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Title	溶液NMR法を用いた糖鎖の構造と水和との連関の解明
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Abstract

Biological functions of carbohydrates are exerted mainly through their interactions with lectins. The hydration as well as the structure of carbohydrates are considered to be important factors for the selectivity and affinity of carbohydrate recognitions. In this study, I elucidated the relationship between hydration and structural characteristics of carbohydrates.

To characterize unique solvation environments according to the geometric characteristics of carbohydrates, I attempted to investigate behaviors both of carbohydrates and waters. By solution NMR analyses and molecular dynamics simulations, in conjunction with chemical synthesis of carbohydrates, it was revealed that carbohydrates modulate their interactions with surrounding water molecules and hydration sphere based on the chemical structure and sequence of carbohydrates. On the other hand, I also found that the hydrophobic interaction between sugar residues is important to regulate the conformation of carbohydrates in solution.

The $^{1}H/^{2}H$ isotope shifts in NMR were applied to study the proton exchanges between carbohydrate and water and between water molecules. To focus on the differences in sequence and linking type, three compounds, GLC1-3MAN, MAN'1-3MAN, and MAN'1-2MAN, were synthesized and analyzed by NMR using H_2O/D_2O mixed solvents. NMR measurements to focus on the carbohydrate hydroxy groups revealed that the carbohydrate–water proton exchange in GLC1-3MAN solution proceeded slower than in the others. Meanwhile, the frequent proton exchange between waters in GLC1-3MAN solution was shown by NMR observations of water signals. The results suggested that GLC1-3MAN promotes water structuring more efficiently than the others. Furthermore, bridging water molecules between the hydroxy groups were identified prominently in GLC1-3MAN by molecular simulations. These results indicate that the presence of water molecules strongly bound to carbohydrates by cross-linking their hydroxy groups is a key factor for the expansion of water networks.

To examine the effect of water on carbohydrates in solution, I also observed the conformational changes of Lewis X (Gal1-4(Fuc1-3)GlcNAc) in water and methanol, as a model carbohydrate. The NMR analyses of synthetic Lewis X carbohydrates revealed that a conformation of Lewis X is stabilized by water and the conformation changes in methanol with increase of the GlcNAc ring puckering. It was suggested that hydrophobic interactions between the Gal and Fuc residues are important for the conformational control of Lewis X.

Based on solution NMR spectroscopy, I established a methodology that approaches the carbohydrate hydrations from both the carbohydrate and water aspects. I succeeded to reveal both the effects of carbohydrate structure on water and the effects of water on carbohydrate structures. This study will promote the understanding of the functioning mechanisms of carbohydrates in aqueous solution. It is also expected that the findings contribute to the development of applicable carbohydrate materials including new drugs and biomarkers.

Keyword: NMR, Carbohydrate, Hydration, Structure, H/D isotope shifts