Glycomics & Lipidomics

Extended Abstract

EDesign, synthesis and characterization of glycolipids and glycoclusters

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Abstract

Glycolipids and glycoclusters that are able to form self-assembled supramolecular structures are interesting compounds with potential applications as new materials for biomedical research. Our group has a long interest in the design, synthesis and study of various monosaccharide derivatives and we have discovered several new classes of glycolipids based low molecular weight gelators (LMWGs). These compounds form unique soft materials such as organogels or hydrogels that may be useful in biomedical research. They can be used as advanced functional materials for controlled release drug delivery and enzyme immobilization. Using naproxen as a model, we have shown that acid sensitive glucosamine derivatives are effective compounds for controlled release bof naproxen from the gel matrix. By incorporating photosensitive functional groups, we have also synthesized and characterized polymerizable diacetylene containing organogels. The resulting polydiacetylenes gels are useful as stimuli-responsive soft materials. Besides these systems, several branched molecules with sugar moieties at the periphery have also been designed and synthesized. These compounds have accurate molecular weight and can form interesting molecular assemblies. The dendritic glycolipids have shown enhanced self-assembling tendencies which mimic the multi-valency effect. In this presentation, our recent studies on bglycolipids that can form supramolecular gels and self-assembling glycoconjugates will be discussed.

A novel glycolipid featuring a glucosylglycerate moiety as a polar head group was synthesized in two steps from sucrose, glycerate, and N-dodecylamine. Glucosylglyceric acid was formed from sucrose and glyceric acid using sucrose synthase as a catalyst, followed by condensation with N-dodecylamine using 4-(4,6-dimethoxy-1,3,5-triazin-2-yl)-4-methylmorpholinium chloride (DMT-MM) as a condensing agent. A white solid compound was recovered with a yield of 21% after purification by hydrophobic column chromatography. The structure and purity of the isolated compound, identified as N-dodecyl glucosylglyceric acid amide (aGGA), were confirmed by 1H and 13C nuclear magnetic resonance and liquid chromatography-electrospray ionization-mass spectrometry. aGGA was soluble in several polar solvents, including acetone, dimethyl formamide, and short chain alcohols. The dissolution of aGGA in water reduced the surface tension to 27.8 mN m-1 at a critical micellar concentration of 1.57 × 10-4 M. In addition, the presence of aGGA at concentrations as low at 0.68 mM protected egg white from heat-induced denaturation. These results suggest that aGGA could be useful as a protein-protecting surfactant.

The structure of a new glycolipid isolated from the acetone-soluble lipids of the strain of Nocardia caviae has been determined. The water-soluble moiety contains one mole of D-glucose and one mole of D(-)-glyceric acid; the lipid moiety is a mixture of myristic, palmitic and stearic acids with small amounts of oleic acid. The structure of the deacylated compound was determined by periodate oxidation, methylation and enzymatic degradation. The localization of fatty acid residues at 2',3' on glucose was established by methylation and mass spectrometry. The structure was confirmed by 13C NMR spectrometry of the glycolipid and of the deacylated compound. This glycolipid is a 2'.3'-di-O-acyl-alpha-D-glucopyranosyl-(1 leads to 2)-D-(-)-glyceric acid.

A glycolipid was found in a strain of Nocardia caviae. It consists of glucose, myristic, palmitic and stearic acids and a polyhydroxylated acid. The structure of this hydroxyacid was demonstrated by the identification of the product glycerol after LiA1H4 reduction of the glycolipid methyl ester and subsequent hydrolysis, by comparison of the infrared spectra of the hydroxyacid and glyceric acid, by gas chromatography of acetylated methyl and ethyl esters of the polyhydroxylated acid and of standard glyceric acid and by mass spectrometry of the diacetylated methyl ester. The hydroxyacid from the glycolipid is D(-)glyceric acid, a compound rarely found amongst natural products.

Three classes of glycolipids (TMM (trehalose monomycolate), TDM (trehalose dimycolate) and GM (glucose mycolate] containing mycolic acids as hydrophobic components were isolated from a strain of Nocardia rubra (Rhodococcus rubrum) and their structures have been partially characterized using infrared spectrometry, gas-liquid chromatography and gas chromatography-mass spectrometry. Acid or alkaline hydrolysis of isolated glycolipids revealed that trehalose was the sole water soluble component in TMM and TDM, while glucose was the hydrophilic component in GM. On the other hand, saturated, monoenoic and dienoic mycolic acids with carbon atoms ranging from C36 to C50 contained constituents of fatty acid moiety at C44. From the analytical results, TMM, TDM and GM were tentatively identified as trehalose monomycolate, trehalose dimycolate and glucose monomycolate, respectively. The mycolic acid composition differed significantly by the glycolipid classes: the highest

amount of saturated mycolic acids were detected in TMM and GM, while a significant amount of dienoic mycolic acids have been found in TDM and the cell wall bound lipid fraction (BL). All these three classes of glycolipids containing mycolic acids showed strong granuloma forming activity in lungs and spleen of ICR mice 1 week after intravenous injection of 100 to 500 micrograms glycolipid in W/O/W micelles containing Freund's incomplete adjuvant.

These results indicated that glycolipids containing shorter carbon chain mycolic acids ranging C40-50, corresponding to less acyl numbers or monosaccharides such as glucose, can also produce foreign body-type granuloma in mice without protein antigens.

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