DESIGNING BIOMIMETIC MATERIALS FOR BIOMEDICAL APPLICATIONS

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The goal of this work is to design nature-inspired biomimetic materials that recapitulate essential features of tissues for biomedical applications including tissue modeling of drug transport and surgical adhesion.

The first part of this work utilizes collagen and glycosaminoglycans to mimic tissues for preclinical modeling of large-molecule drug transport. We first utilize hydrazone crosslinking chemistry with hyaluronic acid to form interpenetrating networks with collagen at different concentrations. The interpenetrating networks enabled a wide range of mechanical properties, including stiffness and swellability, and microstructures, such as pore morphology and size, that can better recapitulate diverse tissues. The mechanical and microstructural differences translated into differences in transport of the macromolecules of different sizes and charges from these matrices. Large macromolecules were impacted by mesh size, whereas small macromolecules were influenced primarily by electrostatic forces. The tunable properties demonstrated by the collagen and crosslinked hyaluronic acid hydrogels can be used to mimic different tissues for early-stage assays to understand drug transport and its relationship to matrix properties.

We then explore how the glycosaminoglycans hyaluronic acid, chondroitin sulfate, and heparin in collagen hydrogels influence drug transport via glycosaminoglycan-drug interactions and network development. Incorporating different types and concentrations of glycosaminoglycans led to glycosaminoglycan-collagen hydrogels with a range of collagen networks and negative charge densities to recapitulate different tissue compositions. Hyaluronic acid increased the overall viscosity of the hydrogel matrix, and chondroitin sulfate and heparin altered collagen fibrillogenesis. All three GAGs formed concentration-dependent polyelectrolyte complexes with positively charged macromolecules. Transport of positively charged macromolecules through collagen gels with chondroitin sulfate and high concentrations of heparin was inhibited due to complexation and charge effects. Conversely, collagen with low concentrations of heparin hastened the transport of macromolecules due to the limited collagen network resulting from fibrillogenesis inhibition. Overall, the addition of different GAGs into tissue models can better recapitulate native tissue to accurately predict therapeutics transport through a variety of tissues.

The second part of this work investigates the impact of pH and oxidation on an elastin- and mussel-inspired surgical sealant. We combined sodium periodate, an oxidizer, with an L-3,4-dihydroxyphenylalanine-modified elastin-like polypeptide to elucidate how the crosslinking mechanism and intermediate formation impacted adhesion, cure time, and stiffness. Formulations resisted burst pressures greater than physiological internal pressures. They did not swell and had stiffnesses similar to those of soft tissues, and their gelation times varied from seconds to hours. Small increases in the formulation pH led to the formation of α,β-dehydrodopamine intermediates which facilitated the development of multiple crosslinking networks. The mussel-inspired elastin-like adhesive can serve as a model of mussel proteins to further improve our understanding of mussel chemistry. This study exemplifies the importance of pH and oxidation on the performance of mussel-inspired adhesives in surgical sealing within physiological environments.