1-AMINO-1-DEOXY-LACTITOL-GRAFTED HYALURONIC ACID: STRUCTURAL AND CONFORMATIONAL CHARACTERIZATION BY MULTIPLE MOLECULAR DYNAMIC SIMULATION

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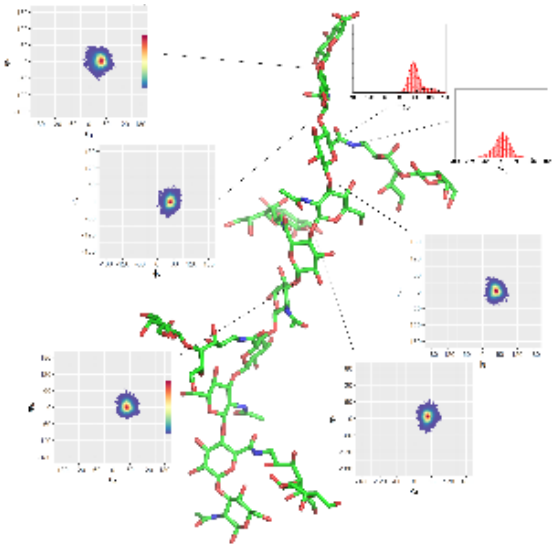
Hyaluronic acid (HA) is a linear non sulfated polysaccharide that is part of the extracellular matrix of animal cells. HA is widely used in cosmetics as an 'anti-age' treatment, combining physical filling, hydration, antioxidant, and degradable capabilities [1]. In addition, HA presents anti-inflammatory properties and modulates cellular activities [2]. Considering these aspects, and the possibility of functionalization with pharmacophores and/or vectorizable groups, HA is a perfect scaffold for drug-delivery polymers. This study focuses on the structural and conformational characterization of the 1-amino-1-deoxy-lactitol-grafted HA in water solution, a new polysaccharide known by the registered name HYLACH® [3], and designed as a broad range therapy for fibrotic disease [4], through the inactivation of galectin-3. In fact, the grafted groups of HYLACH®, that terminate with the β-D-Gal moiety, are known to bind galectin-3. Decasaccharides were constructed *in silico*, repeating the structural units of HA: β(1-3)-D-GlcNAc (1-4) β-D-GlcA and this unit was then grafted with the 1-amino-1-deoxy-lactitol at the carboxyl group of selected GlcA residues, to obtain degrees of grafting (DG) 0%, 50% and 100%. To improve the efficiency of the sampling of the phase space, two independent MD simulations, characterized by different initial backbone conformations, were run for each model. The state-of-the-art GLYCAM06 force field for carbohydrate was used; the 1-amino-1-deoxy-lactitol grafted GlcA residue was parametrized according to preliminary conformational analysis. The backbone conformation, the hydrogen bond network of these oligosaccharides, as well as the size, and conformation of the grafted groups, that are crucial properties for development of these as drug delivery polymers, were investigated. 1-amino-1-deoxy-lactitol grafted HA presents conformation, secondary structure, and hydrogen bond network that slightly but, significantly, differs from that of HA [5] and, furthermore, grafted groups exercise an attractive rather than repulsive force toward the backbone [6].



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