CHARACTERIZATION OF THE FORCES RESPONSIBLE FOR IDURONIC ACID CONFORMATIONAL EQUILIBRIUM

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The iduronic acid (IdoA) is one of the major components of heparin. It presents an unusual mobility, adopting an equilibrium between boat and skew-boat conformations, which is proposed to contribute to the unique heparin binding properties. Since the basis for this equilibrium is not well understood, this work aims to characterize, at atomic level, the forces responsible for IdoA flexibility. Accordingly, the glycosidic linkage of heparin disaccharides was described by energy contour plots, fixing IdoA in its possible conformations ($^1C_4$, $^4C_1$ and ^2S_O) and rotating the Φ and Ψ angles from 0° to 360°, in steps of 30°. The so obtained minimum energy conformations were further submitted to a 10ns molecular dynamics simulation using GROMACS simulation suite and force field. The used methodology allowed us to characterize the major conformations of heparin disaccharides in solution. Through analysis of each conformation, a distinct set of intramolecular interactions was observed to occur as a function of IdoA pyranose conformation. Such interactions, mainly hydrogen bonds, were shown to adequately reproduce the occurrence of each IdoA conformation in solution, being the first work to identify, at the atomic level, the forces responsible for IdoA conformational preference. We expect that these informations contribute to the development of new anticoagulant agents based on the mecanism of action of heparin. Supported by CNPq, CAPES and FAPERGS.