INJECTABLE HYALURONIC ACID BASED HYDROGELS FOR THE REPAIR OF CARTILAGE LESIONS

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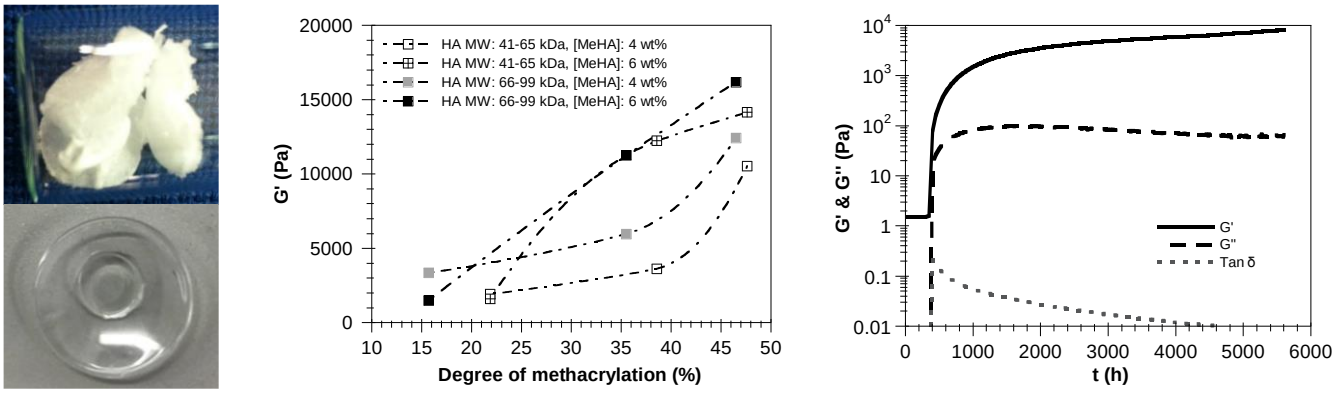
Hyaluronic acid (HA) is a natural polysaccharide which is found natively in cartilage tissue. HA hydrogels are formed by the modification of HA through its carboxyl and hydroxyl groups and subsequent crosslinking. For applications in cartilage repair, it has been found that HA hydrogels not only support and maintain chondrocyte viability and phenotype when cultured in vitro and in vivo, but also that HA hydrogel chemistry supports and promotes the chondrogenic differentiation of mesenchymal stem cells (MSCs). A promising, non-invasive method for the repair of cartilage lesions is based on the use of injectable hydrogels with desirable properties in combination with biomolecules and cells.

In the present study, the synthesis and characterization of injectable HA based hydrogels is assessed. HA is initially modified via reaction with methacrylic anhydride (MA) to methacrylated HA (MeHA) that can be efficiently crosslinked. The effect of HA molecular weight (e.g., 41-65 and 66-99 kDa), anhydride molar excess (e.g., ME: 2, 5 and 10) and type of solvent (e.g., water, water/dimethylformamide) on the degree of methacrylation (DM) is examined. MeHA based hydrogels are subsequently formed using a redox initiator system of ammonium persulfate (APS) and tetramethylethylenediamine (TEMED). The effect of various process parameters (e.g. DM, MeHA concentration, etc) on the final properties of the produced hydrogels (e.g. degree of swelling, storage modulus (G'), degradation rate, etc) is thoroughly assessed. The produced hydrogels are characterized with respect to their gelation kinetics, rheological properties, degree of swelling, and degradation in the presence of hyaluronidase. Additionally, injectable hydrogels are formed using MeHA or MeHA functionalized with a chondroitin sulfate (CS) binding peptide, using a matrix metalloproteinase 7 (MMP7)-degradable peptide, as a crosslinker. Since cells are known to be instructed by the mechanical properties of their matrix, gel stiffness is tuned to favor the chondrogenic differentiation of hMSCs incorporated in the hydrogels. Finally, cell-laden hydrogels will be prepared by dispersing bone marrow derived hMSCs in a solution of MeHA and/or CS-MeHA prior to the crosslinking reaction with the MMP7-sensitive peptide.



a) *b)* *c)*

Figure 10 – a) MeHA and MeHA based hydrogels formed using a redox initiator system (e.g., APS/TEMED) as a crosslinker, b) effect of DM on G' for MeHA based hydrogels formed using APS/TEMED as a crosslinker and c) gelation kinetics of MeHA hydrogel formed using an MMP-7 degradable peptide as a crosslinker.