Rational Design And Enzymatic Synthesis Of galactopyranosil β-(1-X)-glucopyranosil β-(1-4)-glucopyranoside As Galectin Ligand.

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Introduction Protein-carbohydrate interactions are involved in a variety of biological processes, and changes in glycosidic patterns are frequently related to important pathologies. Galectins are a family of proteins with at least one carbohydrate recognition domain (CRD) with affinity for β-galactosides. In particular galectin-1 (Gal-1) has been shown to play a major role in tumor development. Therefore, searching for β-galactosides with higher affinity for Gal-1 than its natural ligands has the potential of generating new compounds with antitumor activity. In this context computational and theoretical chemistry are very useful tools for the design of β-galactosides which could interact properly with the CDR of Gal-1. Glycosidases are an excellent alternative in the synthesis of glycosides. Their high stereoselectivity, allows the synthesis of anomerically pure glycosides in only one step under friendly environmentally conditions, which contributes to the green chemistry field.

Objectives Theoretical evaluation of **galactopyranosil-β-(1-X)-glucopyranosil-β-(1-4)-glucopyranoside** as Gal-1 ligand and further enzymatic synthesis using a β-galactosidase transgalactosylation system.

Material and Methods For all computational simulations (MD, conformational searches and docking experiments) we used the Molecular Operating Environment software (MOE. 2011.10). The crystal structures of the galectin-1 used were bovine (pdbID: 1SLT) and human (pdbID: 1GZW). Enzymatic synthesis was performed using *Aspergillus oryzae* β-galactosidase. *o*-nitrophenyl-β-D-galactopyranoside (ONPG) and cellobiose were used as donor and acceptor of galactosyl group respectively.

Results and Discussion We obtained good quality models for both human and bovine galectin-1 and galactopyranosil-β-(1-X)-glucopyranosil-β-(1-4)-glucopyranoside using molecular dynamics and different conformational search approaches. Docking experiments were analyzed, and preliminary results suggest that the trisaccharide could bind to the receptor with high affinity. Experimental results showed the feasibility of the enzymatic synthesis of compound with general structure β-D-galactopiranosyl-β-D-(1-X)-glucopiranosyl-(1-4)-glucopyranose, under employed conditions using cellobiose as galactosil group acceptor.

Conclusions β-D-galactopiranosyl-β-D-(1-X)-glucopiranosyl-(1-4)-glucopiranose can be enzymatically synthesized and constitutes a promising galectin-1 ligand and therefore, a potential galectin inhibitor.

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