Physical and Bioactive Properties of Glycosaminoglycan Hydrogels Modulated by Polymer Design Parameters and Polymer Ratio

Michael Nguyen[1], Julie Liu[2], Alyssa Panitch[1]

[1]University of California, Davis; [2]Purdue University

Background

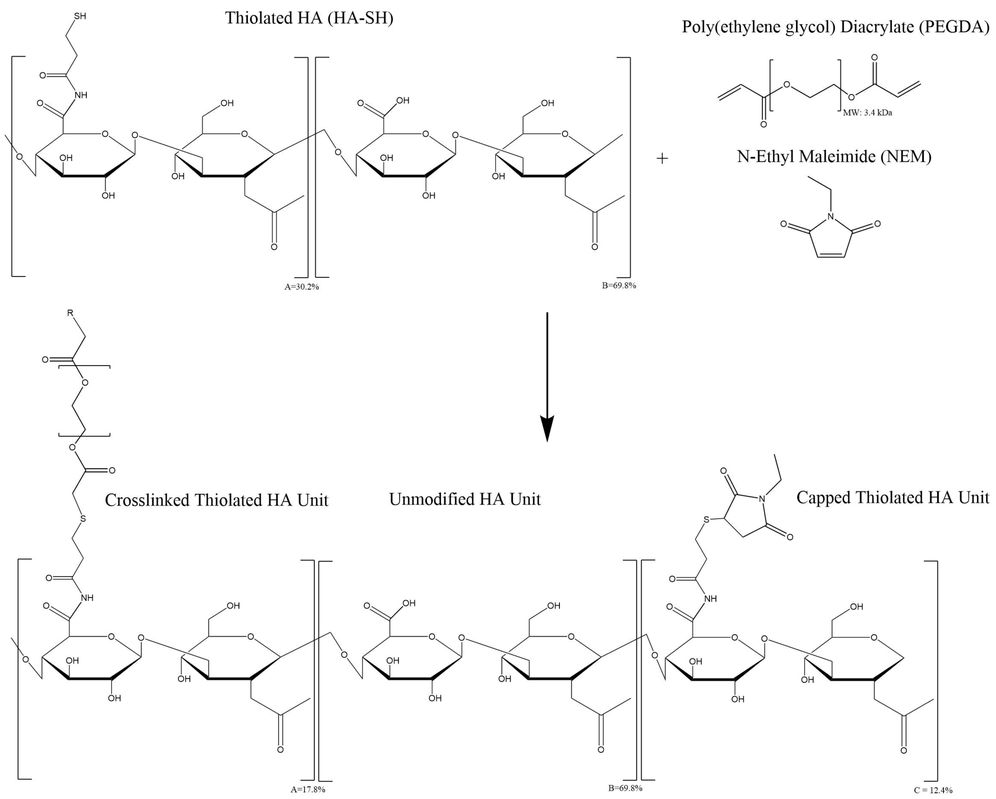
- Glycosaminoglycans, including hyaluronic acid (HA) and chondroitin sulfate (CS) have seen widespread adoption as materials for tissue engineering scaffolds
- Degree of modification of these polymers is not consistent between published studies
- Increased modification can reduce biorecognition and bioactivity of the polymers
- This study investigated the effects of increasing degrees of thiolation (DOT) on the physical and bioactive properties of thiolated HA (HA-SH) and thiolated CS (CS-SH) hydrogels
- The physical and bioactive affects of combining CS-SH and HA-SH into dual polymer network (DPN) hydrogels was also investigated

Materials and Methods

- HA-SH and CS-SH were synthesized using aqueous carbodiimide chemistry with dithio-bis(propionohydrazide) (DTP) providing free thiols
- 1.5 w/v% hydrogels were formed by crosslinking HA-SH and CS-SH with poly(ethylene glycol diacrylate) at varying ratios

Ratio of CS/HA	10:0	7:3	5:5	3:7	0:10
Concentration of CS (w/v%)	1.5	1.05	0.75	0.45	0
Concentration of HA (w/v%)	0	0.45	0.75	1.05	1.5

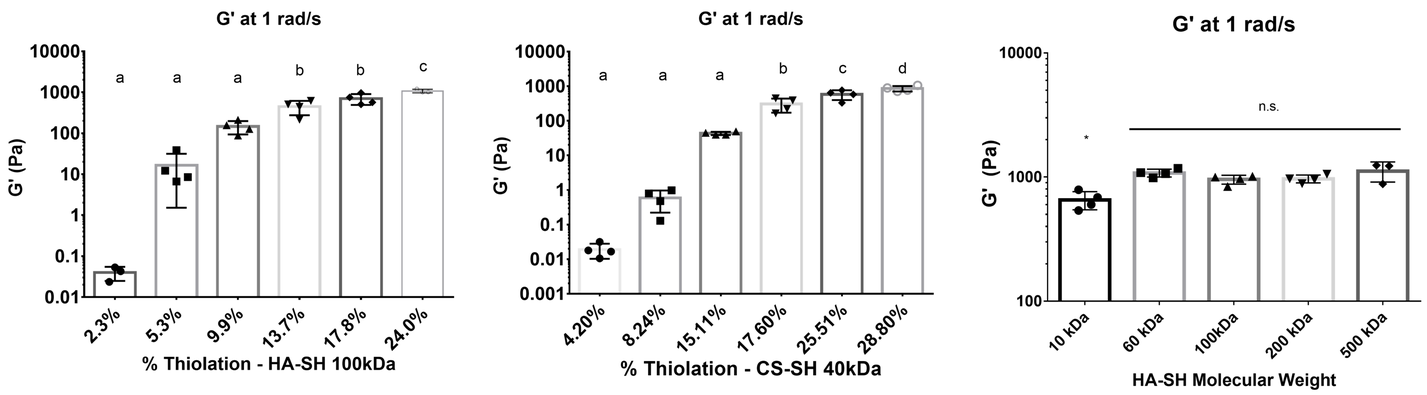
- Gel stiffness, susceptibility to enzymatic degradation, peptide adhesion, and encapsulated cell viability were studied as a function of DOT and GAG ratio
- CS binding peptide YKT and HA binding peptide GAH were used as analogs for protein binding
- Excess thiols were capped with N-ethyl maleimide (NEM) to maintain crosslink density between high (~30%) and low (~17%) DOT hydrogels
- Rabbit mesenchymal stromal cells (MSCs) were used to study cell viability in CS/HA DPN hydrogels



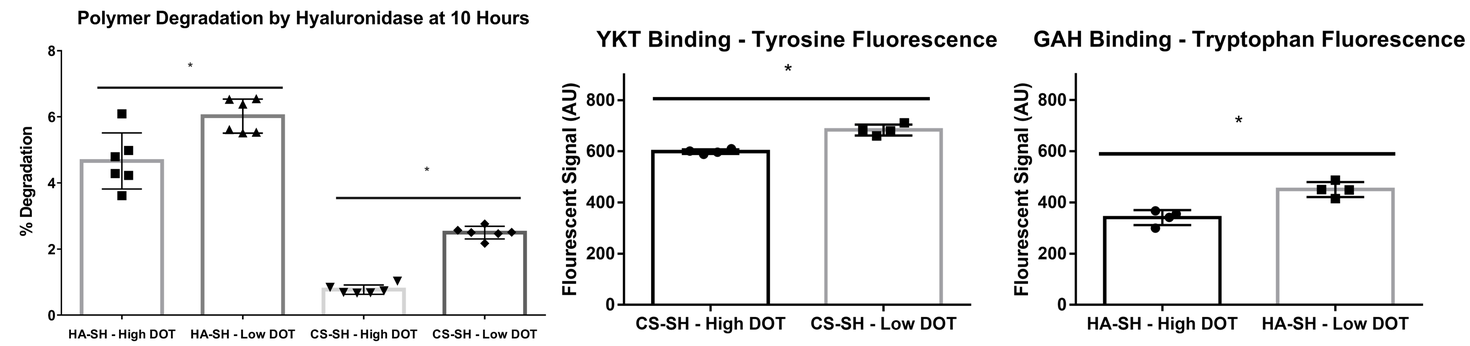
Capping of Free Thiols with NEM

Results

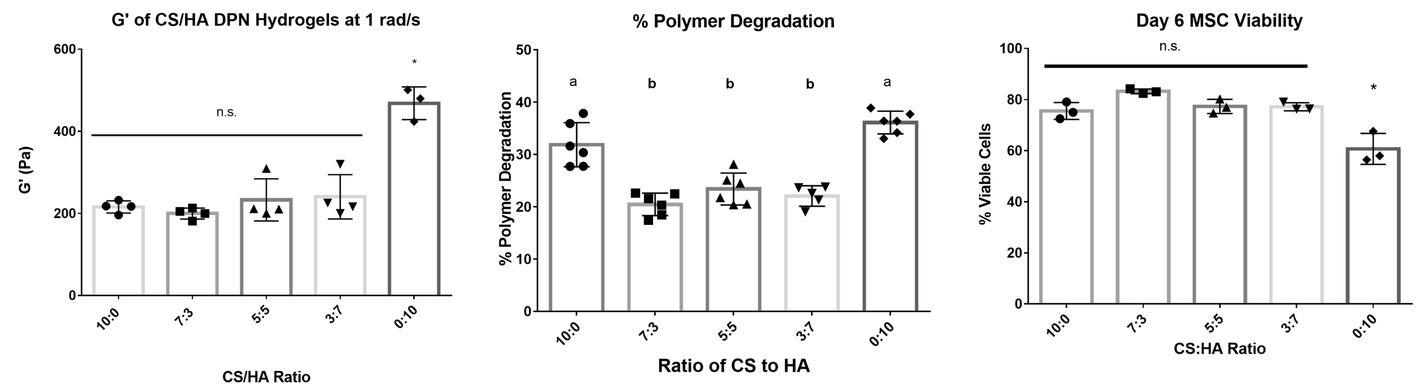
Polymer Parameters Effects on Gel Stiffness

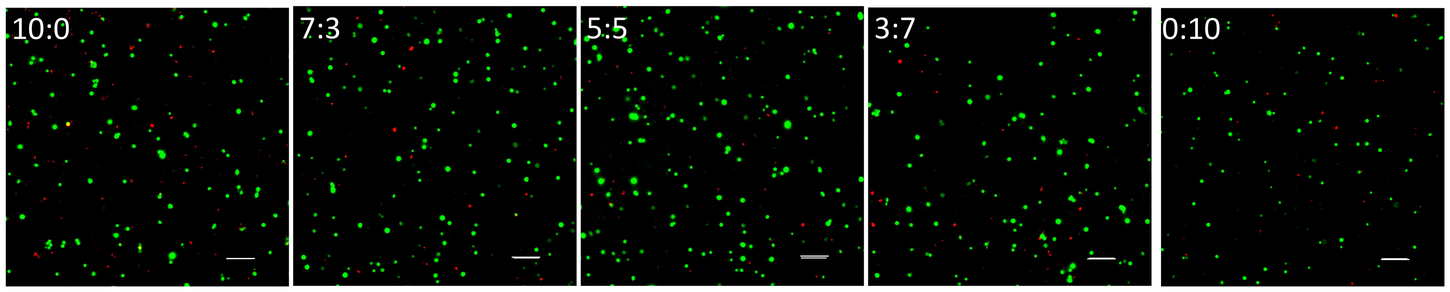


Effect of DOT on Bioactivity



Effects of CS/HA Ratio on DPN Hydrogels





Rabbit MSCs in CS/HA DPN Hydrogels – Live Cells (Green), Dead Cells (Red)

Conclusions

- Increasing the DOT of HA-SH and CS-SH decreases their recognition by hyaluronidase and decreases peptide adhesion to the polymers
- Blending CS-SH and HA-SH into DPN hydrogels modulates hydrogel stiffness and enzymatic degradation rate
- CS-SH presence in hydrogels improves MSC viability

Acknowledgments

We would like to thank the Ripplinger lab at UC Davis for providing the rabbit hind limbs used in this experiment for MSC isolation. This work was funded by the NIH grant T32 HL086350.

UC DAVIS COLLEGE OF ENGINEERING
Biomedical Engineering