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Cyclodextrin-based supramolecular architectures: Syntheses, structures, and applications for drug and gene delivery ☆

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Abstract

The supramolecular structures formed between cyclodextrins (CDs) and polymers have inspired interesting developments of novel supramolecular biomaterials. This review will update the recent progress in studies on supramolecular structures based on CDs and block copolymers, followed by the design and synthesis of CD-based supramolecular hydrogels and biodegradable polyrotaxanes for potential controlled drug delivery, and CD-containing cationic polymers and cationic polyrotaxanes for gene delivery. Supramolecular hydrogels based on the self-assembly of the inclusion complexes between CDs with biodegradable block copolymers could be used as promising injectable drug delivery systems for sustained controlled release of macromolecular drugs. Biodegradable polyrotaxanes with drug-conjugated CDs threaded on a polymer chain with degradable end-caps could be interesting supramolecular prodrugs for controlled and targeting delivery of drugs. CD-containing cationic polymers as gene carriers showed reduced cytotoxicity than non-CD-containing polymer counterparts. More importantly, the polyplexes of CD-containing cationic polymers with DNA could be pegylated through a supramolecular process using inclusion complexation between the CD moieties and a modified PEO. Finally, new cationic polyrotaxanes composed of multiple oligoethylenimine-grafted CDs threaded and end-capped on a block copolymer chain were designed and synthesized as a new class of polymeric gene delivery vectors, where the chain-interlocked cationic cyclic units formed an integrated supramolecular entity to function as a macromolecular gene vector. The development of the supramolecular biomaterials through inclusion complexation has opened up a new approach for designing novel drug and gene delivery systems, which may have many advantages over the systems based on the conventional polymeric materials.

Keywords: Cyclodextrin; Polymers; Supramolecular structures; Inclusion complex; Polypseudorotaxane; Polyrotaxane; Hydrogels; Cationic polymers; Drug delivery; Gene delivery

Contents

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1. Introduction

A supramolecule is a system of two or more molecular entities held together and organized by means of inter-molecular non-covalent binding interactions [1]. The studies on supramolecular structures involving macrocycles have been a fascinating research area because they not only serve as models for understanding natural supramolecular self-assembly and molecular recognition, but also provide precursors for designing novel nanomaterials for electronics, and biomedical and pharmaceutical applications [2–11].

Cyclodextrins (CDs) are a series of natural cyclic oligosaccharides composed of 6, 7, or 8 D(+)-glucose units linked by α-1,4-linkages, and named α-, β-, or γ-CD, respectively (Fig. 1A). The geometry of CDs gives a hydrophobic inner cavity having a depth of ca. 7.0 Å, and an internal diameter of

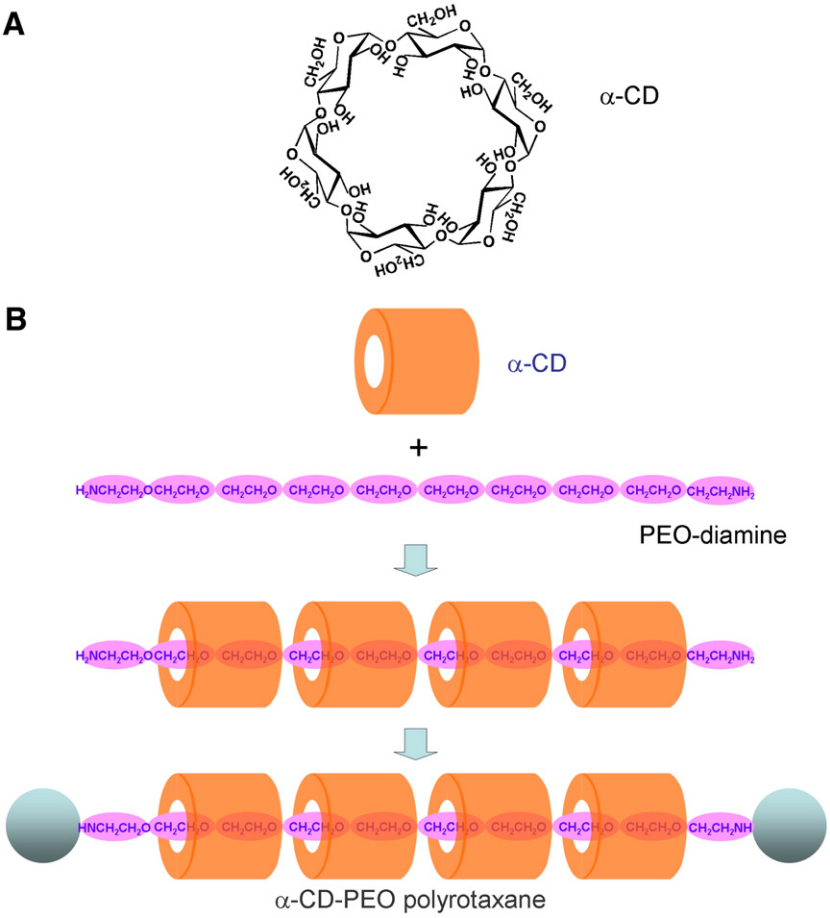

Fig. 1. (A) Structure of α-CD; (B) the synthesis of polyrotaxane from α-CD and PEO-diamine.