NMR Studies and Molecular Modelling of Chondroitin Sulfate Oligosaccharides

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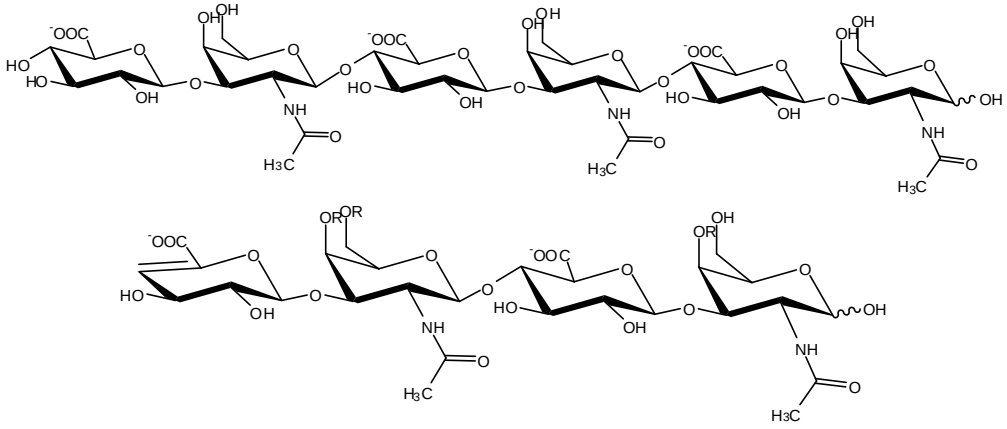
The chondroitin sulphate is an anionic linear polysaccharide largely diffused in connective tissues, in skin and in blood vessels, where it plays structural roles but also takes part to biological processes, like the development of arteriosclerosis plaques[1]. It belongs to the glycosaminoglycans family, and it is characterized by a disaccharidic repeating unit made up by an uronic acid and an amino-sugar, namely the repeating unit is [→4)-β-D-GlcA-(1→3)-β-D-GalNAc-(1][2]. This disaccharide can be modified by the presence of sulfate groups, that can be found at the 4 and/or 6 of the GalNAc, at the position 2 of the GlcA, and more rarely at the position 3 of the GlcA[3]. The sulfation pattern is largely dependent upon the source and the location in the tissues, leading to a high degree of heterogeneity[2]. Not much is known about conformation of this polysaccharide, but combining computational methods and NMR techniques, it is possible to obtain information about the three-dimensional structure of the molecule.

In this work, we present the results of molecular dynamics calculations performed with Amber 9 in explicit solvent and NMR experiments (TOCSY, NOESY, DOSY), performed on different oligosaccharides of chondroitin sulfate:



R= H, SO_3^-

In order to understand, at atomic level, the involvement of chondroitin sulfate in the development of arteriosclerosis, we are also applying NMR techniques to a study of interaction between the polysaccharide and a peptide belonging to the site B of the LDL protein.

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