

UNEXPECTED BINDING OF FLUORINATED DISACCHARIDES TO WGA

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Fluorinated carbohydrates exhibit improved metabolic stability and higher lipophilicity than natural glycans. However, deoxyfluorination of glycans often results in reduced or abrogated binding affinity to their cognate lectins due to the removal of hydrogen bonds with the binding site. We synthesized the complete series of methyl β -glycosides of *N,N'*-diacetylchitobiose (GlcNAc β 1–4GlcNAc β 1-OMe) and LacdiNAc (GalNAc β 1–4GlcNAc β 1-OMe) systematically monofluorinated at all hydroxyl positions and determined the binding affinity of the fluoroanalogues to wheat germ agglutinin (WGA), a plant defense lectin. For the first time, the binding profile of a previously unexplored WGA ligand LacdiNAc was investigated. Unexpectedly, fluorination at the 4-position of the GalNAc moiety in LacdiNAc resulted in a stronger binder than the unmodified LacdiNAc. Even more surprisingly, fluorination at the 6-position of the non-reducing end GlcNAc moiety in chitobiose increased binding to WGA by an order of magnitude (Figure 1). These results demonstrate that systematic deoxyfluorination of carbohydrate lectin ligands can identify analogues that exceed the binding affinity of unmodified parent oligosaccharides [1].

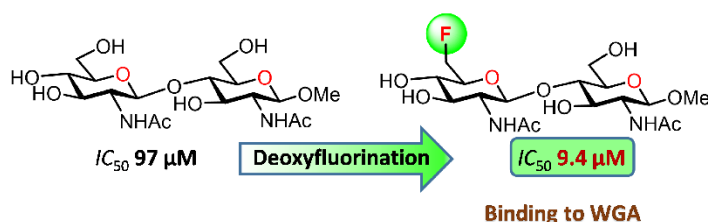


Figure 1. Deoxyfluorination of chitobiose increased binding to WGA

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References:

1. Kurfiřt, M.; Hamala, V.; Beránek, J.; Červenková Šťastná, L.; Červený, J.; Dračínský, M.; Bernášková, J.; Spiwok, V.; Bosáková, Z.; Bojarová, P.; Karban, J., *Bioorg. Chem.* **2024**, *147*, 107395.