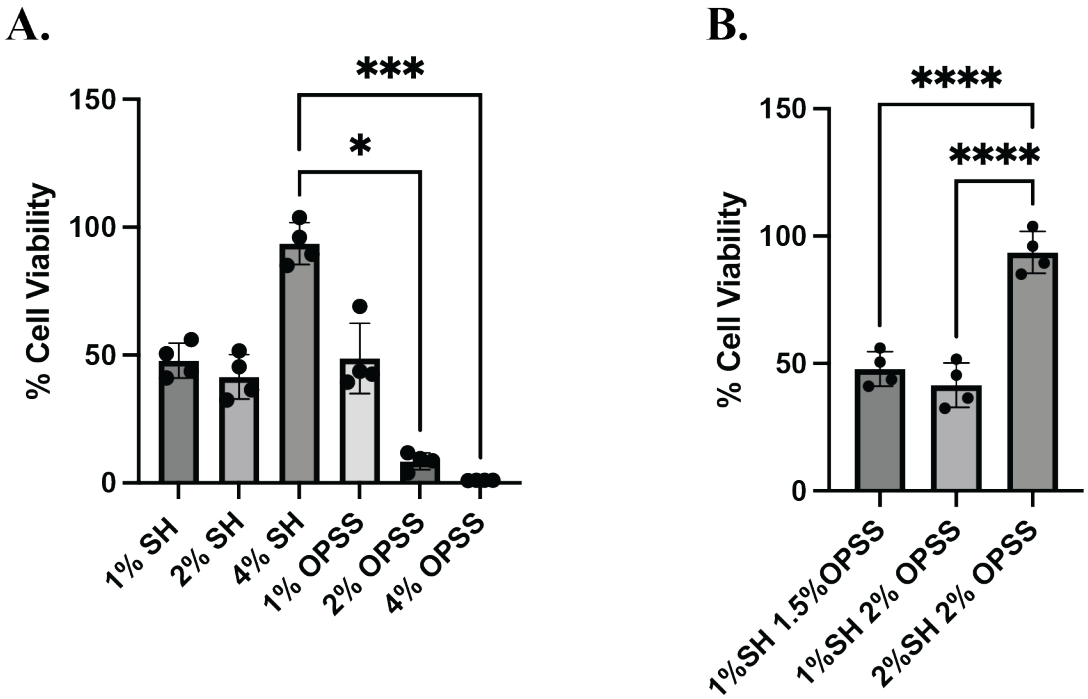

Figure S6. Biocompatibility of rapid forming 5kD PEG gels. Viability of HEK-293T cells following treatment with (A) 4-arm PEG solutions (n=4) * p <0.05 ***p <0.001 for Kruskal-Wallis test. (B) PEG hydrogels (n=4) ****p <0.0001 for one-way ANOVA with Tukey's multiple comparison test.

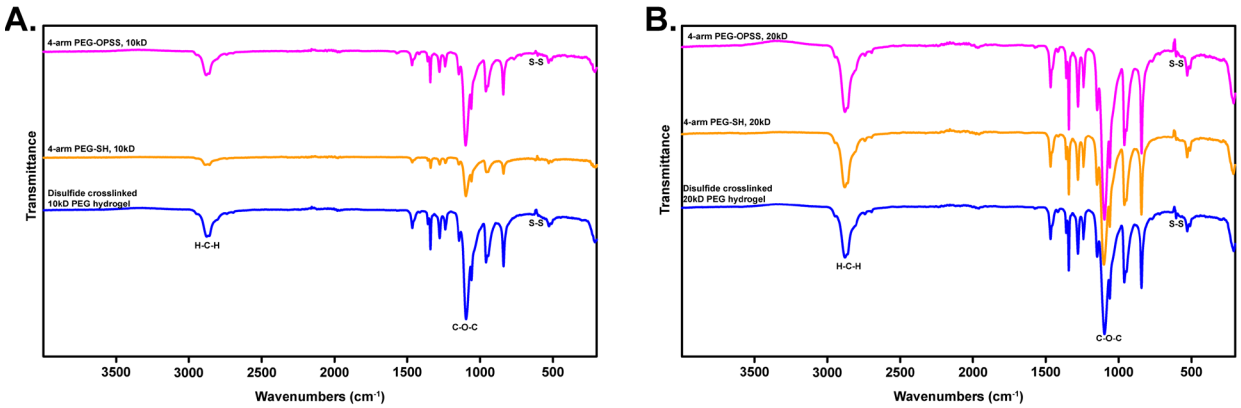

Figure S7. FTIR Spectrum of rapid forming PEG gels. (A) 10kD and (B) 20kD

References:

[1] C. Wischke, H.-H. Borchert, Fluorescein isothiocyanate labelled bovine serum albumin (FITC-BSA) as a model protein drug: opportunities and drawbacks, Pharmazie 61 (2006) 770–774.