Thermodynamic stabilization of conformations in Lewis Antigens

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The Lewis antigens are a well-known family of fucosylated glycans whose structures were thought to be conformationally inflexible, until recently. In this presentation, we present evidence for conformational flexibility between hydrogen bonded conformations and non-hydrogen bonded ones. We show here that the formation of a C-H→O non-conventional hydrogen bond from the H5 of fucose III or II to the pyranose oxygen of galactose II or III, respectively, in Lewis A, Lewis B, Lewis X and Lewis Y, partially stabilizes a "compact structure" of these antigens. This creates NMR spectral conditions that allowed us to analyze Lewis antigen spectra by using the partial stabilization in NMR lineshape analysis. We analyzed temperature dependent spectra in the aggregate together with slow-exchange chemical shifts obtained from fucose monomer. These analyses led us to determine that the ΔG^{o} values for the hydrogen bonded conformers in the Lewis Antigens studied here, range from -1.5 to -1.0 kcal/mol. Lineshape analysis also yielded rate constants which we used to determine the free energy barriers to breaking these hydrogen bonds.

In Lewis Antigen analogs where a rhamnose residue replaces the fucose, the ΔG^{o} values are comparable to those containing a fucose, suggesting that this type of non-conventional hydrogen bond is general and may be used in design of vaccines or drugs to stabilize or destabilize desired conformations.