LECTIN LIGANDS: FROM MULTIVALENCY TO PHOTOSWITCHING

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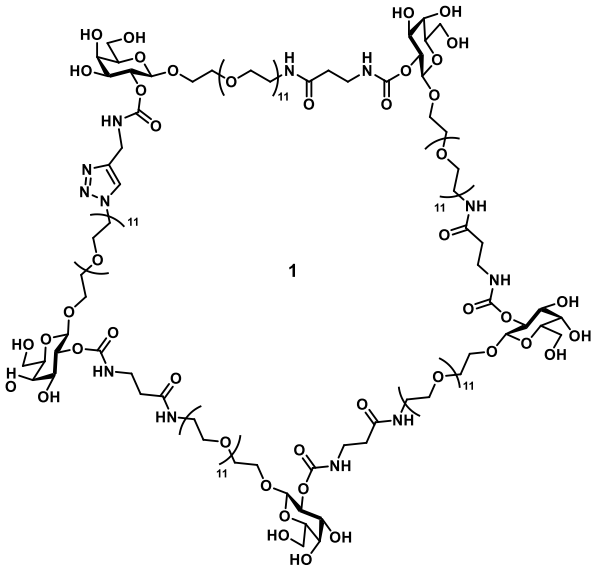
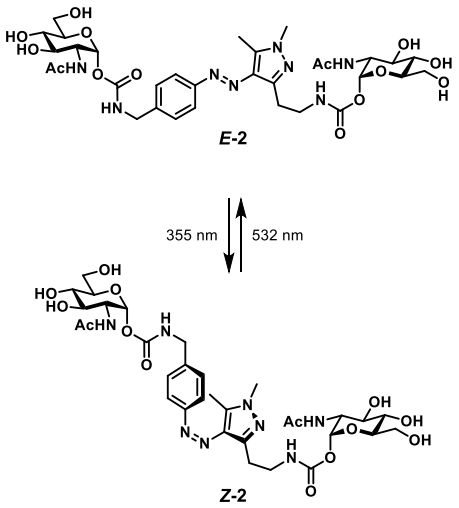
Carbohydrates are involved in a myriad of cellular recognition processes. High-affinity lectin ligands are of high medicinal interest for diagnostic and therapeutic applications. However, the binding affinities between individual carbohydrate epitopes and carbohydrate-binding proteins (lectins) are usually low. Multivalency can drastically enhance binding affinities between the interacting species [1]. In the past, we developed a new design of multivalent lectin ligands, termed inline lectin ligands (iLecs) [2]. iLecs lead to exceptionally high binding affinities without concurrent precipitation of proteins due to crosslinking.
In this communication, I will present recent efforts in the development of iLecs for bacterial AB_5-type toxins. We designed macrocyclic ligand **1** that can bind to five binding site of the B_5-subunit of Shiga toxin simultaneously. Binding affinities were determined with microscale thermophoreses (MST) and showed an increased affinity of the cyclic ligand over its linear precursor.





Furthermore, we developed divalent ligand **2** for the plant lectin wheat germ agglutinin (WGA) that contains an arylazopyrazole photoswitch [3]. The ligand was designed in a way that only the (*E*)-isomer is able to bridge adjacent binding sites of WGA leading to a chelating binding mode. Photoswitching induces an unprecedentedly high change in lectin binding affinity as determined by isothermal titration calorimetry (ITC). Furthermore, we observe a change of the binding mode of the ligand from chelating binding of *E*-**2** to crosslinking binding of *Z*-**2**.

References:
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2. P. Rohse, S. Weickert, M. Drescher, V. Wittmann, *Chem. Sci.* **2020**, *11*, 5227-5237.
3. U. Osswald, J. Boneberg, V. Wittmann, *Chem. Eur. J.* **2022**, *28*, e202200267.