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A synthetic encapsulating emulsifier using complex-forming pentacosadiynoyl cyclosophoraoses (cyclic β-(1, 2)-D-glucan)

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ABSTRACT

A new pentacosadiynoyl cyclosophoraose (P-Cys) was synthesized using a biosourced cyclooligosaccharide with intrinsic complexation capacity. NOESY analysis revealed that switchable molecular behavior of pentacosadiynoyl moiety attached to P-Cys was dependent on the external lipophilicity. Both encapsulation by cyclosophoraose and switchable emulsification by pentacosadiynoyl moiety in P-Cys make it possible to finely formulate a nanoemulsion state for an external hydrophobic guest molecule like Sudan III. Various physicochemical properties of the emulsions of P-Cys were investigated using TEM and DLS. The results indicate that P-Cys is a useful potential platform for the encapsulating emulsification of bioactive molecules for cosmetic and pharmaceutical applications.

Introduction

Emulsions have been widely used in diverse applications of food, pharmaceutical, petrochemical, and cosmetic industries [1–4]. They are thermodynamically metastable two-phase systems composed of at least two immiscible liquids. To facilitate the formation of emulsions or stabilize them, emulsifiers are required. Due to the amphiphilic character, the emulsifier is positioned at the oil surface, where the hydrophilic head-group is directed to the aqueous phase and hydrophobic tail to the oil phase. By reducing the interfacial tension at the oil surface, the emulsifiers can stabilize the emulsion. Further, the emulsifier enhances the bioavailability of encapsulated active molecules by controlling their interactions with biomolecules, cells, or tissues [5,6]. Thus, the development of appropriate emulsifiers is regarded as one of the key aspects in fabricating dispersion or emulsion systems. Although some anionic and non-ionic surfactants show toxic effects on aquatic environment as well as skin irritation [7–9], alkyl polyglucosides (APG), sugar esters, and cyclodextrins (CDs) have been of interest as eco-friendly carbohydrate-based emulsifiers [10–12].

Since triple-bonded unsaturated fatty acids are known to be chemically inert and non-metabolized under physiological condition, they are potential compounds in redox-modulated cellular systems by using pi electrons [13,14]. In addition, diacetylenes are believed to be pharmacologically active constituents in ginseng roots [15]. As an unsaturated fatty acid, 10,12-pentacosadiynoic acid (PCDA) has a diacetylene group, and the lipid construct could be utilized for the encapsulation of cosmetic active molecules such as hydrophobic organic UV filters, dyes, and vitamins [16]. Based on its colloidal stability and biocompatible surface, a poly (ethylene)glycol-PCDA conjugate has also been reported to encapsulate effective component [17,18]. However, emulsion systems containing organic acids with triple bonds have not yet been reported up to date.

Cyclosophoraoses (Cys) are unbranched cyclic β-(1,2)-D-glucans containing 17–23 glucose residues, and produced by *Rhizobium* and *Agrobacterium* species both intracellularly and extracellularly [19]. In particular, it is noted that Cys are involved in

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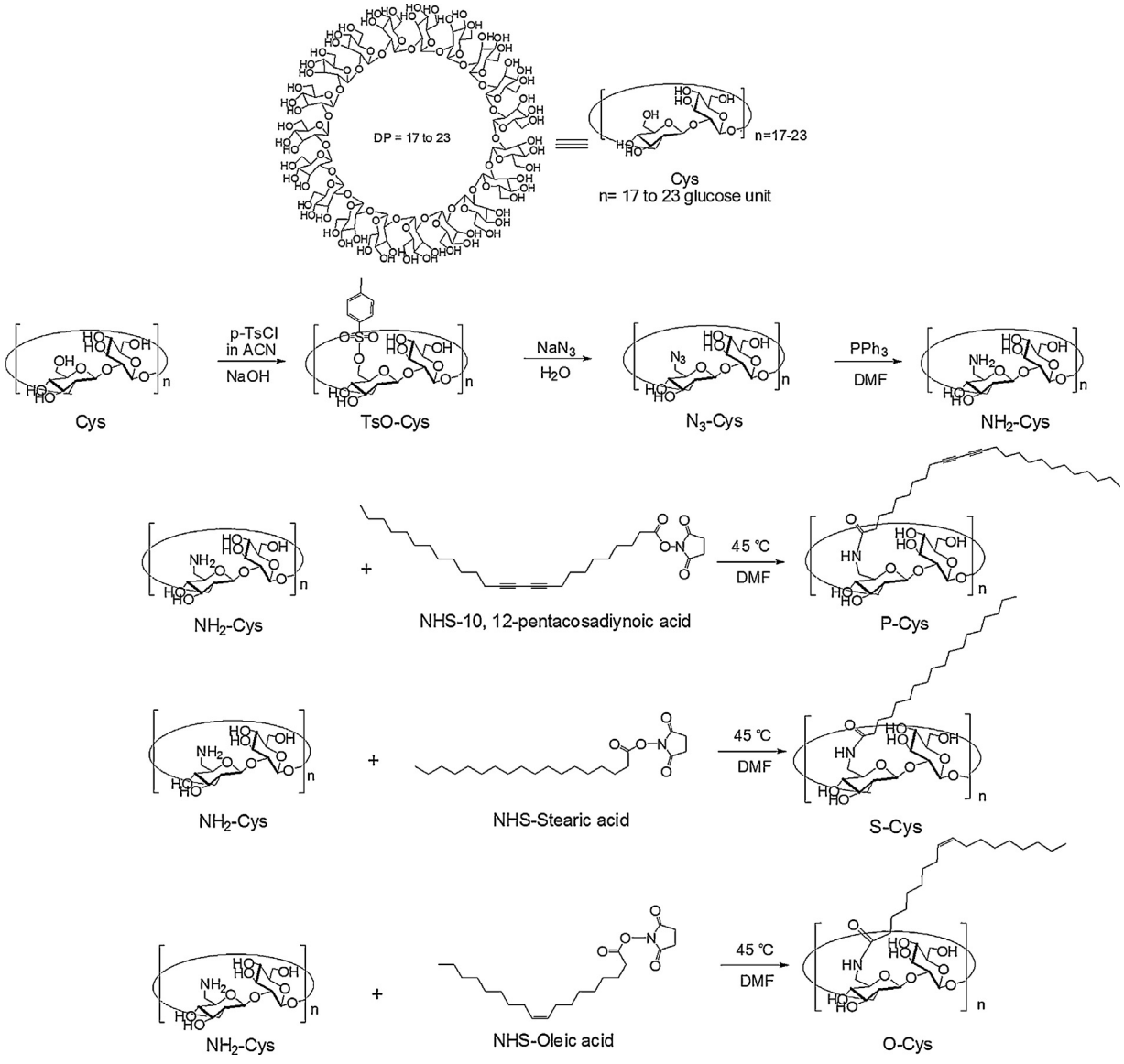
molecular complexation with various plant flavonoids in the symbiotic interaction with plant legumes [20]. Since then, the complexation ability of Cys has been steadily reported with targeting of the non-polar chemicals such as ergosterol, luteolin, vitamin D3 and naproxen [21–24]. Although the accurate three-dimensional structure of Cys is not accessible, the conformational studies support its flexible backbone structure with doughnut-like ring shape [25]. Based on the characteristic conformation, the induced-fit type complexation with hydrophobic molecules is also proposed differently from the well-known macrocyclic host molecule, β-cyclodextrin (β-CD) [26]. As a cyclic α-1,4 linked heptasaccharide, β-CD has relatively rigid structure with the perfect circular cavity, and also been reported to have inclusion complexation behavior [27–29]. This complexing ability of both Cys and CDs can provide some advantages such as protection against light and oxidation, solubilization, improvement in handling, and stability for the effective component in a dispersed system [21,30,31]. Furthermore, the complexing ability of those host molecules can be combined with the interaction of the conjugated hydrophobic tail, where the emulsification and encapsulation are differentiated depending on the host structures.

In the present study, we synthesized pentacosadiynoyl cyclosophoraoses (P-Cys) for the first time by reacting synthetic mono-6-amino-6-deoxy-cyclosophoraoses (NH_2-Cys) with the NHS ester of 10,12-pentacosadiynoic acid (NHS-PCDA) in *N*,*N*-dimethylformamide (DMF), as shown in Scheme 1. Then, the structure and physicochemical properties of the amphiphilic P-Cys molecules were analyzed by matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF/MS), one- and two-dimensional nuclear magnetic resonance (1D, 2D NMR) spectroscopy, transmission electron microscopy (TEM), and dynamic light scattering (DLS). The effective encapsulation of liphophilic substance using sudan III as a model guest molecule was also analysed using NMR and fluorescence spectroscopy.

Experimental

Materials

Oleic acid (*cis*-9-octadecenoic acid) was purchased from TCI (Tokyo Chemical Industry Co., Ltd., Tokyo, Japan). NHS was obtained from Fluka (Sigma–Aldrich Chemical Co., St. Louis, MO,



Scheme 1. Synthesis and structures of fatty amide Cys derivatives.

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