Proteoglycan mimics: Synthesis of brush glycopolymers via oxime condensation

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Abstract

Proteoglycans (PGs) are one of the main components of the extracellular matrix (ECM) where they play a structural role, serve as reservoirs of proteins secreted by cells (growth factors, chemokines and cytokines), and act as co-factors triggering various cell signaling pathways, including inflammation and coagulation cascades.1-2 Because of their functions, PGs have been proposed as therapeutics for a variety of diseases such as thrombosis, amyloid diseases, arthritis and cancer among others.3 Structurally, PGs consist on a protein core with covalently linked pendant glycosaminoglycan (GAG) chains in a bottle brush fashion. The difficulties in PG isolation have stimulated the development of biomimicking glycopolymers, glycodendrimers and nanoparticles based on carbohydrates attached to synthetic polymers with different architectures.3 Most of the synthetic approaches interfere with GAG bioactivity because of a side-on attachment mode. Herein, we propose an alternative approach in which GAGs are linked to poly(2-hydroxyethyl methacrylate) (pHEMA) by end-on oxime ligation at their reducing end to preserve GAGbioactivity. We demonstrate that this approach is feasible for either hyaluronic acid or chondroitin sulfate: they were successfully linked to the synthetic core as confirmed by 1H NMR and gel permeation chromatography. Moreover, the degree of glycosylation can be tuned; we obtained pHEMA with different substitution degrees. The generated glycopolymers may be used to develop more complex bioactive structures such as extracellular matrix or cartilage mimics.