**ENZYMATICALLY STABLE GALECTIN INHIBITORS**

Luboš Plamitzer, Miroslav Hájek, Jakub Kaminský, Petr Pachl, Kamil Parkan,   
Marcela Pávová, Radek Pohl

*Institute of Organic Chemistry and Biochemistry of the Czech Academy of Sciences –   
Molecular Spectroscopy Group – Flemingovo náměstí 2, 160 00, Prague, Czechia*

Over the last two decades, human galectins (particularly galectin-1, -3, -7 and -9) have become attractive targets for anti-cancer and anti-inflammatory drug development.   
In addition, galectin-1 enhances the binding affinity of human immunodeficiency virus type-1 (HIV-1) glycoprotein gp120 to host cells and increases viral infectivity [1].

Recently, we have introduced a modular stereoselective synthesis of *C*-disaccharides that is based on sp3-sp2 cross-coupling reactions followed by stereoselective oxidative-reductive transformations [2]. Since lactose and TDG are known scaffolds in preparation of galectin-1 and galectin-3 inhibitors, the initial goal was therefore to prepare their carba-analogues. We have found that CDG (β-d-Gal*p*-*C*-(1🡪1)-β-d-Gal*p*) occupies in free unbound state predominantly one conformation, which is very similar to the conformation of TDG, and therefore perfectly arranged to fit into the binding site of galectin-1. However, the determination of bidding affinity of CDG (*K*d= 416 μM) to galectin-1 by isothermal titration calorimetry showed repeatedly *K*d worse than for lactose (*K*d = 327 μM). Moreover, TDG binds to galectin-1 about 6 times stronger than lactose (*K*d = 57 μM). This difference in binding affinities of CDG and TDG might be therefore attributed to special geometric arrangement in proximity of sulfide bridge.

We have tested prepared glycomimetics in our optimized viral entry assay using LuSIV cells infected with HIV-1 and in red blood cells hemagglutination assay. Both assays show that CDG has comparable effect as TDG. These biochemical and biological findings, together with molecular modeling, will serve as a basis for further synthesis of novel glycomimetics with improved efficiency, stability and bioavailability.

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