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Versatility of cyclodextrins in self-assembly systems of amphiphiles

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ABSTRACT

Recently, cyclodextrins (CDs) were found to play important yet complicated (or even apparently opposite sometimes) roles in self-assembly systems of amphiphiles or surfactants. Herein, we try to review and clarify the versatility of CDs in surfactant assembly systems by 1) classifying the roles played by CDs into two groups (modulator and building unit) and four subgroups (destructive and constructive modulators, amphiphilic and unamphiphilic building units), 2) comparing these subgroups, and 3) analyzing mechanisms. As a modulator, although CDs by themselves do not participate into the final surfactant aggregates, they can greatly affect the aggregates in two ways. In most cases CDs will destroy the aggregates by depleting surfactant molecules from the aggregates (destructive), or in certain cases CDs can promote the aggregates to grow by selectively removing the less-aggregatable surfactant molecules from the aggregates (constructive). As an amphiphilic building unit, CDs can be chemically (by chemical bonds) or physically (by host–guest interaction) attached to a hydrophobic moiety, and the resultant compounds act as classic amphiphiles. As an unamphiphilic building unit, CD/surfactant complexes or even CDs on their own can assemble into aggregates in an unconventional, unamphiphilic manner driven by CD–CD H-bonds. Moreover, special emphasis is put on two recently appeared aspects: the constructive modulator and unamphiphilic building unit.

Contents

1. Introduction

Amphiphiles (or surfactants) are molecules that consists hydrophobic and hydrophilic moieties. They can self assemble in solution into

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structurally well-defined aggregates, as governed by a delicate balance between different noncovalent interactions, in particular hydrophobic and solvation interactions [1,2]. Not only is the self-assembly of amphiphiles ubiquitous in chemistry, materials science, industry, and commerce, but also does it provide a path towards ordered, functional assemblies, which might ultimately lead to intellectual organisms [3–5]. Construction and modulation of self-assembly therefore receives constant attention, for which many approaches have been developed ranging from molecular modification and additive introduction to stimuli responses [6–9]. Alternatively, cyclodextrins (CDs) may provide a host–guest approach to construct and modulate self-assembly.

CDs are donutlike oligosaccharides with hydrophobic cavities and hydrophilic outer surface, which can form inclusion complexes with most surfactants in high binding constants [10–15]. Loads of work has demonstrated that CDs can play important roles in surfactant or surfactant-based assembly systems with many applications such as viscoelasticity control [16–21], DNA decompaction [22–25], and protein reconstruction [26–28]. The roles played by CDs are, however, complicated and different (or even contradictory) from case to case. For example, it was generally accepted that CDs can destruct aggregates like surfactant micelles [29,30] or surfactant/polymer gel network [16], whereas it was recently revealed that CDs are able to transform mixed surfactant micelles into vesicles [31,32]. Moreover, the exterior of CDs (abundant with OH groups) was normally thought to be hydrophilic to dissolve CD/surfactant complexes into water or to maintain the solvation of CD based aggregates, but the OH-abundant exterior was found in recent reports to act as a "self-philic" moiety to drive the self-assembly of CD/surfactant complexes or even of the CDs themselves [33–44].

In this review, we attempt to elucidate the versatility and complexity of CDs in surfactant assembly systems according to the following vein. Sections 2 and 3 will briefly discuss some basic aspects of CDs and CD/surfactant complexes, with implication on the versatility of CDs. Sections 4 to 7, being the main contents of this review, will classify the roles played by CDs into two groups (modulator and building unit) and four subgroups (destructive and constructive modulators, amphiphilic and unamphiphilic building units) and will give in-depth comparison and analysis. At last, Section 8 would draw a conclusion and give a perspective.

2. Molecular structures of CDs

CDs consist of identical α-D-glucopyranose units, the C1 to C6 of which are marked in Fig. 1. These units are linked by α-1,4 glycosidic bonds to form a circle. The circle is shaped as a hollow, truncated cone rather than a perfect cylinder due to the chair conformation of the glucopyranose units. The bigger edge of the cone is usually called "head", while the smaller edge "tail". CD's secondary hydroxyl groups (C2-OH and C3-OH) locate at the head, whereas CD's primary hydroxyl groups (C6-OH) at the tail. Most commonly used CDs include natural α-, β- and γ-CD with six, seven, and eight glucopyranose units, respectively, as well as their hydroxypropyl and methylated derivatives (HPCDs and MCDs).

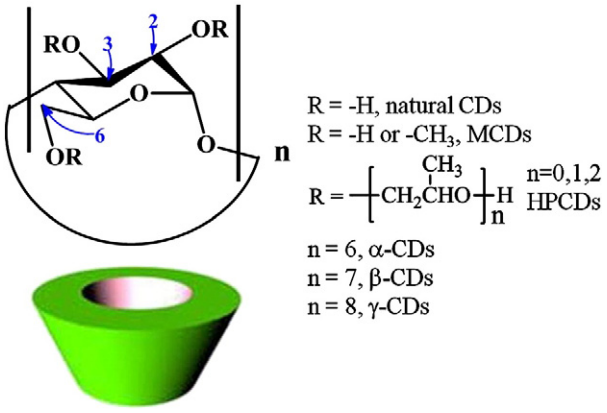

Fig. 1. Molecular structures of CD, HPCD, and MCD.

The central cavity of CDs is lined by the skeletal carbons and ethereal oxygens of the glucose residues, which makes it much less hydrophilic than the aqueous environment. The polarity of the cavity was estimated to be similar to that of a water/ethanol mixture, a somewhat hydrophobic environment. On the other hand, the hydroxyl groups of sugar residue at edges of the CD cone, giving a hydrophilic exterior. The hydrophobic potential map of α-CD is profiled in a very intuitive and informative way in Fig. 2 (calculated by Lichtenthaler et al. using a MOLCAD program [45,46]). It can be clearly seen that the cavity is hydrophobic while the exterior is hydrophilic (yet the tail is less hydrophilic). The hydrophobicity of the cavity enables the accommodation of a broad range of hydrophobic guests like alkyl chains of surfactants. The hosting ability of CDs is a key point for us to understand the behavior of CDs in CD/surfactant systems. The hydrophilic exterior usually imparts CDs and their complexes considerable solubility in water.

Although the OH groups on the exterior, in most cases, form H-bonds with water to dissolve the CDs or CD complexes (solvation), they can, in some situations, form CD–CD H-bonds to induce aggregation and even precipitation (self-assembly) [33–44]. For example, relatively strong CD–CD H-bonding in the crystal state was identified and was thought to be responsible for the limited aqueous solubility of natural CDs (in particular β-CD) in comparison to that of the comparable acyclic oligosaccharides. Substitution of any of the H-bond forming OH groups, even by relatively hydrophobic methoxy functions, will result in dramatic improvement of aqueous solubility. As will be shown, depending on the kind of H-bonds, the outer surface of CDs can be either hydrophilic (CD–water H-bonds, maintaining solvation, Sections 4 to 6) or "self-philic" (CD–CD H-bonds, driving self-assembly, Section 7).

3. Basics of CD/surfactant complexes

3.1. Thermodynamics

CDs are able to form host–guest complexes with most surfactants in 1:1 (denoted as surfactant@CD) or 2:1 (denoted as surfactant@2CD) stoichiometries with high binding constants by including surfactant's hydrophobic tails into CD cavities [47–74]. Fig. 3 lists the molecular structures and abbreviations of some common surfactants. The driving forces for CD/surfactant complex formation include, primarily, release of enthalpy-rich water molecules from the cavity (i.e. water molecules that cannot have a full complement of hydrogen bonds), van der Waals interactions, and hydrophobic interactions, as well as secondarily, hydrogen bonds, electrostatic interactions, release of conformational and steric strain, etc. The thermodynamic quantities for CD/surfactant complexation are, strictly speaking, a consequence of the weighted contributions of these interactions, which is, however, hard to handle in practice. Therefore, the size-match concept (a simple and effective concept that anticipates the highest binding constants for the best size-matching host–guest pairs) were more often used to explain and predict the thermodynamic quantities. The following discussion will demonstrate that the rather straightforward idea of size match does provide us a useful qualitative frame to understand the thermodynamic data.

1) For surfactant homologues, the binding constant increases substantially with the increase of tail length (Fig. 4, with data from [12,29,52,66,74]) because the CD cavity is more likely to be fully occupied by the longer tails. This increase, however, is much less pronounced for hydrocarbon chain longer than 14 carbons, probably because the CD cavity is "saturated" by the C14 chain.