Supporting Information

Development and optimization of an ocular hydrogel adhesive patch using definitive screening design (DSD)

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Table S1. Hydrogel compositions based on different concentrations of polymers used for Design of experiment (DoE) by JMP® software

#	GelMA[1] %(w/v)	Instagel[2] %(w/v)	PEGDA[3] %(w/v)	HAMA[4] %(w/v)	HAGM[5] %(w/v)	Replicates
1	0	0	0	0	3	2
2	0	0	0	3	0	2
3	0	0	1	0	0	2
4	0	0	1	3	0	2
5	0	3	0	0	0	2
6	0	4	1	0	3	2
7	0	6.5	0.5	1	0	2
8	0	6.5	1	0	0.5	2
9	0	7	0	0	3	2
10	0	7	0	3	0	2
11	3	0	0	0	0	2
12	4	0	1	0	3	2
13	4	0	1	3	0	2
14	6.5	0	0.5	1	0	2
15	6.5	0	1	0.5	0	2
16	7	0	0	0	3	2
17	7	0	0	1	0	2

[1]Referred to as GelMA B300, [2]Commercial name of GelMA B225, [3]Poly ethylene glycol diacrylate, [4]Methacrylated hyaluronic acid and [5]Glycidyl methacrylated hyaluronic acid.

Table S2. Physicochemical characteristics of single polymers 10% (w/v) for GelMA (B300 and B225), 3% (w/v) for HAMA and HAGM, and PEGDA.

Polymer	MW (kDa)[1]	DM[2]
GelMA B300	60-100	81%
GelMA B225, Instagel	40-60	78%
HAGM	1.5-1.8 x 10^3	12%
HAMA	1.5-1.8 x 10^3	33%
PEGDA	35 x 10^3	85%

[1]Molecular weight, [2]Degree of modification determined by [1]HNMR

Table S3. Optimized hydrogel formulations at different concentrations and weight ratios of GelMA B300 and HAGM.

#	Formulations	GelMA %(w/v)	HAGM %(w/v)	GelMA: HAGM ratio
1	G7HG3	7	3	2.3
2	G14HG3	14	3	4.7
3	G14HG6	14	6	2.3
4	G7HG6	7	6	1.2

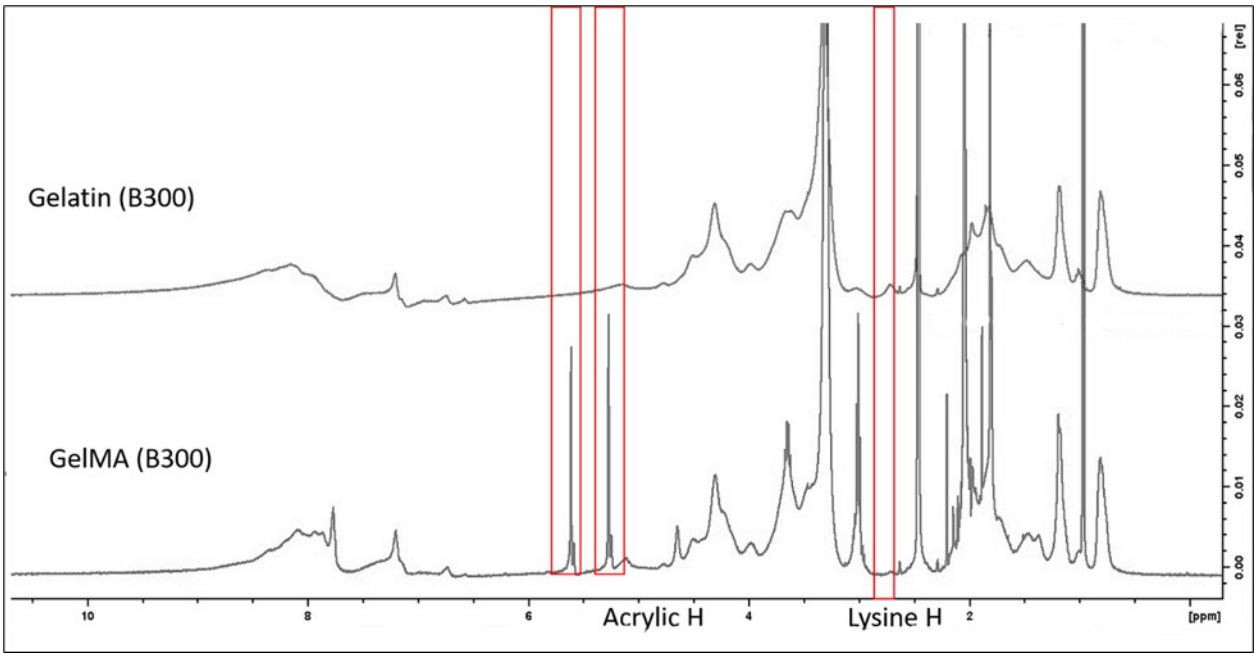

Figure S1. ^{1}HNMR characterization of porcine derived methacrylated gelatin (GelMA B300) compared to its native form gelatin (B300).

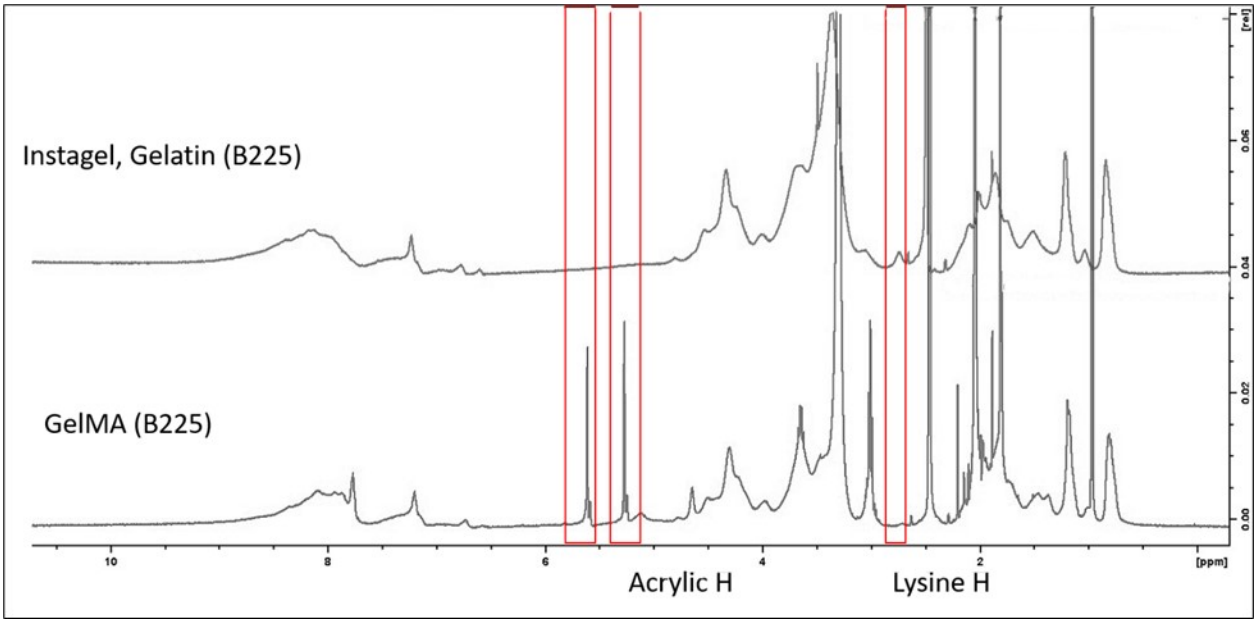

Figure S2. ^{1}HNMR characterization of porcine derived methacrylated gelatin (GelMA B225) compared to its native form gelatin (B225) or Instagel.

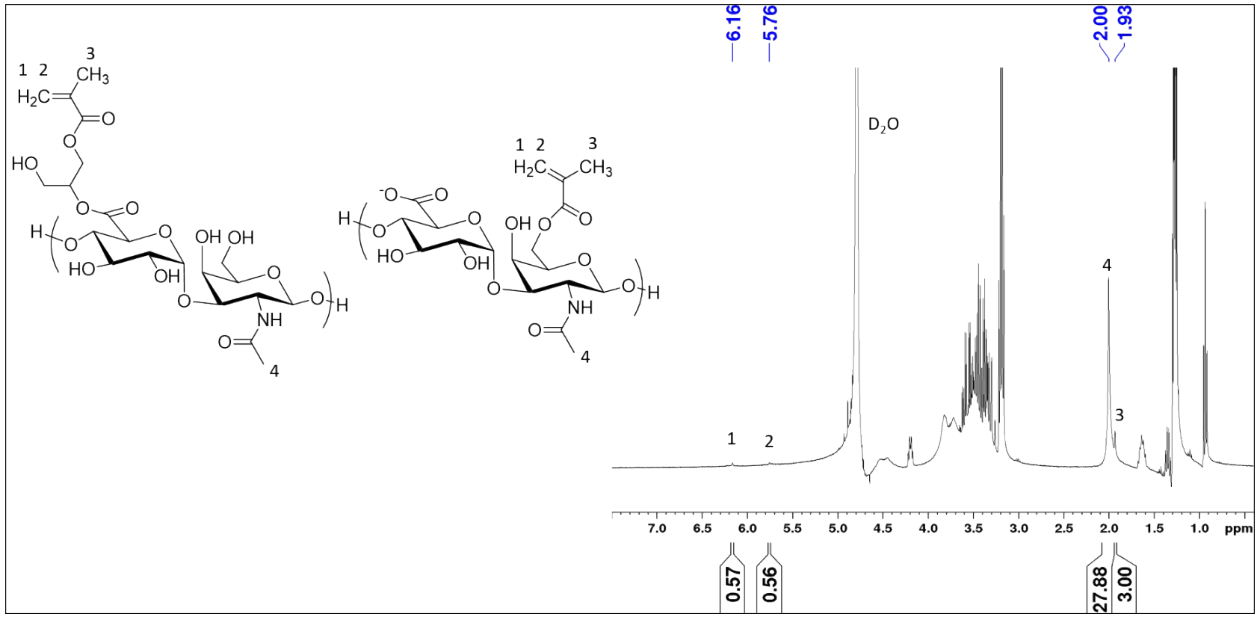

Figure S3. [1]HNMR characterization of glycidyl methacrylated hyaluronic acid (HAGM).

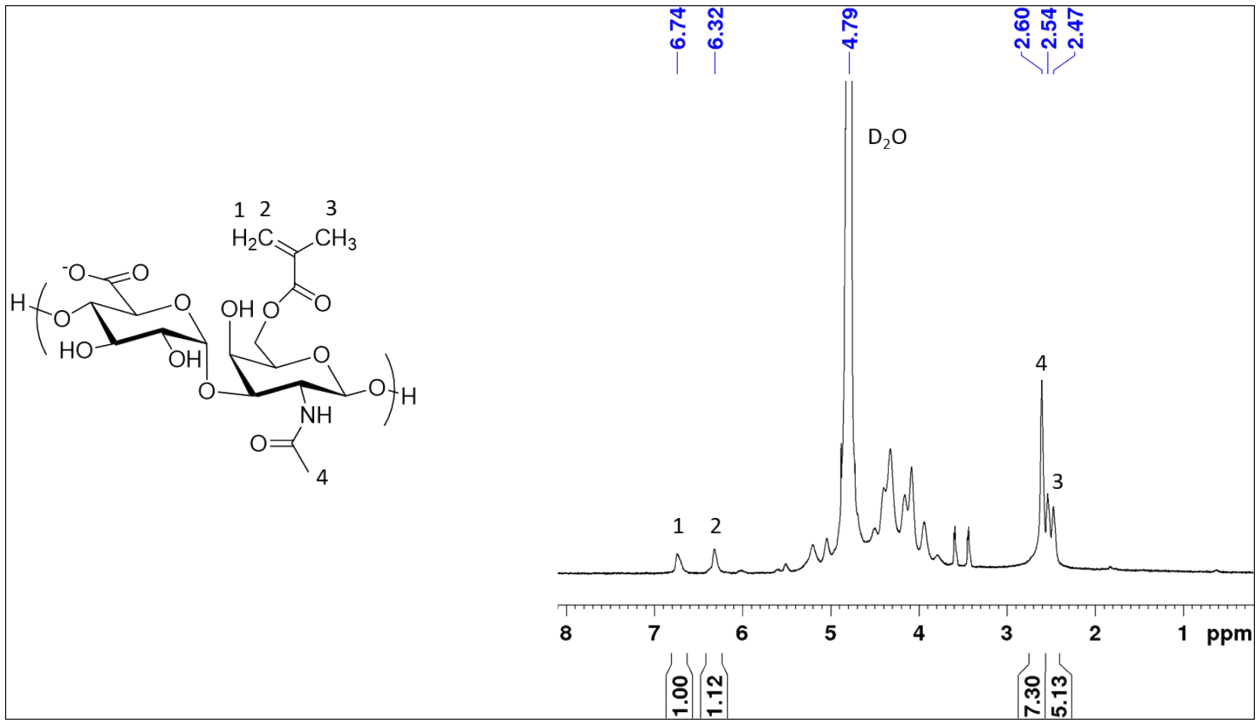

Figure S4. [1]HNMR characterization of methacrylated hyaluronic acid (HAMA).

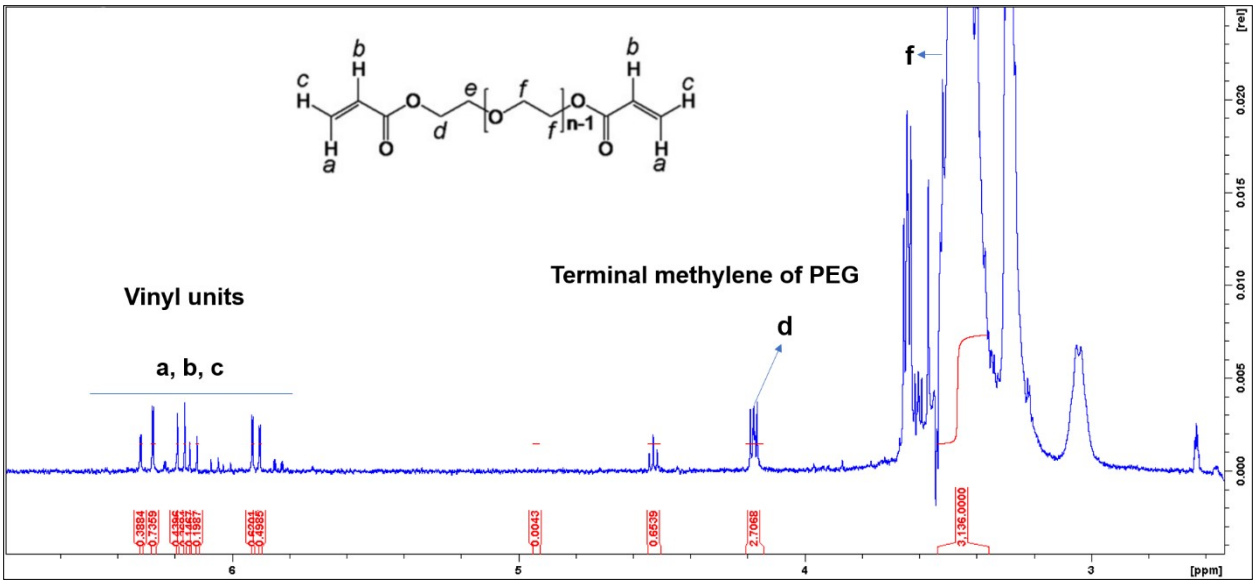

Figure S5. [1]HNMR characterization of diacylated polyethylene glycol (PEGDA)

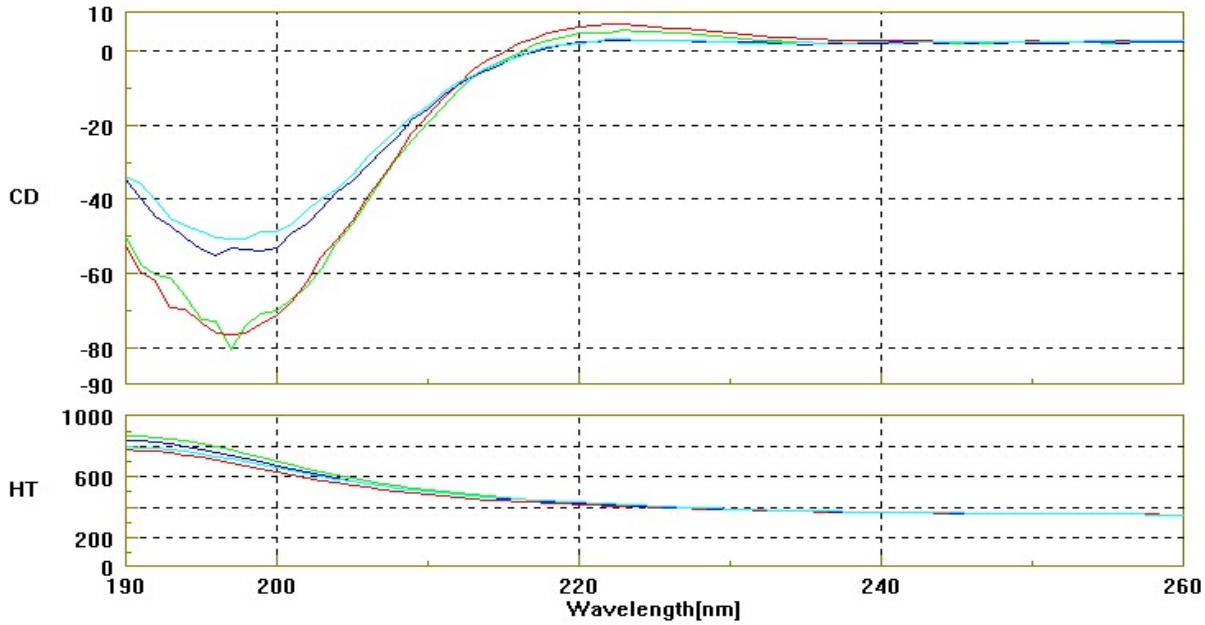

Figure S6. Circular dichroism (CD) spectra of 0.03% GelMA B300 (blue), GelMA B225 (cyan), [orcine gelatin B300 (red), and porcine gelatin B225 (green) dissolved in water. The bottom half is dynode voltage, labeled as high tension (HT).

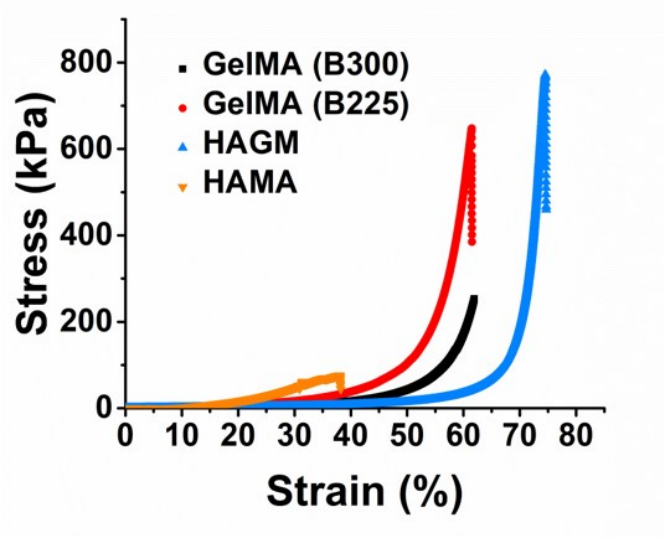

Figure S7. Representative compressive stress-strain curves of photocrosslinked hydrogels prepared with 10%(w/v) GelMA (300 and 225) and 3% (w/v) HAGMA and HAMA.

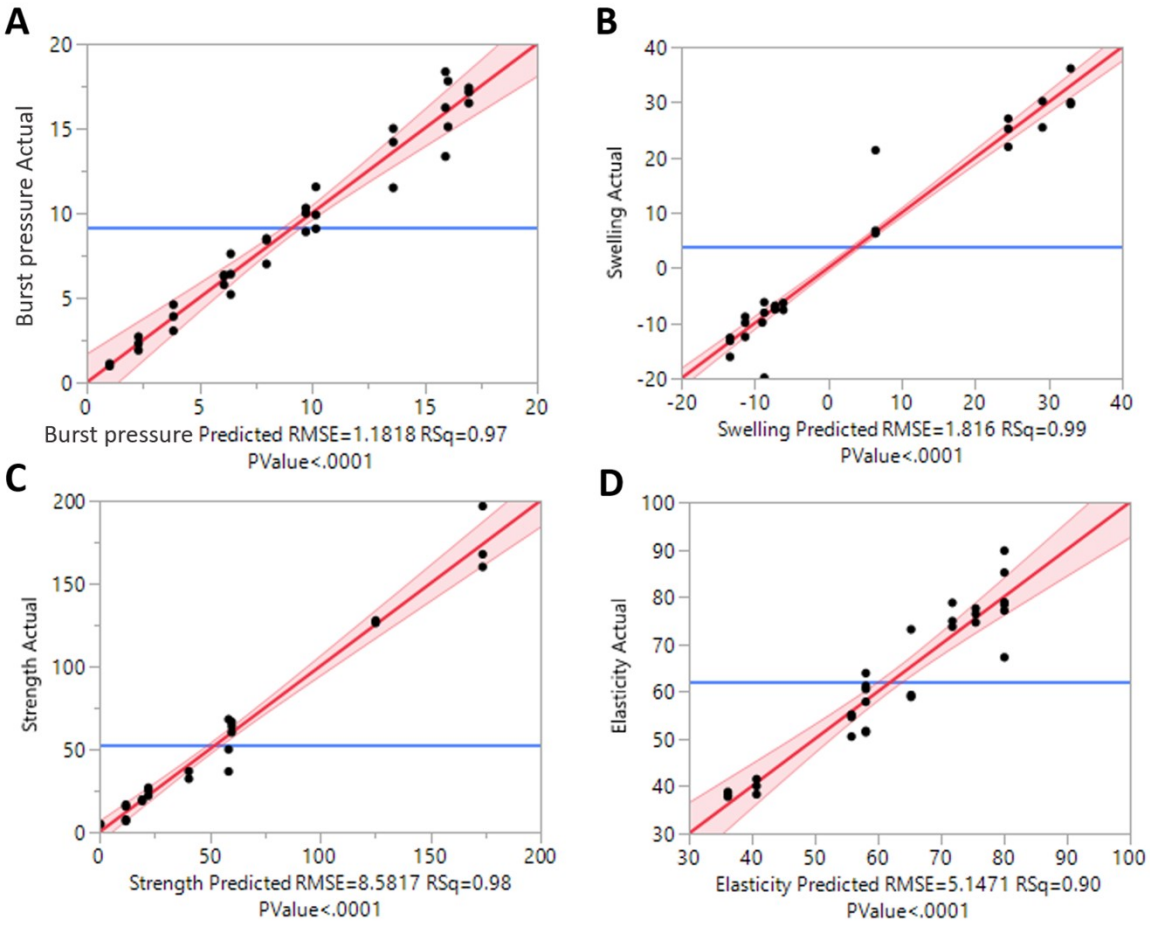

Figure S8. Scatterplots of experimental versus predicted values for (A) Burst pressure, (B) Swelling ratio, (C) compression modulus, and (D) Elasticity.

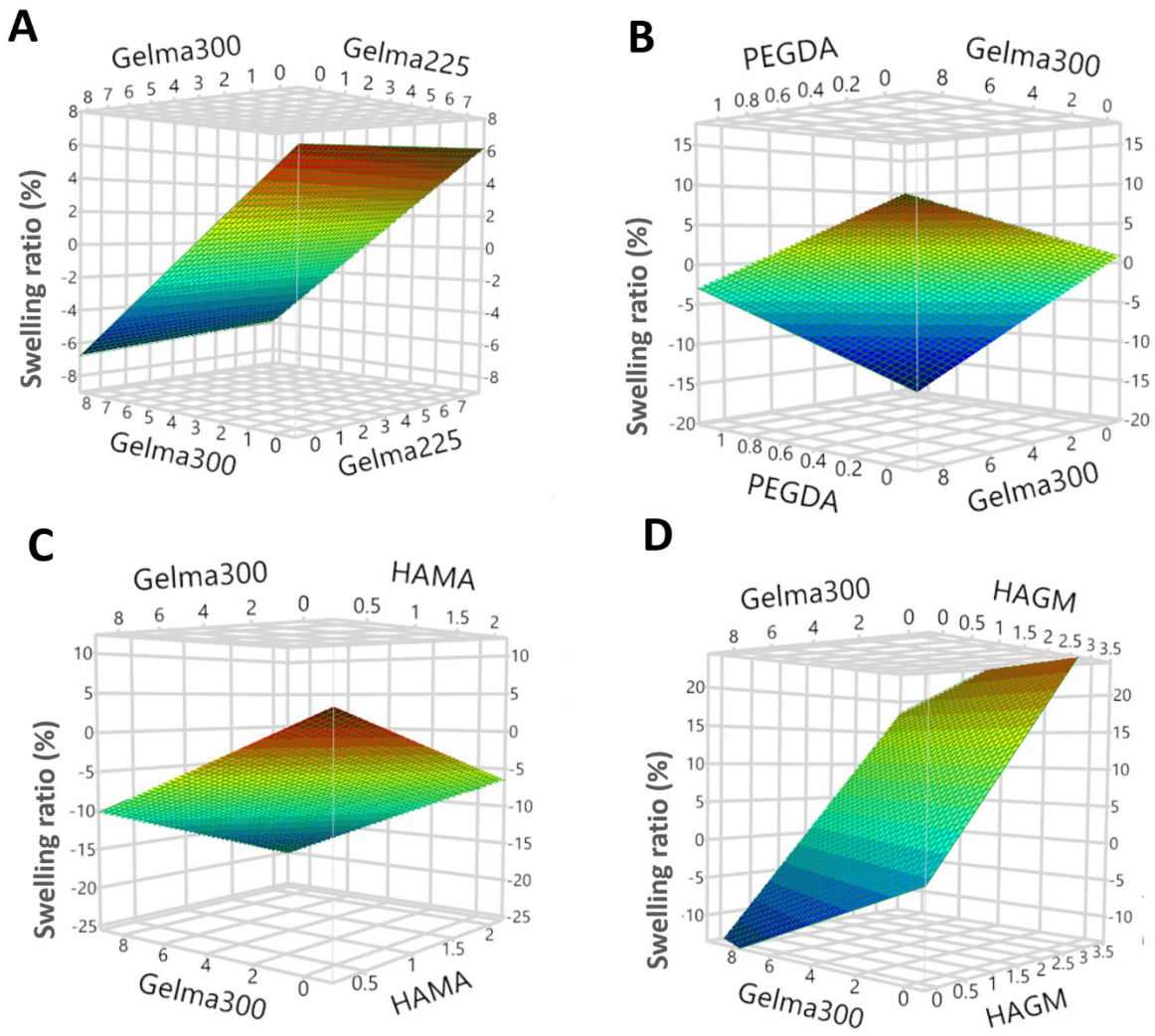

Figure S9. Response surface estimated by definitive screening design (DSD) for swelling ratio. (A) As a function of GelMA B300 and GelMA B225 concentrations, (B) as a function of GelMA B300 and PEGDA concentrations, (C) as a function of HAMA and GelMA B300 concentrations, (D) as a function of GelMA B300 of HAGM concentrations. Only positive Z values were considered.

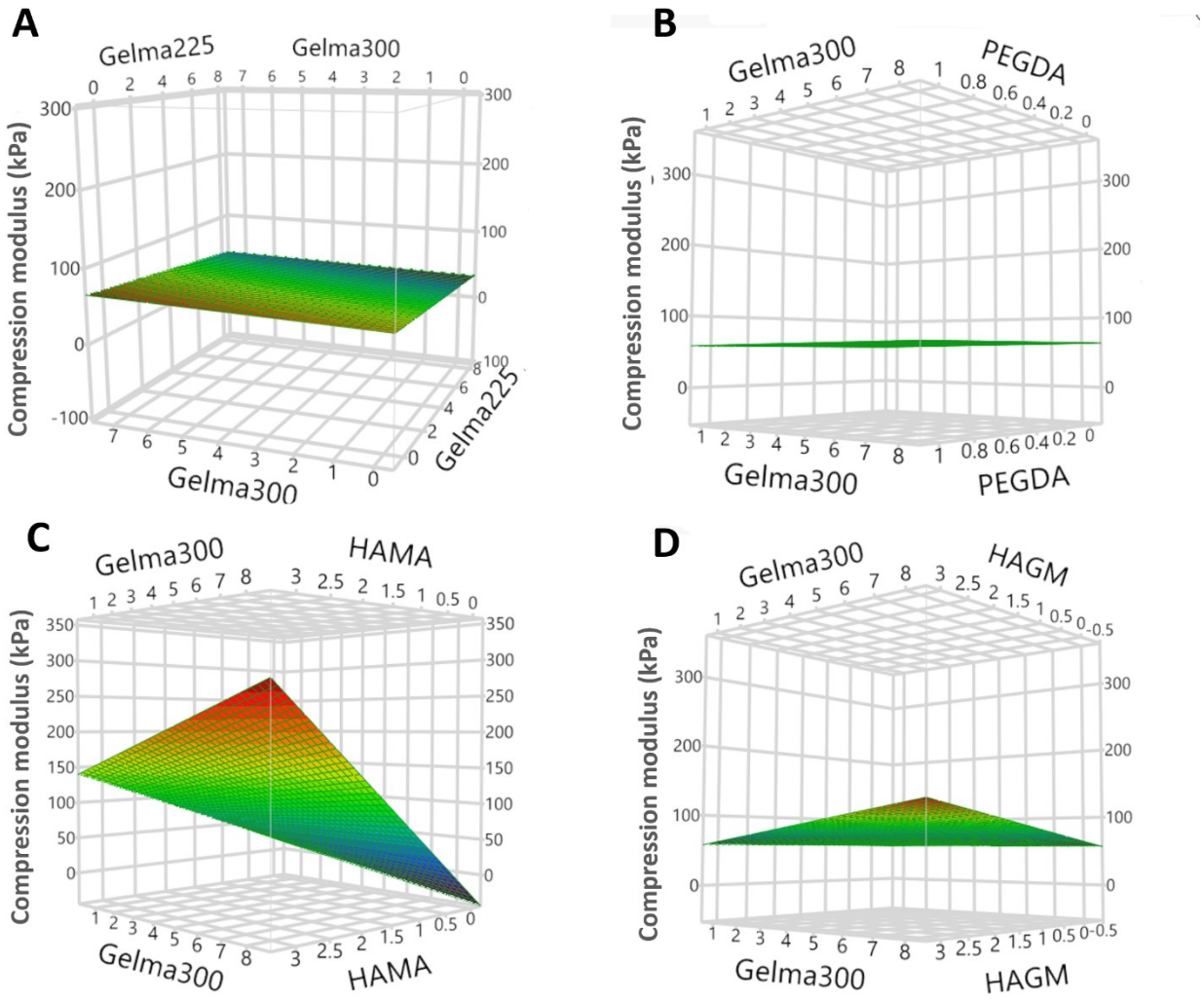

Figure S10. Response surface estimated by definitive screening design (DSD) for compression modulus. (A) As a function of GelMA B300 and GelMA B225 concentrations, (B) as a function of GelMA B300 and PEGDA concentrations, (C) as a function of GelMA B300 and HAMA concentrations, (D) and as a function of GelMA B300 of HAGM concentrations. Only positive Z values were considered.

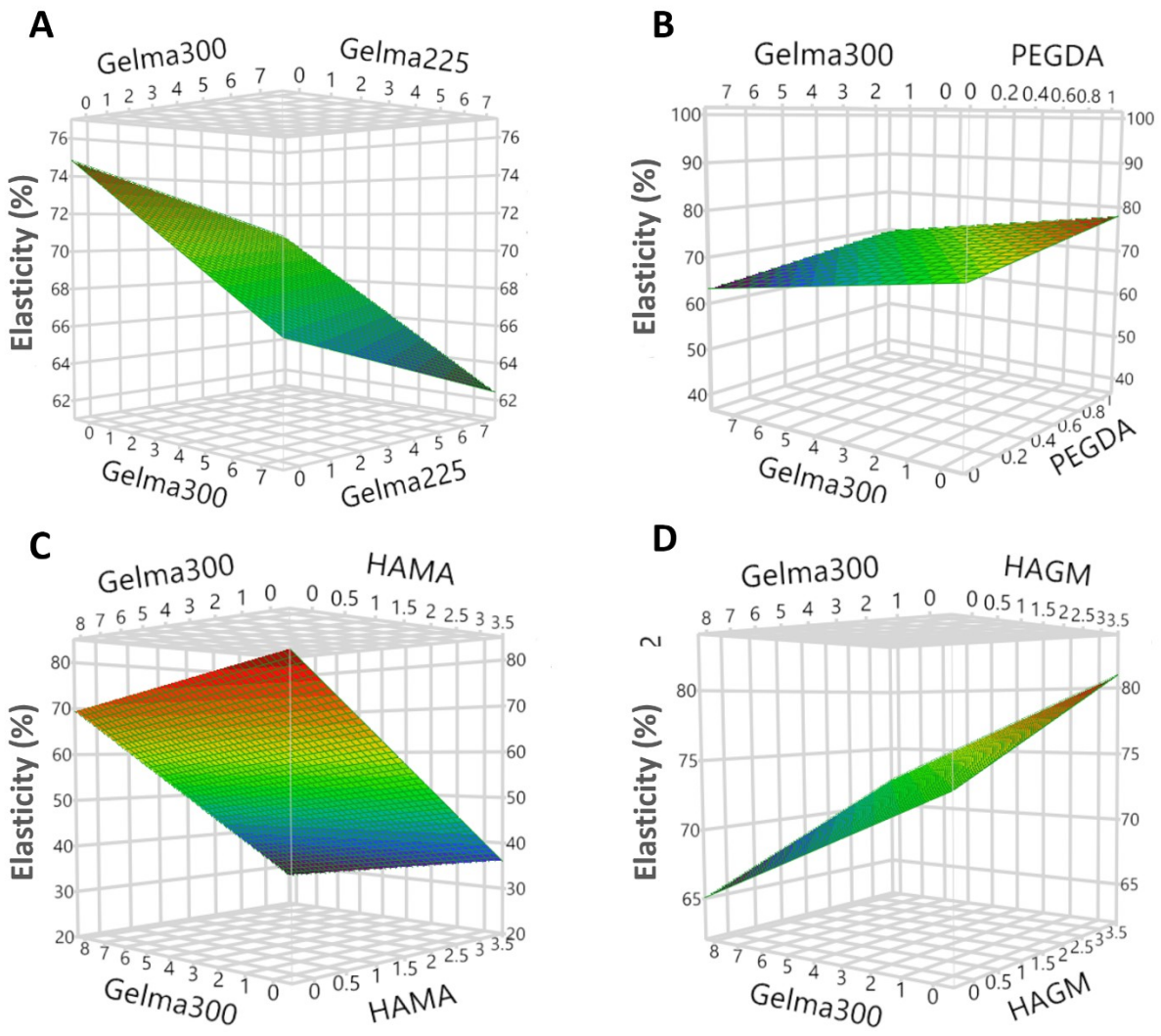

Figure S11. Response surface estimated by definitive screening design (DSD) for elasticity (maximum strain). (A) As a function of GelMA B300 and GelMA B225 concentrations, (B) as a function of GelMA B300 and PEGDA concentrations, (C) as a function of GelMA B300 and HAMA concentrations, and (D) as a function of GelMA B300 of HAGM concentrations. Only positive Z values were considered.

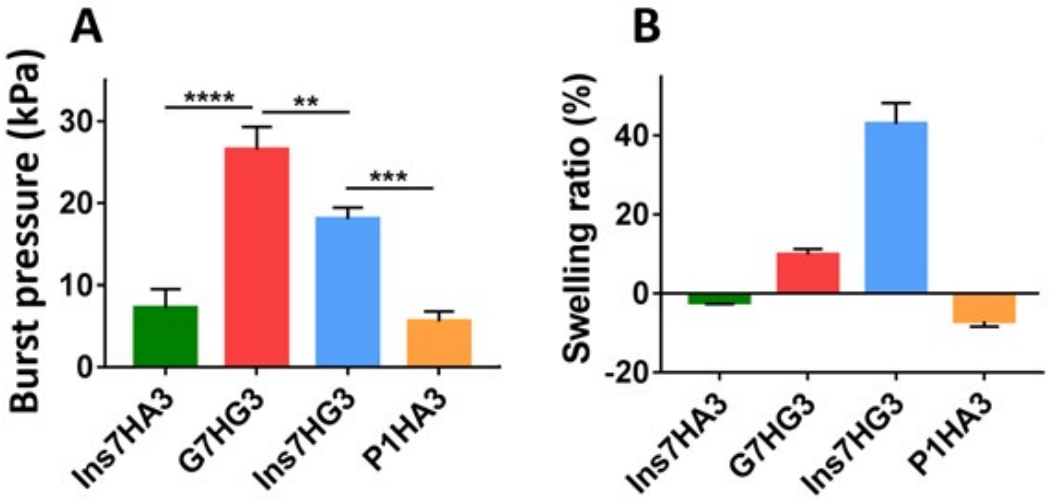

Figure S12. Characterization of GelPatch formulations suggested by augmented design of JMP® software. (A) Burst pressure measured using collagen sheets and **(B)** swelling ratios of various formulations in DPBS at 37°C.

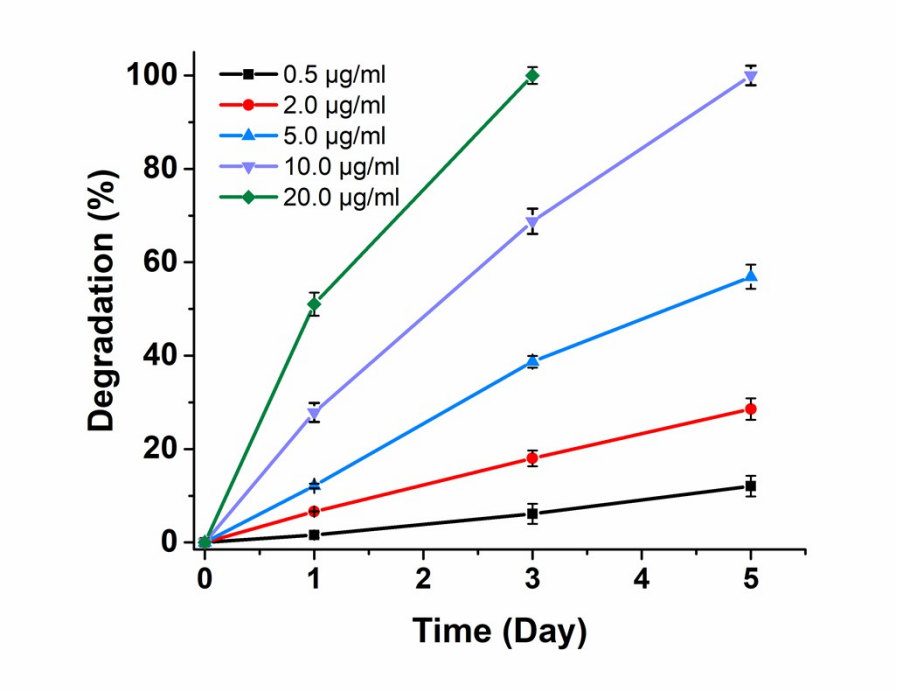

Figure S13. *In vitro* degradation of optimized GelPatch formulation (G7HG3) in the presence of various concentrations of collagenase type II and Hyaluronidase (type I-S) in DPBS and 37°C. Data are represented as mean ± SD, n =3.

Movie S1. (.mp4 format). This movie shows the *ex vivo* adhesion and retention of the optimized GelPatch formulation (G7HG3) to the scleral ocular surface after 4 days of incubation in organ batch.

Movie S2. (.mp4 format). This movie shows *ex vivo* adhesion and retention of the optimized GelPatch formulation (G7HG3) upon subconjunctival injection and crosslinking after 4 days of incubation in organ bath.