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Copper-Catalyzed Azide–Alkyne Cycloaddition in the Synthesis of Polydiacetylene: "Click Glycoliposome" as Biosensors for the Specific Detection of Lectins

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Abstract: Supramolecular self-assembly of conjugated diacetylenic amphiphile-tethered ligands photopolymerize to afford polydiacetylene (PDA) functional liposomes. Upon specific interaction with a variety of biological analytes in aqueous solution, PDA exhibits rapid colorimetric transitions. The PDA nanoassemblies, which are excellent membrane mimics, include an ene–yne polymeric reporter responsible for the chromatic transitions and the molecular recognition elements that are responsible for selective and specific binding to the biological target. A bottleneck in the fabrication of these colorimetric biosensors is the preparation of the diacetylenic monomer embedded with the recognition element of choice. In the present work, we make use of copper-catalyzed azide–alkyne cycloaddition (CuAAC) as key step in the preparation of sugar-coated liposome biosensors. The regioselective click ligation of the triacetylenic *N*-(2-propynyl)pentacosa-10,12-diynamide (NPPCDAM) with a variety of mannose- and lactose-tethered azides afforded chemo- and regioselectively the corresponding 1,2,3-triazole. The obtained diacetylenic monomers were incorporated efficiently into vesicles to afford functional mannose- and lactose-coated glycoliposomes. The obtained PDA-based click glycoliposomes have been characterized by using transmission electronic microscopy (TEM), dynamic light scattering (DLS), and UV/Vis spectroscopy. The efficiency of the reported approach was demonstrated by the rapid optimization of the hydrophilic spacer between the lipidic matrix and the mannose head group for the colorimetric detection of Concavalin A.

Keywords: biosensors · carbohydrates · click chemistry · lectins · polydiacetylene

Introduction

Living cell membrane is the paradigmatic example of a highly evolved self-assembled nanostructure that combines molecular-recognition elements and signal-transduction functions.[1] In most eukaryotic and prokaryotic cells, the extracellular part of the membrane is covered by a dense layer of glycolipids, glycoproteins, and proteglycans named glycocalyx. After decades spent assigning the glycocalyx a simple role of safeguarding the cells against foreign attacks, recent investigations have confirmed the prime role of carbohydrates in critical biological events including cell adhesion, inflammation, tumor cell metastasis, and pathogen infection.[2] Interestingly, it has been demonstrated that the weak interaction between individual glycoligand and the corresponding lectin (on the millimolar range) is compensated by multivalent display of sugar epitopes through the so-called cluster effect.[3] Thus synthetic model systems able to emulate the densely glycosylated membrane are of great interest in glycobiology to assist in the study of carbohydrate functions and to interfere with native binding events.[4] In this sense, tridimensional liposomes and vesicles, which are considered to be similar to the first cells on earth, are excellent membrane mimics.[5] Among the tridimensional liposomes developed so far, those based on glycosylated polydiacetylene (PDA) are by far the most advanced synthetic membrane mimics.[6] Within these supramolecular assemblies, the

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