Towards applying paramagnetic NMR to study the conformation of Heparin/Heparan Sulfate

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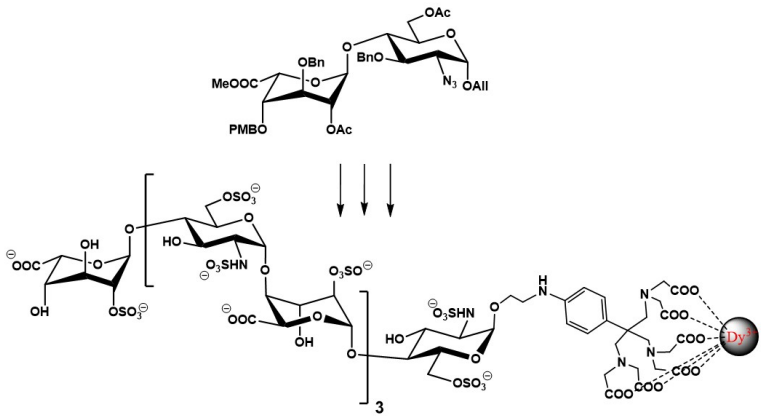
Heparin (HP) and Heparan sulfate (HS) are linear sulfated polysaccharides found in the extracellular enviroment. They are involved in multiple biological functions, such as cell growth and adhesion, virus recognition, and cancer metastasis. These multifaceted biological impacts arise from their molecular diversity, conformational flexibility and sulfatation pattern.

Many HP/HS-protein interactions have been described from affinity-based procedures and X-ray crystallography. Moreover, different approaches have been employed to assess their conformations and interactions in solution by NMR. Indeed, it is evident that these molecules display conformational flexibility at different levels, from the L-IdoA residues to their overall shape. Despite fundamental advances, the NMR-based interpretation of their conformational, dynamic, and interactions features remain a challenging process, especially for long saccharides. The intrinsic homogeneity of these chains, which display numerous disaccharide repeating units, makes the full and unambiguous NMR assignment a rather exigent task, even at very high field. We herein propose the use of paramagnetic NMR; in particular, pseudo-contact shifts (PCSs), to elucidate the conformation and interactions of these molecules. On this basis, a new synthetic approach has been developed to conjugate the target HP/HS to a paramagnetic probe, which allows measuring PCS. These results expand the applications of paramagnetic NMR to chemically synthetized HP/HS and pave the way for further analysis of their interactions with proteins.



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