Available online at www.sciencedirect.com

ScienceDirect

Current Opinion in
Colloid & Interface Science

Recent advances in assemblies of cyclodextrins and amphiphiles: construction and regulation

Kaerdun Liu, Cheng Ma, Tongyue Wu, Weilin Qi, Yun Yan and Jianbin Huang

Abstract

Cyclodextrins (CDs) had been regarded as destructors in molecular assembly systems for a long time until CD/surfactants were found to assemble into high order structure driven by hydrogen bonding between CDs. Thereafter, intensive researches have been conducted on construction and regulation of CD–amphiphile systems. Here, we summarized the recent progress on construction and regulation of CDs and amphiphiles assembly. The scope of amphiphiles have been extended from surfactants (ionic surfactants, zwitterion surfactants, nonionic surfactants, gemini surfactant, and so on), to nontypical amphiphiles (amines, aromatic molecules, alkanes, and so on). Owing to the abundant choices of guest amphiphiles and dynamic nature of host–guest inclusive interaction, numerous regulation methods (such as enzyme, light, pH, concentration, temperature, and so on) have been used in CD–amphiphile systems. Moreover, remarks and future perspectives are also discussed at the end of this review, which is expected to stimulate progress on both mechanism and application level.

Addresses

Beijing National Laboratory for Molecular Sciences (BNLMS), State Key Laboratory for Structural Chemistry of Unstable and Stable Species, College of Chemistry and Molecular Engineering, Peking University, Beijing, 100871, PR China

Corresponding author: Huang, Jianbin (jbhuang@pku.edu.cn)

Current Opinion in Colloid & Interface Science 2020, **45**:44–56

This reviews comes from a themed issue on **Surfactants**

Edited by **Romain Bordes** and **Yilin Wang**

For a complete overview see the Issue and the Editorial

https://doi.org/10.1016/j.cocis.2019.11.007

Keywords

Cyclodextrins, Amphiphiles, Non-typical amphiphiles, Regulation, Light, Enzyme.

Introduction

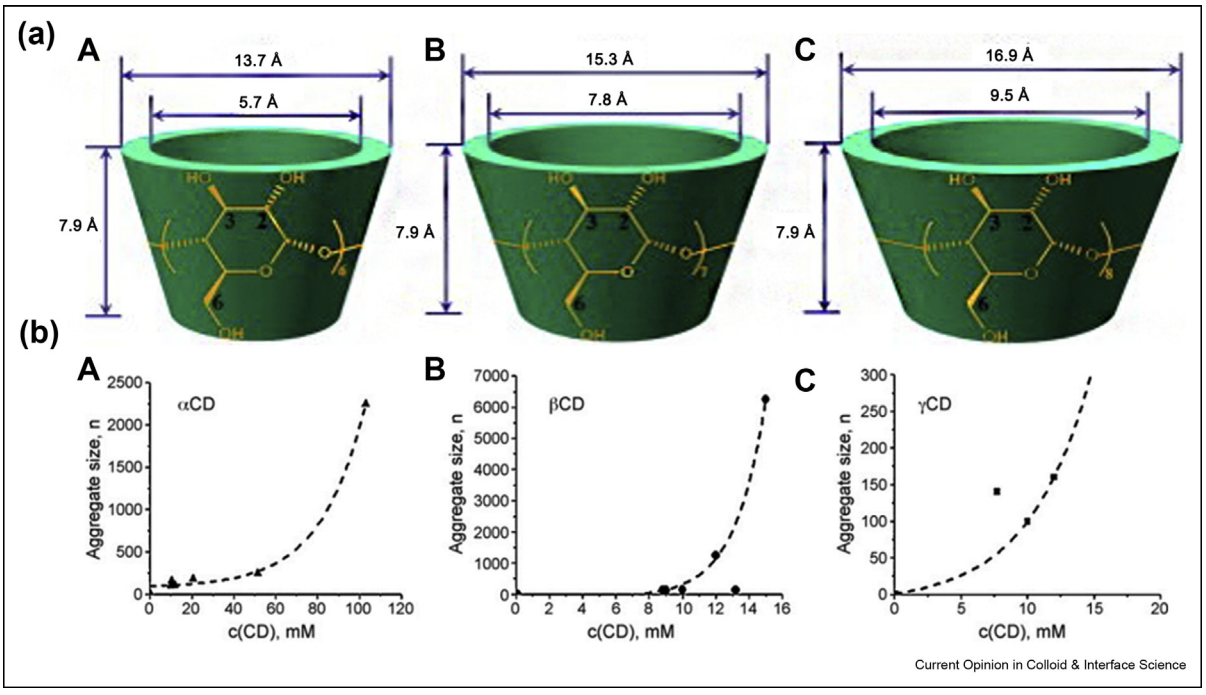
Cyclodextrins (CDs) are cyclic oligosaccharides produced by enzymatic degradation of one of the most essential polysaccharides, starch. Since the first discovery in 1891, CDs have drawn intensive attention. And applications of CDs have been found in almost all sectors of industry, especially pharmacy, food, chemistry, chromatography, catalysis, biotechnology, agriculture, cosmetics, hygiene, medicine, textiles, and environment [1].

The uniqueness of CDs comes from its cage structure. Most commonly used CDs include natural α, β, and γ-CDs with six, seven, and eight α-D-glucopyranose units, respectively, which are linked by α-1,4 glycosidic bonds to form a ring (Figure 1 (a)). CD has a hollow, truncated cone appearance, and a donut, toroidal-like shape. The outer side of the toroid is hydrophilic because of the hydroxyl groups of the glucopyranose units, while the central cavity of CDs is lined by skeletal carbons and ethereal oxygens of glucose residues, which makes it much less hydrophilic than the aqueous environment. Thus, the hydrophobicity of cavity enables the favorable inclusion of hydrophobic parts of guest molecules (mainly amphiphiles) in a process known as host–guest assembly to form inclusive complex [2].

The assemblies from CD–amphiphile–inclusive complexes received intensive attention because of several advantages. Firstly, CDs, as natural products from starch, endow CD–amphiphile assemblies with high biocompatibility. Moreover, the CDs–amphiphiles–inclusive complexes have crystalline structure, representing clear mechanism during assembly. Therefore, it is appealing to fabricate CD–amphiphile assemblies with high biocompatibility and clear mechanism. However, from a historical view, CDs were firstly regarded as destructor for assemblies because the hydroxyl groups (-OH) on the exterior of CD–amphiphile–inclusive complexes would improve the solubility of complex, meaning no high order structure will appear.

To obtain high-order assembly structure from CD–amphiphile complexes, two strategies were used. First strategy is to chemically modify CDs by introducing hydrophobic groups, which may reduce the biocompatibility of natural CDs. Second one is to thread CDs on high molecular weight polymers [4], where the crystalline property of CD–amphiphile complexes is usually absent. It was still a challenge to fabricate high-order assembly structures from natural CDs and small

Figure 1



Structure and aggregation of CDs. (a) Molecular structures and dimensions of various CDs: (A) α-CD; (B) β-CD; and (C) γ-CD. **(b)** Average size of native CDs aggregates versus CD concentration obtained by light scattering. (n is the number of molecules) [3]. CD, cyclodextrin.

amphiphiles until Jiang et al. [5,6] reported a pioneering research on assembly of β-CDs and surfactant sodium dodecyl sulfate (SDS) in 2010.

The key conceptual advances are hydrogen bonds between CDs, which can be the driving force to fabricate high-order assembly structure from inclusive complex. It has been known for some time that natural CDs are able to self-assemble into aggregates because of hydrogen bonds between CDs [3,7]. As shown in Figure 1 (b), α/β/γ-CD can assemble into aggregates, while the largest aggregates are observed from β-CD assemblies [8]. The driving force for native CDs to aggregate is CD−CD hydrogen bond. However, native CD aggregates do not have well-ordered structure and tunable properties of regulation, which can be provided by assemblies with amphiphiles. Therefore, the general hierarchical assembly process leading to high order structure from CDs and amphiphiles can be described as following: firstly, the formation of inclusive complex occurs driven by host−guest interactions, then the inclusive complex can further assemble into high-order assembly structure driven by hydrogen bonding on the exterior of inclusive complex.

Since the report of SDS−β-CDs assembly in 2010 [5,6], numerous research studies have been conducted to explore the construction of assemblies from CDs and amphiphiles, to extend the scope of amphiphiles from typical surfactants to nontypical amphiphiles, and to regulate CD−amphiphile assemblies upon stimuli including light, pH, enzyme, and so on.

There were already some reviews covering the modulator role of CDs in amphiphile assembly [9,10]. In this review, we want to summarize the recent advances on construction and regulation in assemblies of CDs and amphiphiles. Construction of CDs and amphiphiles assembly will mainly cover the construction of CD−amphiphile assemblies. Regulation of CD and amphiphile assembly will emphasize the regulation of assemblies of CDs and amphiphiles. Remarks and perspectives is the remarks and perspective.

Construction of CDs and amphiphiles assembly

Assembly of CDs and polymers

We first briefly review the assembly of CDs and amphiphilic polymers, since researchers used polymer to thread CDs before CD−CD hydrogen bonding was used. Native CDs can directly assemble onto polymer chains to form so-called poly (pseudo)rotaxane [11−13]. The resulting assembly is reminiscent of beads on a string. Early work on poly (pseudo)rotaxane started with threading multiple CDs onto poly (ethylene glycol)

(PEG) polymer chains to create crystalline inclusion complex [4]. Besides PEG polymer, alkyl chain can also serve as linear line to thread α-CDs [14]. The chemical structure of polymers can be varied to alter material properties of poly (pseudo)rotaxane, especially the structure and sequence of the threading polymer [15–17]. Apart from synthetic polymers, biological polymers can also assemble with CDs. For example, CD can serve as an important and promising method to control the assembly behavior of DNA [18,19].

Shortly thereafter, polymer–CD polyrotaxanes were used to create hydrogels. It should be noted that polymer–CD hydrogels did not form initially upon threading and were dependent on self-association of α-CDs through hydrogen bonding to form physical cross-links between the linear poly (pseudo)rotaxane chains [20–22]. These research studies illustrate the importance of CD–CD hydrogen bonds in formation of high-order assembly structures.

In brief, polymers can form inclusive complex with CDs and thread CDs on polymer chain. Although CDs on polymer with high molecular weight can be obtained, the assembly mechanism is usually uncertain, (for example, the diversity of polymer mass and the number of threaded CDs are not accurate during assembly) and CDs are not driving components during assembly. Still, some researches have shown importance and possibility to directly use hydrogen bonding between CDs to fabricate high order structures.

Assembly of CDs and surfactants

Learning the importance of hydrogen bonding between CDs, Jiang et al. [5,6] reported breaking through assembly of β-CDs and surfactant SDS in 2010 driving by strong hydrogen bonding between β-CD–SDS–inclusive complexes. Thereafter, plenty assembly examples with detailed mechanism between CDs and surfactants were reported.

Surfactants are classic amphiphiles containing both hydrophobic groups and hydrophilic groups. Usually, the hydrophobic groups of surfactants can be incorporated into CDs, leading to CD–surfactant inclusion complex [2]. Then CD–surfactant complex as a building block can further assemble into various high order structures driven by hydrogen bond between CDs. This two-step hierarchical assembly process is universal for many types of surfactants. In this assembly process, the structure of surfactants will determine the association strength and ratio with CDs, and hydrogen bonding and other interactions (such as electrostatic interaction between charged group on anionic or cationic surfactants) will determine the crystalline assembly of CD–surfactant complexes.

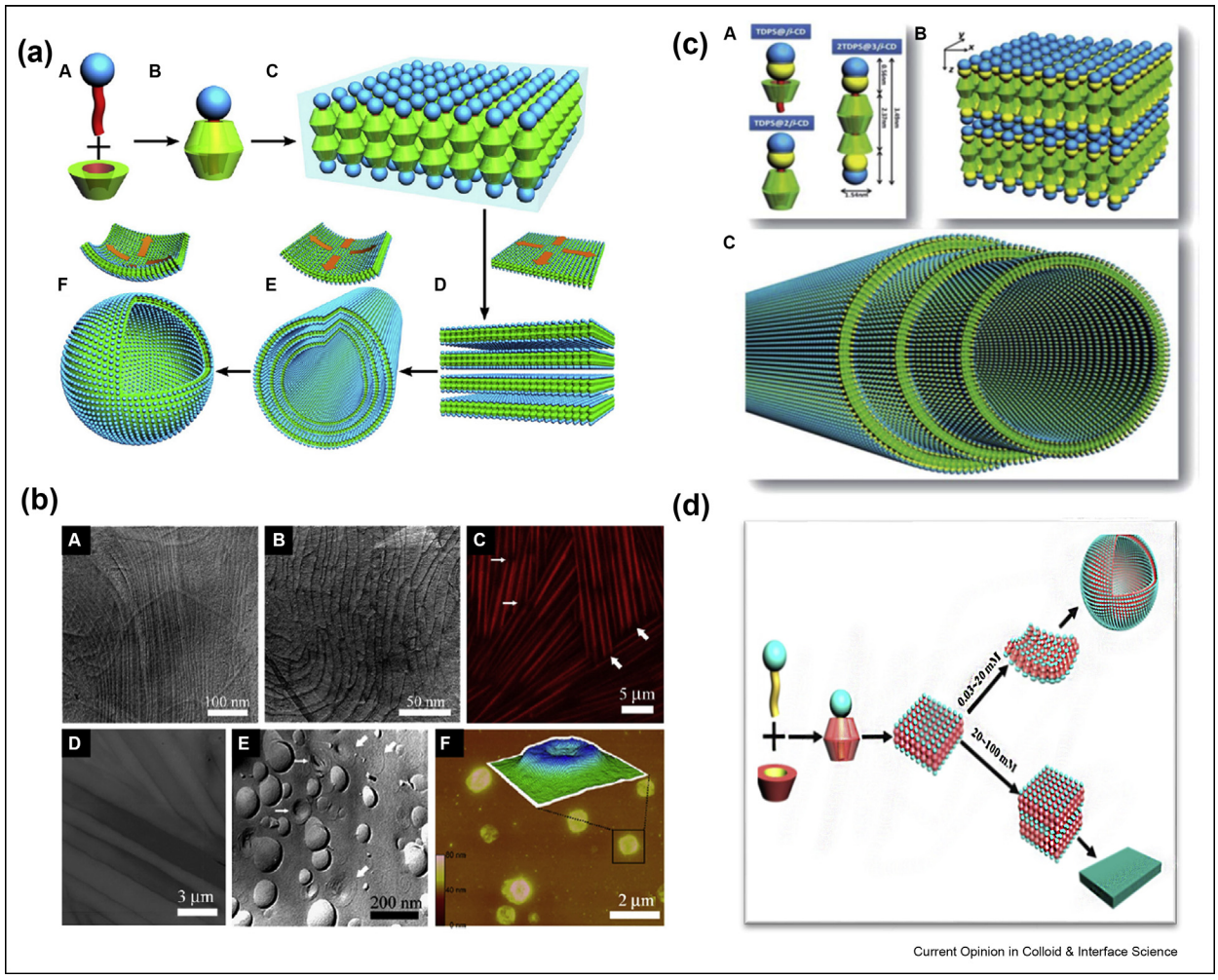
In 2010, Jiang et al. [5,6] reported that anionic surfactant, SDS and β-CDs can form 1:2 complex (denoted as SDS@2β-CD), which can further assemble into well-defined lamellae, tube, vesicles in concentrated or semiconcentrated aqueous solution (Figure 2 (a)). SDS and β-CDs are able to form host–guest complexes in 2:1 stoichiometry with high binding constants by including SDS's hydrophobic tails into CD cavities. Then SDS@2β-CDs, as building blocks, can assemble into channel-type crystalline bilayer membrane. The membrane can laterally expand into infinite two-dimensional lamellar structures at high concentrations, disconnect and scroll up along one axis into one dimensional multilamellar microtubes upon dilution, and further close along another axis into dispersed vesicles upon further dilution.

Detailed analysis confirms the SDS@2β-CD as building blocks and structure of SDS@2β-CD channel-type crystalline bilayer membrane. Morphologies of SDS–β-CD assemblies are observed by confocal laser scanning microscope (CLSM), transmission electron microscopy (TEM), and atomic force microscope (AFM). Figure 2 (b) (A) and (B) are full of numerous parallel lines with a uniform interval, typical for cross section of lamellar structure. Figure 2 (b) (C) and (D) are prevailed by pairs of parallel lines, indicating the one-dimensional tubular structure. Figure 2 (b) (E) and (F) are dominant by spherical structures, corresponding to vesicles. Hydrogen bonds between CDs and electrostatic interactions of charged head group of SDS were proposed as driving forces.

Besides anionic surfactant SDS, zwitterion surfactants can also form inclusion complex with β-CDs and further assemble into high-ordered structure in a similar mechanism [23]. Tetradecyl dimethylammonium propane sulfonate (TDPS, Figure 2 (c)) and β-CDs can form *2*TDPS@3β-CD building block. The *2*TDPS@3β-CD complex laterally expands into lamellae, the lamellae stack together in the perpendicular direction to form a 3D array, and the array eventually folds up into the microtubes.

The TDPS–β-CD microtubes are long, flexible, bundling, and entangling (in great contrast to the previously described SDS@2β-CD microtubes), and they can thus form an extensive 3D network and eventually a strong hydrogel. Compared with SDS@2β-CD nanotubes, TDPS–β-CD microtubes are more flexible, resulted from the surfactant headgroups: zwitterionic for TDPS (electrostatic repulsion minimized) and anionic for SDS (highly electrostatically repulsive). Similarly, hydrogen bonds between CD and CDs and electrostatic interactions of charged head group of TDPS are driving forces of TDPS–β-CD assembly.

Figure 2

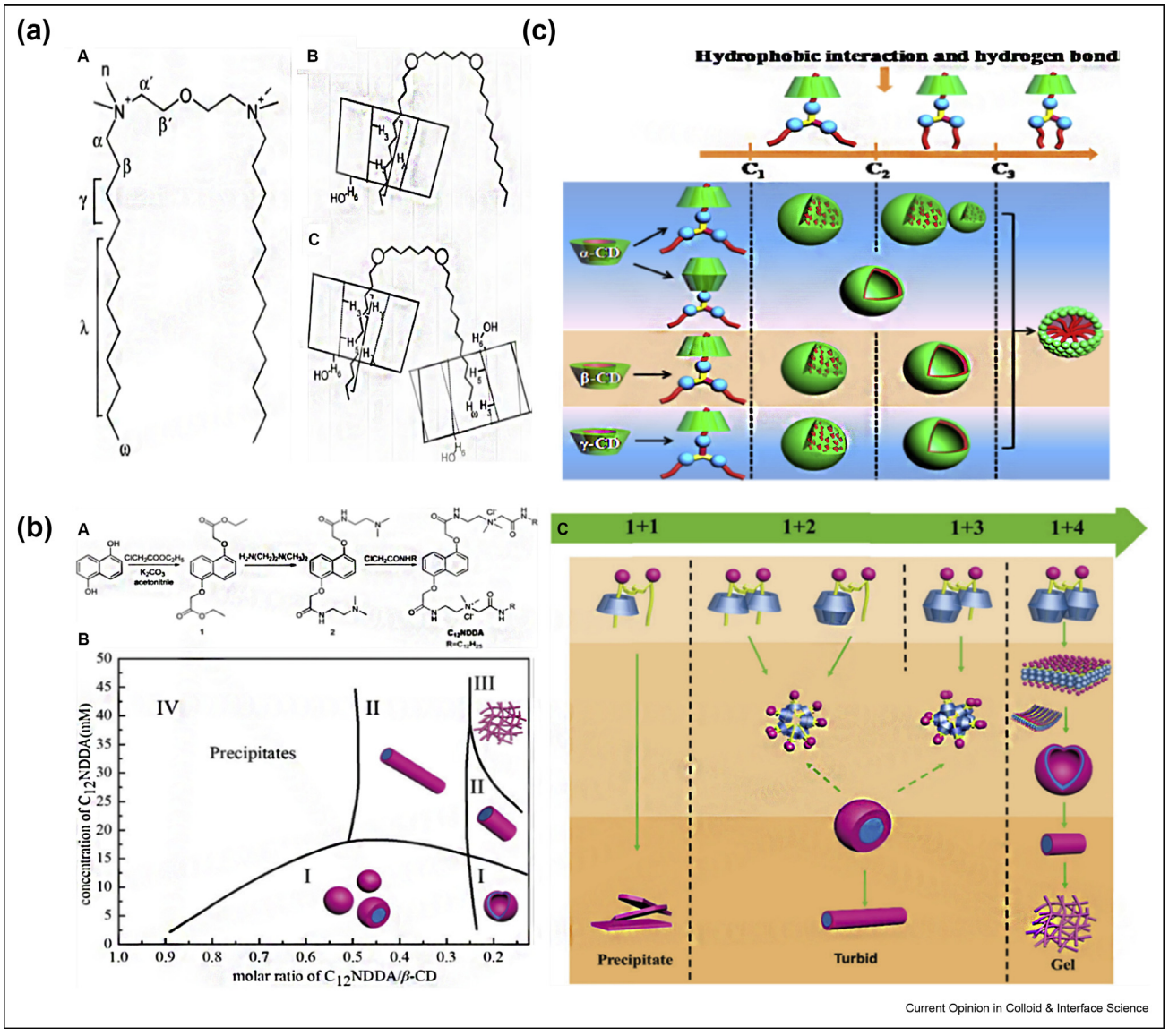


Assembly of β-CD with SDS, TDPS and tween20. (a) Schematic self-assembly behavior of SDS@2β-CD. (A) SDS and β-CD monomers, (B) SDS@2β-CD complex, (C) and SDS@2β-CD bilayer membrane with a channel-type crystalline structure. (D), (E), and (F) the aggregates transform upon dilution from lamellae via microtubes to vesicles [5,6]. **(b)** Morphology of SDS@2β-CD aggregates. (A) (B), FF-TEM images of lamellae. c) d), CLSM and TEM graphics of microtubes, respectively. (E) (F), FF-TEM and AFM images of vesicles, respectively [5,6]. **(c)** (A), Schematic illustrations of different TDPS−β-CD complexes. (B) An array of the 2TDPS@3β-CD complex. (C) a microtube of the 2TDPS@3β-CD complex [23]. **(d)** Schematic illustrations of the self-assembly behavior of tween 20−β-CD complexes [24]. CD, cyclodextrin, SDS, sodium dodecyl sulfate, TDPS, tetradecyl dimethylammonium propane sulfonate; TEM, transmission electron microscopy; FF-TEM, freeze fracture transmission electron microscopy; CLSM, confocal laser scanning microscope; AFM, atomic force microscope.

Apart from ionic surfactants, nonionic surfactant can also assemble with CD and form various ordered structures [24,25]. Assembly of Tween 20 with β-CD was investigated in detail [24]. Tween 20 and β-CD can form 1:2 inclusion complex (Tween 20@2β-CD) as building unit. Tween 20@2β-CD will tend to assemble in a parallel way to form infinite two-dimensional bilayer driven by hydrogen bonding (Figure 2 (d)). In dilute concentration range (c = 0.03−20 mM), the bilayer membranes bend into vesicles. In concentrated range (c = 6−25 wt % or 20−100 mM), the bilayer membranes stack closely into lamellar flakes. Moreover, many other nonionic surfactants, including AEO3, AEO9, Tween 40, Tween 60, Tween 80, and Triton ×100, can also assemble with β-CD and obtain vesicle structure in a similar way.

Surfactants with special topology (such as gemini/bola type surfactants) can also assemble with CDs. β-CD can interact with hydrophobic carbon chains and with polyethylene oxide chain of a nonionic gemini surfactant to form inclusion complex [26,27]. Micelles or rod-like structure can be obtained at different concentration regions. β-CD can also interact with hydrophobic carbon chains of cationic gemini surfactants. Bis (dodecyl dimethylammonium)diethyl ether dibromide (12-EO_1-12) and β-CD assembly was investigated by NMR

Figure 3



Assembly of β-CD with geimini and trimeric surfactants. (a) (A), Molecular structure of 12-EO_1-12 gemini surfactant. Schematic illustration of assembly structure of gemini@β-CD (B) and gemini@2β-CD (C) [28]. **(b)** (A) molecular structure of C12NDDA gemini surfactant. (B) Phase diagram of the C12NDDA−β-CD−H2O system at 25 C. (C) Schematic summary of the aggregation transitions of the β-CD−C12NDDA complexes with varying C12NDDA concentrations and molar ratios of C12NDDA with β-CD [29]. **(c)** Aggregates transitions of the CD−DTAD complexes with the increase of concentration. β-CD and γ-CD will form 1:1 complex with DTAD, while α-CD can form 1:1 and 2:1 complex. DTAD−CD complex will assemble into large solid spherical aggregates, vesicles and micelles upon increasing concentration [30]. C12NDDA, novel cationic gemini surfactant with a spacer containing naphthalene and amides. CD, cyclodextrin. DTAD, tri(dodecyldimethylammonioacetoxy)diethyltriamine trichloride, a novel cationic ammonium trimericsurfactant.

techniques (Figure 3 (a)) [28]. Analysis of the ^{1}H NMR spectra and self-diffusion coefficients reveal the formation of gemini@β-CD and gemini@2β-CD (1:1 and 1:2 complex) with a calculated stability constant for the second binding step higher than that of the first. Detailed assembly structure was illustrated in Figure 3 (a) (B) (C). At low concentrations of β-CD, one of the hydrocarbon tails of the surfactant enters the cavity through the wide rim, with the other chain interacting with the external surface of the β-CD. By contrast, at higher concentrations of β-CD, the two hydrocarbon tails are included in two β-CD cavities.

Inclusion complex of gemini surfactant and β-CD can also further assemble into various structures [29,31]. Figure 3 (b) shows a novel cationic gemini surfactant (C12NDDA) with a spacer containing naphthalene and amides. Tuning the C12NDDA concentration and the

C12NDDA−β-CD molar ratio allowed the production of different assembled aggregate morphologies such as micelles, vesicles, nanowires, nanorods, and hydrogels (Figure 3 (b) (C)). Detailed investigation revealed that C12NDDA could form inclusion complex with β-CD as C12NDDA@β-CD, C12NDDA@2β-CD, C12NDDA@3β-CD, and C12NDDA@4β-CD. C12NDDA@β-CD has an 'exposed' hydrocarbon chain, which lead to precipitate because of strong hydrophobic interactions. As for C12NDDA@2β-CD and C12NDDA@3β-CD, the amount of β-CD was insufficient to interact with all the hydrophobic arms of C12NDDA; thus, the complex tended to restack into spherical micelles with the hydrophobic moieties aggregated in the core and the hydrophilic moieties stretched into water. Moreover, the inclusion complexes assembled into micelles because of hydrophobic interactions, hydrogen bonding, and van der Waals forces. In C12NDDA@4β-CD complex, two hydrophobic chains of a C12NDDA molecule was combined with four β-CD molecules, leading to channel-type bilayer membranes. As the concentration of C12NDDA increased, the bilayer membranes closed laterally along two in-plane axes to generate vesicles. When the concentration of C12NDDA increased to 38 mM, the vesicles expanded into nanorod structures that could further cross-link in a disordered manner to generate an opaque and thermoreversible hydrogel through hydrogen bond interactions, π-π stacking, and electrostatic forces.

Moreover, trimeric surfactants with three hydrophilic groups and three hydrophobic groups can also assemble with CDs. Tri(dodecyldimethylammonioacetoxy)diethyltriamine trichloride (DTAD) is a novel cationic ammonium trimeric surfactant with a star-shaped asymmetric spacer (chemical structure shown in Figure 3 (c)) [30]. Upon adding CDs with different cavity size, the α-CD@DTAD, 2α-CD@DTAD, β-CD@DTAD, and γ-CD@DTAD complexes are fabricated. Compared with DTAD itself, these CD−DTAD complexes show much lower critical aggregation concentration and form more diverse aggregate structures with varying the concentration, larger vesicles, or spherical solid aggregates of ∼50 nm first and then smaller micelles of ∼10 nm. The aggregate transitions are controlled by the discrepancy in the intensity of hydrogen bonds and hydrophobic interaction, and the changes of molecular configuration as illustrated in Figure 3 (c). These different assembly structures can alter antibacterial activity, and the formation of vesicles is approved to be in favor of the improvement of the mildness.

In brief, many types of surfactants (ionic surfactants, zwitterion surfactants, nonionic surfactants, gemini surfactant, and so on.) can form inclusion complexes with CDs driven by host−guest interactions. These inclusion complexes can further assemble into various structures including vesicles, nanotubes, fiber, lamellae, and so on, driven by hydrogen bonding between CDs. The broad spectrum of surfactants and final assembly structures will provide us abundant choices and promising applications.

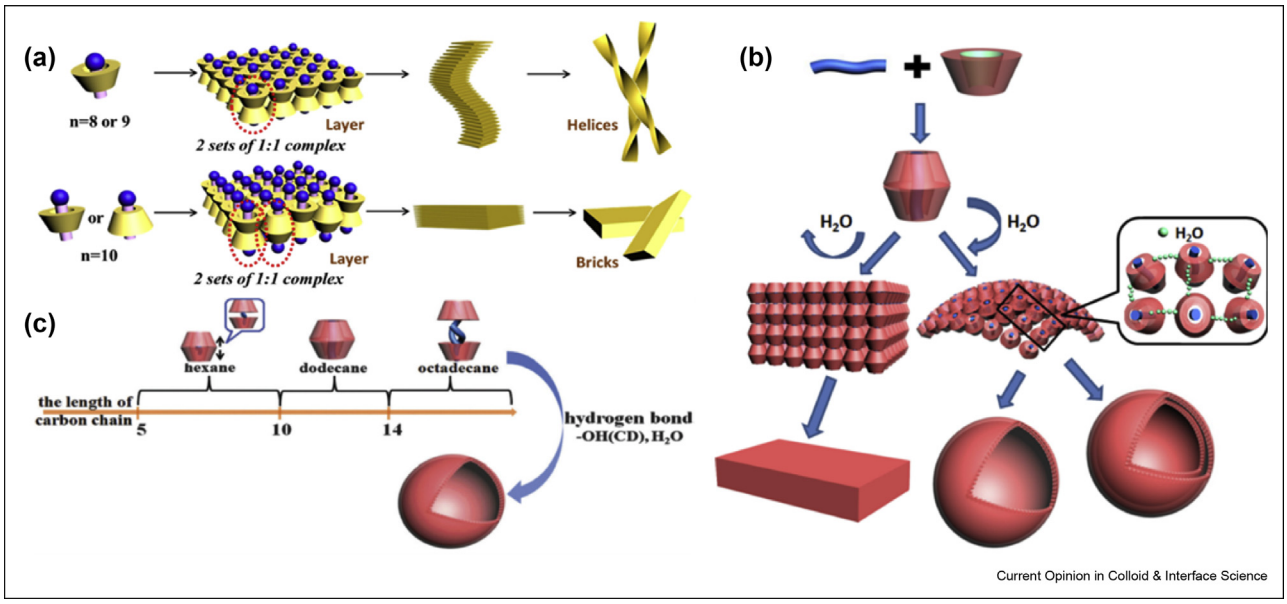
Assembly of CDs and nontypical amphiphiles

As shown before, CDs can assemble with amphiphiles including polymers and surfactants driven by inclusion of hydrophobic groups into cavity of CDs and hydrogen bonding between inclusive complexes. Besides surfactants, recent studies also demonstrate the assembly between CDs and nontypical amphiphiles (such as amines [32], aromatic molecules [33], and so on.), even nonamphiphiles (such as alkene [34,35], and so on). Similarly, these guest molecules can form inclusion complexes with CDs, which further assemble into ordered structures.

Alkyl amines are polar molecules consisting hydrophobic alkyl chains and hydrophilic NH_2. After introducing alkyl amines $CH_3(CH_2)_{n-1}NH_2$ (n = 8, 9, 10) into β-CD solution, the inclusion complex was formed and white precipitates were observed (Figure 4 (a)) [32]. Detailed investigation revealed that $CH_3(CH_2)_{n-1}NH_2$ (n = 8, 9, 10) and β-CD formed 1:1 inclusion complex, which can further assemble into channel-type crystalline layer. Interestingly, $CH_3(CH_2)_{n-1}NH_2$ (n = 8, 9) are oriented predominantly toward the wider rim of β-CD, while $CH_3(CH_2)_{n-1}NH_2$ (n = 10) threaded through both the narrower and wider rim of β-CD. The orientation of alkyl amine is determined by hydrogen interaction between NH_2 group of alkyl amine and OH group of CDs. Interestingly, the selective orientation of $CH_3(CH_2)_{n-1}NH_2$ (n = 8, 9) in β-CD leads to helices, whereas dual orientation of $CH_3(CH_2)_{n-1}NH_2$ (n = 10) results in planar bricks observed by scanning electron microscopy (SEM).

Beyond nontypical amphiphiles alkyl amines, researchers even extend the scope of guest molecules that can assemble with CDs to fully hydrophobic molecules. Dodecane and β-CD were found to form inclusive complex dodecane@2β-CD (Figure 4 (b)) [34]. Because the extending length of dodecane is much shorter than the sum of two β-CDs, the dodecane molecule was completely buried in the channel formed by two β-CD molecules. Thus, dodecane was not directly involved in the interactions between the dodecane@2β-CD supramolecular complexes, so that the self-assembly of dodecane@2β-CD is simply that of the channel type β-CD dimers which is dominated by hydrogen bonds. The dodecane@2β-CD complex will form vesicles at low concentration but bricks at high

Figure 4



Assembly of β-CD with alkyl amines and alkanes. (a) $CH_3(CH_2)_{7,8}NH_2$ is oriented toward to the wider rim of β-CD, and $CH_3(CH_2)_9NH_2$ is oriented toward to both the wider and narrower rims of β-CD. The selective orientation of the $CH_3(CH_2)_{7,8}NH_2$ leads to helices, whereas the dual orientation of $CH_3(CH_2)_9NH_2$ results in planar bricks [32]. **(b)** Schematic illustration for the self-assembling behavior of the dimers of 2β-CD threaded by one dodecane. The dimer is a supramolecular building block of dodecane@2β-CD [34]. **(c)** Schematic illustration of the self-assembly behavior of alkane/β-CD building blocks [35]. CD, cyclodextrin

concentration related with water-mediated hydrogen bond. At low concentrations, more water molecules are expected to bridge the dodecane@2β-CD supramolecular building blocks. The uneven distribution of water molecules in the outer and inner side of the membrane leads to the curvature for vesicles. At high concentrations, dodecane@2β-CD complexes are adequate for parallel packing leading to bricks.

More systematically, influence of chain length of alkanes on assemblies with CDs are studied (Figure 4 (c)) [35]. In the case of short-chained alkanes with 5−10 carbons, the building block is channel type 2alkane@2β-CD, which can be looked on as the dimer of alkane@β-CD. Upon increasing the chain length to 12−14 carbons, the building blocks take the form of alkane@2β-CD. Interestingly, upon further increasing the chain length to 16 and 18 carbons, the building block changes back to the form of 2alkane@2β-CD but with nonchannel type arrangement of β-CD. All these inclusion complexes as building blocks can self-assemble into unilamellar and bilamellar vesicles in dilute solutions. Similar to dodecane@2β-CD assembly, water was found to act as a structural mediator of hydrogen bonds in vesicle formation.

In summary, nontypical amphiphiles (including amines, aromatic molecules, alkanes) can assemble with CDs to form inclusion complex and further assemble into ordered structures (helices, vesicles, and so on) driven by CD−CD hydrogen bonds. In this process, guest molecules can influence the inclusion formation by polar head NH_2 or chain length, leading to controllable assembly structures. Combining with previous 2.1−2.3 sections, we overviewed the assembly of CDs and many types of guest amphiphiles, including polymers, surfactants (ionic surfactants, zwitterion surfactants, nonionic surfactants, gemini surfactant, and so on), and nontypical amphiphiles (amines, aromatic molecules, alkanes, and so on). Guest amphiphiles can form inclusion complex with CDs, and CD−CD hydrogen bond can induce further assembly of these inclusion complex to form various types of ordered structures. Because of the broad spectrum of guest amphiphiles and dynamic nature of host−guest inclusive interaction, researchers also illustrate plenty of ways to regulate CD−amphiphile assemblies to fabricate smart responsive systems (covered in Regulation of CD and amphiphile assembly).

Regulation of CD and amphiphile assembly

In general, assemblies of CDs and amphiphiles occur in sequence: first CDs and amphiphiles form inclusion complexes, then these complexes further assemble into ordered structures. The ways to regulate the aforementioned assemblies can be roughly divided into several categories: (1) to regulate the structure of CDs by enzyme and so on; (2) to regulate guest amphiphiles,

for example, by introducing light-, pH-, coordination-responsive moieties into guest amphiphiles; (3) to regulate host–guest interactions and hydrogen bonding between CDs and amphiphiles by concentration, temperature, and so on. In this section, we will give an overview of the progress in this aspect. Although more exciting developments are still being made, the examples presented herein clearly demonstrate the numerous opportunities and practical applications that can stem from the diversity and complexity of CD-based stimuli-responsive assembly systems.

Enzymes

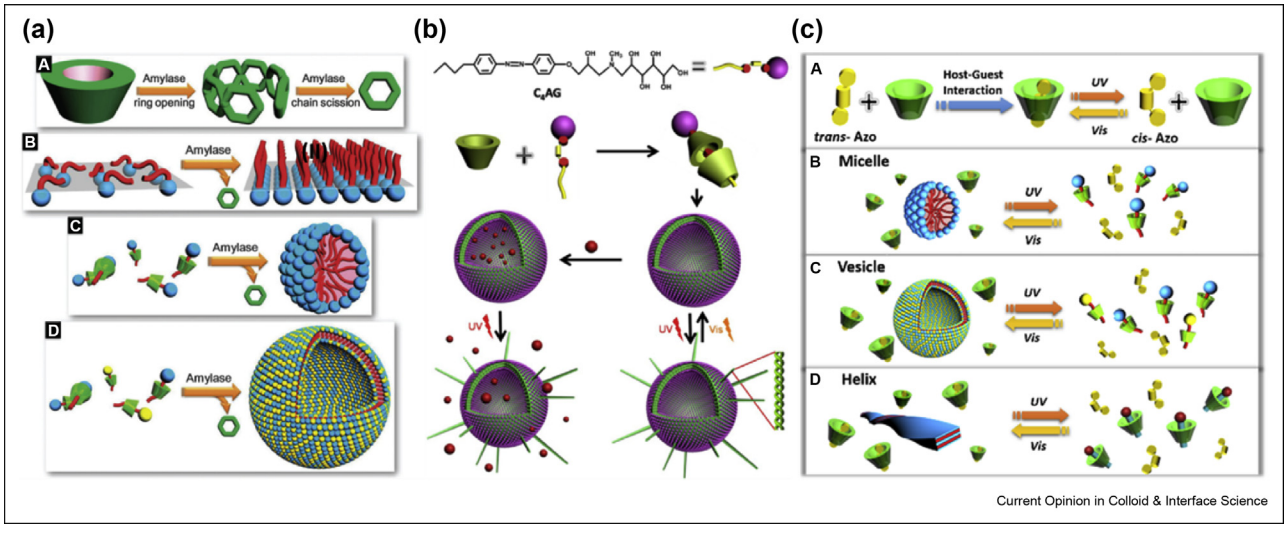
Historically, CDs were firstly found from the enzymatic production of starch [1] and closely related to several biological pathways. On the other hand, the hydrophobic cavity of CDs has long been investigated as artificial enzymes mimicking the substrate-binding pockets of natural enzymes [36]. Recently, considerable research studies have focused on introducing enzyme-responsive sites into CD–amphiphile assemblies.

The direct and general approach to enzymatically regulate CD–amphiphile assemblies is biodegradation of CD glucose bonds by α-amylase. α-Amylase can cleave α-1,4 linkages between glucose units of starch molecules including CDs, which will degrade CDs in two steps (ring opening and chain scission) giving glucose in the end. Biodegradation of CDs would lead to disassembly of CD–amphiphile assemblies. However, in some cases where CDs play destructive roles, degradation of CDs can trigger assembly of amphiphiles [9]. For example, surfactants (including TDPS, CTAB, SDS, and Triton ×100) can be released from the cavity of CDs after treatment of α-amylase. Consequently, released surfactants can form monolayers, micelles, and vesicles (Figure 5 (a)) [37].

This strategy of enzyme regulation by α-amylase has also been used in other CD–amphiphile systems, such as CDs/bola amphiphiles [40], to tune physical properties of assembly. The bola-form covalent amphiphile could self-assemble in solution, forming sheet-like aggregates and displaying weak fluorescence because of aggregation caused quenching. The addition of β-CD led to the formation of host–guest complex, prohibiting the aggregation of naphthalene and accompanying with the significant recovery of fluorescence. Upon the addition of α-amylase, with the degradation β-CD, the fluorescence would quench gradually and significantly. Quantitatively, the quenching rate linearly correlated to the concentration of α-amylase, which makes it promising to diagnose the α-amylase–associated diseases.

Besides enzymatic degradation of CDs, a variety of enzyme-responsive guest amphiphiles have also been extensively used in construction of enzyme-responsive CD–amphiphile assembly systems, such as disruption of protamine by trypsin [41], rupture of myristoylcholine chloride by butyrylcholinesterase (BChE) [42], and so on. BChE-responsive supramolecular nanoparticles are fabricated by hepa-carboxyl–modified CDs (carboxyl-CDs) as the macrocyclic host and cationic enzyme-cleavable guest myristoylcholine as enzymatically responsive guest. After the treatment of BChE, myristoylcholine can be cleaved into myristic acid and choline, leading disassembly of nanoparticles.

Figure 5



Enzyme and light methods to regulate CD-amphiphiles assembly. (a) Schematic illustrations of the degradation of (A) β-CD by α-amylase, (B) enzyme-triggered monolayer formation, (C) enzyme-triggered micellization, (D) and enzyme-triggered vesicle formation [37]. **(b)** Schematic illustration of photo-triggered release from the bacteria-like C_4AG@2β-CD vesicles [38]. **(c)** Schematic illustrations of the construction (A) a photoresponsive self-assembly using Azo@CD in (B) micelle, (C) vesicle, and (D) helix systems [39]. CD, cyclodextrin

As described previously, it is clear that enzyme-responsive CD—amphiphile assembly offers huge space of regulation and applications. Taking advantage of the facile degradation of CDs by enzymes, we anticipate that almost all CD—amphiphile assemblies can respond to enzymes, which brings about limitless possibility to regulate CD—amphiphile assemblies. In addition, since numerous enzyme—substrate pairs have been found in biological research, many substrates are suitable to be introduced into amphiphiles to fabricate specific enzyme-responsive assemblies. Moreover, enzyme-responsive CD—amphiphile assemblies may also be important in disease diagnosis because many diseases are associated with abnormal enzymatic expression and activity.

Light

Light-regulated CD—amphiphile systems usually relate with light-responsive amphiphiles. Light-responsive assemblies attract much attention because of convenience, rapid response, remote control, and no chemical contamination. Typically, guest amphiphiles contain photoresponsive moieties including azobezene, arylazopyrazole, 0-nitrobezylester, pyrenylmethyl ester, coumarin, and anthracene [43].

Among the aforementioned photo-responsive moieties, azobezene groups are a family of most widely used light-responsive moieties because of their unique properties of isomerization in *trans—cis* structures. *Trans* azobenzene isomerized from *cis*-azobenzene under 365 nm UV light irradiation can be included by α-CD and β-CD. However, *cis* azobenzene isomerized from *trans*-azobenzene under approximately 450 nm UV light irradiation is relatively hard to include in the cavity of α-CD and β-CD. The isomerization is reversible and controllable through alternating the light. The huge difference of binding ability between *trans/cis* azobenzene and CDs provides researchers with unlimited opportunities for remote and reversible control over assembly structures [39,44,45] and related properties such as phase transition [46], drug release [38], optical properties [47], and so on.

Photo-controlled inclusion and exclusion of azobenzene-containing amphiphiles with CDs can undergo reversible assembly and disassembly, leading to reversible transformation of assembly structure. For example, cationic surfactant 1-[10-(4-phenylazophenoxy) decyl]pyridinium bromide (termed AzoC10) can form vesicle-like aggregates in aqueous solution [44]. After addition of α-CD, AzoC10 and α-CD would form inclusion complex, leading to disassembly of vesicle. *Trans*-AzoC10 will undergo photo-induced isomerization under UV light and resultant cis-Az0C10 has a much smaller binding constant with α-CD compared with *trans*-AzoC10, leading to reassembly to vesicle structure.

Besides the vesicle morphology, other morphologies manipulated by light can also be achieved in CD—Azo system. Amphiphiles containing axially chiral 1,1′-binaphthyl and photoresponsive azobenzene moieties can form inclusion complex with α-CD and bis-SC4A host molecules [45]. The inclusion complex can extend to polymer-like structure (so-called supramolecular polymer) P because of unique structure of bis-SC4A. *Trans*-Azo—based P has more flexible and shorter length aggregates under cryo-TEM, while after UV irradiation *cis*-Azo based P can assemble into linear single-helical supramolecular polymer molecules with diameters of *ca.* 2 nm and lengths of hundreds of nanometers to micrometers. This could be ascribed to the fact that UV-irradiated P containing *cis*-azobenzene has a more straight structure compared with the P containing *trans*-azobenzene. Interestingly, the single-helical structure of irradiated supramolecular polymer P can be observed, resulted from the introduction of the axially chiral 1,1′-binaphthyl units in amphiphiles.

Beyond assembly structure transformation upon light in CD—Azo system, the related properties of the system can also be manipulated, which resulted from assembly transformation. For example, some researchers focus on light-controlled phase transition, especially gel—sol transition [46]. Azobenzene units functionalized with a guanidinium group were used as the photoswitches and incorporated through a host—guest inclusion method involving α-CD functionalized with 2,6-pyridinedicarboxylic acid groups. The guanidinium groups could associate with the negatively charged surface of sodium polyacrylate exfoliated laponite nanosheets (SPLNs) through electrostatic interactions, thus connecting the organic and inorganic components of the hydrogel. Owing to the conformation-dependent binding behavior between Azo moieties with α-CD, light could control the isomerization of azobenzene, which induces assembly or disassembly of the inclusion complexes and further leads to sol—gel phase transition of hydrogels.

Apart from phase transition, other functions were investigated in CD—Azo system. Light-controlled drug release is an attracting topic for precise delivery and release of drug. This can be achieved in amphiphilic [4-butyl-40-(oxy-2, 3-epoxypropyl)azobenzene] (C_4AG) and β-CD aqueous system (Figure 5 (b)) [38]. C_4AG and β-CD can form inclusion complex at molar ratio of 1:2 as $C_4AG@2\beta$-CD, and C_4AG $@2\beta$-CD complex can further self-assemble into vesicles in water. Upon UV irradiation, many hairs may develop from the surface of the vesicle, just similar to cilia of bacteria. Concomitantly, this triggers the release of the loaded drug. The transformation process is reversible and repeatable with alternative UV—visible light irradiation. In this way, vesicles with photo-controlled on and off membrane can be obtained, which can be used in photo-controlled smart drug carrier.

In general, CD–Azo system can serve as a universal control unit in molecule assembly system [39]. β-CD and 4-(phenylazo)benzoic acid sodium salt form an Azo@CD photoresponsive factor to couple with light-inert amphiphilic assemblies that successfully make a general approach for controlling the morphology of amphiphilic aggregates by UV or visible light irradiation (Figure 5 (c)). The key point of this strategy is the different capabilities of forming host–guest inclusions with CD, that is, *trans*-azobenzene > alkyl chain of amphiphilic molecules > *cis*-azobenzene. The inclusion of *trans*-Azo@CD can stably coexist with light-inert amphiphilic aggregates under visible light. Upon UV light irradiation, with the transformation from *trans*-Azo to *cis*-Azo, CDs are released into the solution and form new inclusions with amphiphilic molecules, which lead to the disassembly of the light-inert aggregations. The morphology of amphiphilic assemblies, such as micelles, vesicles, and helixes, and phase behavior, such as gel formation, can be modulated upon light irradiation using this method.

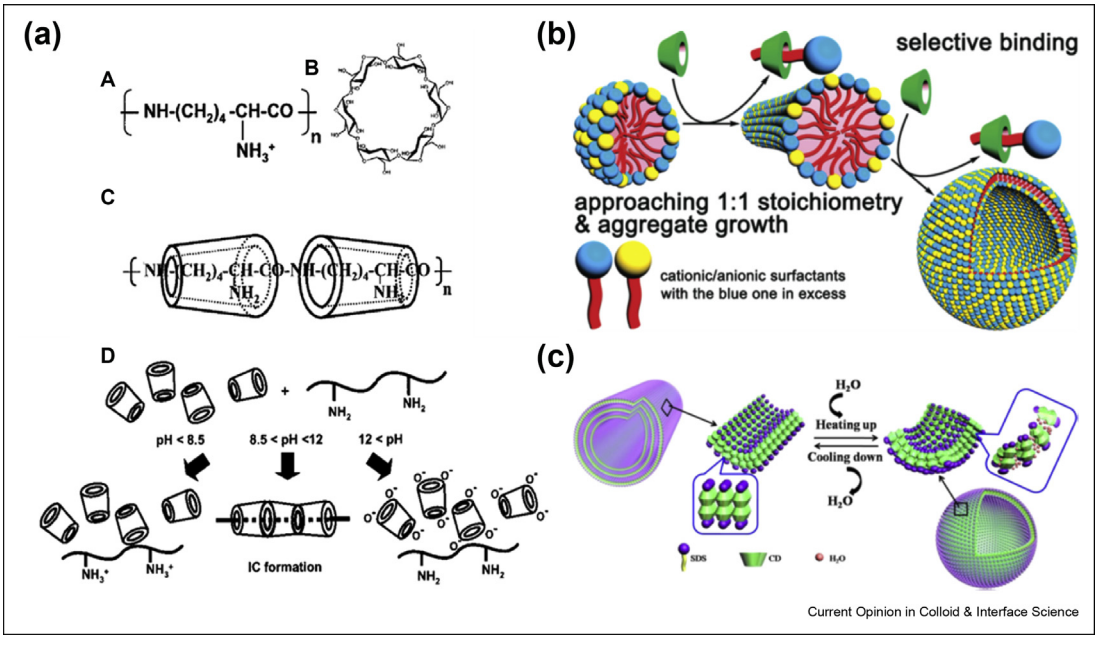
Others

Besides enzymes and light, other stimulus (such as pH, concentration, temperature, and so on) can also regulate CD–amphiphile assemblies. Among these stimuli, pH regulates guest amphiphiles of acid–base form. Concentration and temperature mainly affect the host–guest interaction between CDs and amphiphiles.

Similar to biomolecules, pH has a great impact on CD–amphiphile assemblies. Usually, molecules containing pH-responsive groups (such as peptides, carbonate groups, amine group, and so on) have been used in the construction of pH-responsive CD–amphiphile systems. For example, cationic poly (ε-lysine) can thread α-CDs to obtain inclusive polypseudorotaxane at condition of $8.5 < pH < 12$ (Figure 6 (a)) [48]. Although the inclusion complexation could be observed in the pH 8.5–12, no inclusive polypseudorotaxane was found in acidic and highly alkaline conditions. This pH-dependent complexation is closely related to the protonation of amino side groups (pKa = 9) and the dissociation of hydroxyl groups (pKa = 11.3) of α-CD. α-CD cannot include any polymer chains containing the protonized amino side groups in acidic conditions, and also the ionized form of α-CD in highly alkaline conditions more than pH > 11.5 cannot work as a host for any guests. This illustrates pH is a feasible and powerful method to regulate CD–amphiphile assemblies and further applications have been intensively studied [49–51].

Concentration is a common factor affecting assembly behavior in aqueous assembly system. As illustrated in previous examples [5,24,29,32,34,35], concentration and molar ratio of CDs and amphiphiles could lead to various assembly structures. Moreover, CDs can serve as modulators to anionic–cationic surfactant assembly system because anionic–cationic surfactants can be included into hollow of CDs. In nonstoichiometrical

Figure 6



pH, concentrationand temperature methods to regulate CD-amphiphiles assembly. (a) (A) Poly (ε-lysine), (B) α-CD, and (C) the inclusion polypseudorotaxane by α-CD and poly (ε-lysine). (D) Schematic illustration for pH-dependent inclusion complexation [47]. **(b)** Schematic illustration of aggregate growth in mixed cationic–anionic surfactant systems induced by β-CD [52]. **(c)** Schematic aggregate morphology transition of SDS@2β-CD complexes with the variation of the temperature [53]. CD, cyclodextrin.

mixed cationic–anionic surfactants systems, upon addition of β-CD, the aggregate undergoes a micellar elongation and a following micelle-to-vesicle transition, which in turn greatly influences the viscosity and absorbance of the solutions (Figure 6 (b)) [52]. It was found that the selective binding of β-CD toward the major component of a cationic–anionic surfactant mixture is thought to be responsible. This selectivity removes the excess part of the major component from the aggregates, shifts the surfactant compositions in the aggregates toward an electroneutral mixing stoichiometry, and thus gives rise to the observed aggregate growth and concomitant variations in solution properties. This is an excellent example of using CD–amphiphile assemblies to regulate local concentration of other assembly system, which gives us inspirations for precise control of assembly system.

Temperature has long been used as a convenient tool to control molecular self-assembly because noncovalent interaction can be largely affected by temperature. In CD–amphiphile system, temperature will influence the hydrogen bonding and finally influence the assembly behavior because CD–CD hydrogen bond is the main driving force for CD–amphiphile complexes to assemble. In SDS and β-CD (β-CD) system, SDS and β-CD form a channel-type SDS@2β-CD supramolecular unit, which further self-assembles into nonamphiphilic vesicles and microtubes driven by hydrogen bonding [5]. Vesicle and tubular structures existed at the concentration range of 4–6% and 6–25% at 25 C, respectively. Upon decrease in temperature, the vesicles in the concentration range of 4–6% will transform into microtubes, whereas with increase in temperature, the microtubes that are formed in the concentration range of 6–25% transform into vesicles. The achievement of the transformation between the microtubes and vesicles depends upon the variation of the strength of hydrogen bonds (Figure 6 (c) [53]). At low temperatures and high concentrations, the hydrogen bonding between CDs is very strong, so that microtubes are the favorite structures. Under opposite conditions, the hydrogen bonding between water and CDs becomes dominant. This unique behavior may shed light on importance of hydrogen bonding in CD-based inclusion complexes and offer a reversible regulation method.

To summarize, various amphiphiles can be chosen to fabricate CD–amphiphile systems, which can response to stimuli including light, pH, enzyme, and so on. Moreover, because the host–guest interaction and hydrogen binding in CD–amphiphile assemblies are noncovalent and dynamic interaction, various techniques (including temperature, concentration, and so on) can be applied to control this host–guest interaction. These studies concerning regulation of CD–amphiphile assemblies will not only help us understand the principle rules of assembly but also benefit applications of CD–amphiphile assemblies.

Remarks and perspectives

In this review, we summarized the recent progress on assemblies of CDs and amphiphiles, focusing on aspects of construction and regulation. The scope of amphiphiles used to fabricate CD–amphiphile assemblies has been widely extended from polymers (PEGs, block polymers, and so on), surfactants (ionic surfactants, zwitterion surfactants, nonionic surfactants, gemini surfactant, and so on), to nontypical amphiphiles (amines, aromatic molecules, alkanes, and so on). In general, these guest amphiphiles can form inclusion complexes with CDs, and CD–CD hydrogen bond can induce further assembly into various high order structures. Owing to the abundant choices of guest amphiphiles and dynamic nature of host–guest–inclusive interaction, elegant and convenient regulation methods (such as enzyme, light, pH, concentration, temperature, and so on) have been used to regulate CD–amphiphile assemblies.

Although remarkable advances have been made in this field, a great deal of effort is needed:

(1) Mechanism of assembly and relationship between molecular structure and assembly behavior. Although recent study revealed guest orientation inside CDs using 2D-NMR [32], detailed mechanism is still worth careful investigations. For example, the orientation and alignment of inclusion complex in channel-type bilayers, factors affecting curvature of assembly structure, interactions between polar heads on surfactants, and so on. These details not only enrich the scientific knowledge but also give us hints for understanding mysterious of assemblies in nature. Biological systems are usually assembled by various noncovalent interactions, among which hydrogen bonding is a vital one. Therefore, assembly of CDs and amphiphiles driven by hydrogen bonding will offer understanding for biological assembly process. Recently, it was found that crystalline bilayer constructed from channel-type CDs might resemble structure of a capsid in nature [54].

(2) Applications based on CD–amphiphile assemblies. Construction and regulation of CD–amphiphile assemblies offer great opportunities to construct responsive functional materials for colloidal science, biomedical application, and so on. Besides, ordered structure of CD–amphiphile assemblies also provides model systems for further applications. For example, CD–SDS microtubes were used as a confined space to investigate basic assembly of colloidal particles inside the assemblies [55]. This shows us a promising example to use CD–

amphiphile assemblies to promote advances in colloidal and many other fields. Moreover, CD–amphiphile assemblies are also promising for biomedicine because CDs are highly biocompatible and are widely used in the pharmaceutical industry.

In conclusion, we have witnessed substantial advancement in assembly between CDs and amphiphiles from construction to regulation. Moreover, CD–amphiphile assemblies with ordered structure and multiple responsiveness can be promising in both fundamental and application level. Indeed, more discoveries can be stimulated to illustrate the assembly mechanism and essential applications, beneficial for us to understand dynamic nature of host–guest interactions and master assembly system, which may be helpful for problems such as food shortage, disease, and pollution.

Conflict of interest statement

Nothing declared.

References

Papers of particular interest, published within the period of review, have been highlighted as:

* of special interest
** of outstanding interest

1. * Crini G: **Review: a history of cyclodextrins**. *Chem Rev* 2014, **114**:10940–10975.
This is a recent review on research history of cyclodextrins, including discovery, identification and its applications.

2. Valente AJ, Söderman O: **The formation of host–guest complexes between surfactants and cyclodextrins**. *Adv Colloid Interface Sci* 2014, **205**:156–176.

3. Messner M, Kurkov SV, Jansook P, Loftsson T: **Self-assembled cyclodextrin aggregates and nanoparticles**. *Int J Pharm* 2010, **387**:199–208.

4. Harada A, Li J, Kamachi M: **The molecular necklace: a rotaxane containing many threaded α-cyclodextrins**. *Nature* 1992, **356**:325.

5. ** Jiang L, Peng Y, Yan Y, Deng M, Wang Y, Huang J: **"Annular Ring" microtubes formed by SDS@ 2β-CD complexes in aqueous solution**. *Soft Matter* 2010, **6**:1731–1736.
This pioneering work reports the formation of microtubes constructed from SDS and β-CD, and illustrates an reasonable assembly mechanism. Also, this paper points out the unique and indispensable role of hydrogen bond in CD/amphiphiles assembly.

6. ** Jiang L, Peng Y, Yan Y, Huang J: **Aqueous self-assembly of SDS@ 2β-CD complexes: lamellae and vesicles**. *Soft Matter* 2011, **7**:1726–1731.
This paper expands the assembly diagram of SDS and β-CD, obtaining lamellae, vasicles and microtubes upon different concentrations.

7. Coleman AW, Nicolis I, Keller N, Dalbiez JP: **Aggregation of cyclodextrins: an explanation of the abnormal solubility of β-cyclodextrin**. *J Incl Phenom Macrocycl Chem* 1992, **13**:139–143.

8. Bonini M, Rossi S, Karlsson G, Almgren M, Lo Nostro P, Baglioni P: **Self-assembly of β-cyclodextrin in water. Part 1: cryo-TEM and dynamic and static light scattering**. *Langmuir* 2006, **22**:1478–1484.

9. * Jiang L, Yan Y, Huang J: **Versatility of cyclodextrins in self-assembly systems of amphiphiles**. *Adv Colloid Interface Sci* 2011, **169**:13–25.
This is a review on versatile roles of cyclodextrins in self-assembly system. The versatality of cyclodextrins are classfied into destructive and constructive modulators, amphiphlic and unamphiphilic building units.

10. * Yan Y, Jiang L, Huang J: **Unveil the potential function of CD in surfactant systems**. *Phys Chem Chem Phys* 2011, **13**:9074–9082.
This is a review on functions of amphiphiles/CD assembly system.

11. van de Manakker F, Vermonden T, van Nostrum CF, Hennink WE: **Cyclodextrin-based polymeric materials: synthesis, properties, and pharmaceutical/biomedical applications**. *Biomacromolecules* 2009, **10**:3157–3175.

12. Mantooth SM, Munoz-Robles BG, Webber MJ: **Dynamic hydrogels from host–guest supramolecular interactions**. *Macromol Biosci* 2019, **19**:1800281.

13. Lo Nostro P, Lopes JR, Cardelli C: **Formation of cyclodextrin-based polypseudorotaxanes: solvent effect and kinetic study**. *Langmuir* 2001, **17**:4610–4615.

14. Isnin R, Kaifer AE: **Novel class of asymmetric zwitterionic rotaxanes based on alpha-cyclodextrin**. *J Am Chem Soc* 1991, **113**:8188–8190.

15. Li J, Li X, Zhou Z, Ni X, Leong KW: **Formation of supramolecular hydrogels induced by inclusion complexation between pluronics and α-cyclodextrin**. *Macromolecules* 2001, **34**:7236–7237.

16. Li WS, Chung WS, Chao I: **A computational study of regioselectivity in a cyclodextrin-mediated Diels-Alder reaction: revelation of site selectivity and the importance of shallow binding and multiple binding modes**. *Chemistry* 2003, **9**:951–962.

17. Karim AA, Loh XJ: **Design of a micellized α-cyclodextrin based supramolecular hydrogel system**. *Soft Matter* 2015, **11**:5425–5434.

18. Alves P, Mesquita O, Rocha M: **Controlling cooperativity in β-cyclodextrin–DNA binding reactions**. *J Phys Chem Lett* 2015, **6**:3549–3554.

19. Cao M, Deng M, Wang X-L, Wang Y: **Decompaction of cationic gemini surfactant-induced DNA condensates by β-cyclodextrin or anionic surfactant**. *J Phys Chem B* 2008, **112**:13648–13654.

20. Araki J, Ito K: **Recent advances in the preparation of cyclodextrin-based polyrotaxanes and their applications to soft materials**. *Soft Matter* 2007, **3**:1456–1473.

21. Wang J, Qi W, Lei N, Chen X: **Lamellar hydrogel fabricated by host-guest interaction between α-cyclodextrin and amphiphilic phytosterol ethoxylates**. *Colloids Surf A Physicochem Eng Asp* 2019, **570**:462–470.

22. Liu KL, Zhang Z, Li J: **Supramolecular hydrogels based on cyclodextrin–polymer polypseudorotaxanes: materials design and hydrogel properties**. *Soft Matter* 2011, **7**:11290–11297.

23. ** Jiang LX, Yan Y, Huang JB: **Zwitterionic surfactant/cyclodextrin hydrogel: microtubes and multiple responses**. *Soft Matter* 2011, **7**:10417–10423.
This paper reports the assembly of zwitterionic surfactant TDPS and CDs. TDPS/CDs hydrogels are obtained and assembly mechnism is studied in detail.

24. ** Zhou C, Cheng X, Zhao Q, Yan Y, Wang J, Huang J: **Self-assembly of nonionic surfactant tween 20@ 2β-CD inclusion complexes in dilute solution**. *Langmuir* 2013, **29**:13175–13182.
This paper reports the assembly of nonionic surfactant tween-20 and CDs.

25. Xu H-N, Ma S-F, Chen W: **Unique role of β-cyclodextrin in modifying aggregation of Triton X-114 in aqueous solutions**. *Soft Matter* 2012, **8**:3856–3863.

26. Alami E, Abrahmsen-Alami S, Eastoe J, Grillo I, Heenan RK: **Interactions between a nonionic gemini surfactant and cyclodextrins investigated by small-angle neutron scattering**. *J Colloid Interface Sci* 2002, **255**:403–409.

27. Abrahmsen-Alami S, Alami E, Eastoe J, Cosgrove T: **Interaction between a novel gemini surfactant and cyclodextrin: NMR and surface tension studies**. *J Colloid Interface Sci* 2002, **246**: 191–202.

28. Guerrero-Martínez A, González-Gaitano G, Viñas MH, Tardajos G: **Inclusion complexes between β-cyclodextrin and a gemini surfactant in aqueous solution: an NMR study**. *J Phys Chem B* 2006, **110**:13819–13828.

29. Zhu B, Jia L, Guo X, Yin J, Zhao Z, Chen N, *et al.*: **Controllable assembly of a novel cationic gemini surfactant containing a naphthalene and amide spacer with β-cyclodextrin**. *Soft Matter* 2019, **15**:3198–3207.

30. Zhou C, Wang D, Cao M, Chen Y, Liu Z, Wu C, *et al.*: **Self-aggregation, antibacterial activity, and mildness of cyclodextrin/cationic trimeric surfactant complexes**. *ACS Appl Mater Interfaces* 2016, **8**:30811–30823.

31. Shen J, Song L, Xin X, Wu D, Wang S, Chen R, *et al.*: **Self-assembled supramolecular hydrogel induced by β-cyclodextrin and ionic liquid-type imidazolium gemini surfactant**. *Colloids Surf A Physicochem Eng Asp* 2016, **509**:512–520.

32. Wang X, Li M, Song P, Lv X, Liu Z, Huang J, *et al.*: **Reversible manipulation of supramolecular chirality using host–guest dynamics between β-cyclodextrin and alkyl amines**. *Chem Eur J* 2018, **24**:13734–13739.

33. Li S, Zhang L, Wang B, Ma M, Xing P, Chu X, *et al.*: **An easy approach for constructing vesicles by using aromatic molecules with β-cyclodextrin**. *Soft Matter* 2015, **11**:1767–1777.

34. ** Zhou C, Cheng X, Zhao Q, Yan Y, Wang J, Huang J: **Self-assembly of channel type β-CD dimers induced by dodecane**. *Sci Rep* 2014, **4**:7533.
This paper reports the assembly of dodecane and CDs, expending the scope of host molecules from typical surfactants to non-amphiphilic dodecanes.

35. * Zhou C, Huang J, Yan Y: **Chain length dependent alkane/beta-cyclodextrin nonamphiphilic supramolecular building blocks**. *Soft Matter* 2016, **12**:1579–1585.
This paper reveals the effect of chain length on alkane/CDs assembly system.

36. Aghahosseini H, Ramazani A: **General overview on cyclodextrin-based artificial enzymes' activity**. *Curr Org Chem* 2016, **20**:2817–2836.

37. Wu C, Fan W, Zhou Y, Luo Y, Gelinsky M, Chang J, *et al.*: **3D-printing of highly uniform CaSiO 3 ceramic scaffolds: preparation, characterization and in vivo osteogenesis**. *J Mater Chem* 2012, **22**:12288–12295.

38. Zhao Q, Wang Y, Yan Y, Huang J: **Smart nanocarrier: self-assembly of bacteria-like vesicles with photoswitchable cilia**. *ACS Nano* 2014, **8**:11341–11349.

39. ** Zhao Q, Lian Z, Gao X, Yan Y, Huang J: **General approach to construct photoresponsive self-assembly in a light-inert amphiphilic system**. *Langmuir* 2016, **32**:11973–11979.
This paper proposes a general way to introduce light responsiveness into light-inert assembly system by incorporating azobenen derivatives and CDs into target assembly system.

40. Kang Y, Cai Z, Tang X, Liu K, Wang G, Zhang X: **An amylase-responsive bolaform supra-amphiphile**. *ACS Appl Mater Interfaces* 2016, **8**:4927–4933.

41. Hou XF, Chen Y, Liu Y: **Enzyme-responsive protein/polysaccharide supramolecular nanoparticles**. *Soft Matter* 2015, **11**:2488–2493.

42. Han X, Chen Y, Sun HL, Liu Y: **Enzyme-responsive supramolecular nanoparticles based on carboxyl-modified cyclodextrins for dual substrate loading**. *Asian J Org Chem* 2018, **7**: 870–874.

43. Zhang X, Ma X, Wang K, Lin S, Zhu S, Dai Y, *et al.*: **Recent advances in cyclodextrin-based light-responsive supramolecular systems**. *Macromol Rapid Commun* 2018, **39**:1800142.

44. Wang Y, Ma N, Wang Z, Zhang X: **Photocontrolled reversible supramolecular assemblies of an azobenzene-containing surfactant with α-cyclodextrin**. *Angew Chem Int Ed* 2007, **46**: 2823–2826.

45. Sun R, Xue C, Ma X, Gao M, Tian H, Li Q: **Light-driven linear helical supramolecular polymer formed by molecular-recognition-directed self-assembly of bis(p-sulfonatocalix[4]arene) and pseudorotaxane**. *J Am Chem Soc* 2013, **135**: 5990–5993.

46. Li Z, Wang G, Wang Y, Li H: **Reversible phase transition of robust luminescent hybrid hydrogels**. *Angew Chem Int Ed* 2018, **57**:2194–2198.

47. Xie F, Ouyang G, Qin L, Liu M: **Supra-dendron gelator based on azobenzene–cyclodextrin host–guest interactions: photoswitched optical and chiroptical reversibility**. *Chem Eur J* 2016, **22**:18208–18214.

48. Huh KM, Tomita H, Ooya T, Lee WK, Sasaki S, Yui N: **pH dependence of inclusion complexation between cationic poly(ε-lysine) and α-cyclodextrin**. *Macromolecules* 2002, **35**: 3775–3777.

49. Park C, Oh K, Lee SC, Kim C: **Controlled release of guest molecules from mesoporous silica particles based on a pH-responsive polypseudorotaxane motif**. *Angew Chem Int Ed Engl* 2007, **46**:1455–1457.

50. Joung YK, Ooya T, Yamaguchi M, Yui N: **Modulating rheological properties of supramolecular networks by pH-responsive double-axle intrusion into γ-cyclodextrin**. *Adv Mater* 2007, **19**: 396–400.

51. Guo W, Wang J, Lee SJ, Dong F, Park SS, Ha CS: **A general pH-responsive supramolecular nanovalve based on mesoporous organosilica hollow nanospheres**. *Chem Eur J* 2010, **16**: 8641–8646.

52. Jiang L, Deng M, Wang Y, Liang D, Yan Y, Huang J: **Special effect of β-cyclodextrin on the aggregation behavior of mixed cationic/anionic surfactant systems**. *J Phys Chem B* 2009, **113**:7498–7504.

53. Zhou C, Cheng X, Yan Y, Wang J, Huang J: **Reversible transition between SDS@ 2β-CD microtubes and vesicles triggered by temperature**. *Langmuir* 2014, **30**:3381–3386.

54. Yang S, Yan Y, Huang J, Petukhov AV, Kroon-Batenburg LMJ, Drechsler M, *et al.*: **Giant capsids from lattice self-assembly of cyclodextrin complexes**. *Nat Commun* 2017, **8**:15856.

55. Jiang L, de Folter JW, Huang J, Philipse AP, Kegel WK, Petukhov AV: **Helical colloidal sphere structures through thermo-reversible Co-assembly with molecular microtubes**. *Angew Chem Int Ed* 2013, **52**:3364–3368.