学 位 論 文 内 容 の 要 旨

博士（環境科学）　　氏 名 韓 彬（Bin Han）

学 位 論 文 題 名

Studies on synthesis and characterization of cyclodextrin-based glyco-clusters
（シクロデキストリンを基盤とした糖鎖クラスターの合成と特性評価に関する研究）

Lectin is a carbohydrate-binding protein. In a variety of everyday biological phenomena, carbohydrate-lectin recognition is a very important process. Oligosaccharides are now known to mediate cell-cell recognition, it could influence physiological phenomena and activities which could be happening at every moment such as the moderation of enzymes and other proteins, the various functions in the immune response, and the infection of cells by bacteria and viruses. Cell-surface lectins plays as a vital role in the process of intercellular recognition due to its specific recognition ability to corresponsive carbohydrate groups. In addition, carbohydrate moieties which attached to membrane glycoproteins and glycolipids constitute the potential recognition sites for carbohydrate-mediated interactions between cells and drug molecule carriers bearing targeting ligands. Taken the specific recognition ability of part carbohydrate compounds to cell-surface lectins into consideration, some representative carbohydrates could be hypothesized as ideal targeting ligands in the construction of molecular vehicle for bioactive compounds, which should be confirmed by biological evaluation.

As stated in chapter 1, the D-mannose, maltose and melibiose that could be obtained from natural environment easily were selected as starting materials to prepare cyclodextrin-based glyco-clusters. The three kinds of cyclodextrin-based glyco-clusters could be regarded as potential host molecular model due to the specific binding abilities of α-mannosyl, α-glucosyl and α-galactosyl residues to lectins. It is significant to study the lectin recognition abilities of these cyclodextrin-based glyco-clusters, but firstly the research on inclusion abilities should be necessary.

In chapter 2, the Man-CD was successfully obtained by slightly modified Cu-mediated “click reaction” and characterized by ^{1}H and 2D NMR spectrum. The illustration for its detailed peak assignment is significant and will be useful to the inclusion application of Man-CD. Meanwhile, the Mal-CD and Meli-CD were also prepared by using Cu-mediated “click reaction” and characterized by brief ^{1}H NMR spectrum temporarily. As

it is stated, the study on inclusion behavior of Man-CD, Mal-CD and Meli-CD is necessary with the consideration of multi-substituted groups and complicated space distribution.

In chapter 3, the ibuprofen sodium salt (IBUNa) was selected as an ideal guest molecular model in the research on inclusion properties of cyclodextrin-based glyco-clusters, with the consideration of its molecular properties and mature application. The inclusion properties of glyco-clusters were studied by using NMR spectrum to calculate the stoichiometry and associate constants (Ks) values for inclusion complexes. Experimental results showed that β-CD/IBUNa, Man-CD/IBUNa, Mal-CD/IBUNa and Meli-CD/IBUNa inclusion complexes are all 1:1 inclusion stoichiometry. The Ks values were evaluated by curve fitting of proton chemical shift changes of IBUNa, showed the $0.87 \times 10^4\ M^{-1}$ (β-CD/IBUNa), $2.9 \times 10^4\ M^{-1}$ (Man-CD/IBUNa), $0.64 \times 10^4\ M^{-1}$ (Mal-CD/IBUNa) and $1.9 \times 10^4\ M^{-1}$ (Meli-CD/IBUNa) respectively.

In chapter 4, the inclusion conformations of β-CD/IBUNa and Man-CD/IBUNa complexes were deduced through the 2D ROESY and NOESY spectra. Interestingly, the β-CD/IBUNa complex has two potential inclusion modes but the Man-CD/IBUNa has only one potential inclusion mode, indicating that the substituted sugar groups may have an influence on the inclusion behavior.

Three kinds of cyclodextrin-based glyco-clusters were prepared by Cu-mediated “click reaction”, the detailed procedure fulfilled will be useful to the construction of other kinds of sugar-clusters. Detailed information about NMR peak assignments of Man-CD was illustrated temporarily, and detailed peak assignments of Mal-CD and Meli-CD are still in processing. The inclusion abilities of Man-CD, Mal-CD and Meli-CD were studied by NMR method and compared, showed the 1:1 inclusion stoichiometry and different associate constants (Ks) values for IBUNa. The inclusion abilities of cyclodextrin-based glyco-clusters were confirmed, these findings would be useful for designing new drug delivery system when considerate the combination with biological evaluation such as lectin recognition ability.