Nanostructures

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Synthesis of Supramolecular Nanocapsules Based on Threading of Multiple Cyclodextrins over Polymers on Gold Nanoparticles**

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Polymer nanocapsules, or hollow polymer nanospheres, have attracted increasing interest because of their great potential for applications in chemistry, materials, biomedicine, and biotechnology.[1,2] Currently, methods towards the production of polymeric nanocapsules include cross-linking of self-assembled block copolymer micelles,[3–5] emulsion polymerization,[6,7] dendrimer modification,[8–10] and layer-by-layer adsorption of polyelectrolytes[11–14] or polymerization[15] on spherical nanoparticles as templates. Multiple α-cyclodextrin (α-CD) rings were found to thread over a polymer such as poly(ethylene glycol) (PEG) and form a supramolecular polyrotaxane structure,[16–19] which has inspired the development of interesting nanostructures such as molecular tubes,[20,21] as well as various supramolecular materials for electronics[22–24] and biomaterials[25–29] applications. Formation of polyrotaxane films on gold surfaces was also detected using surface plasmon spectroscopy.[30]

Herein, we demonstrate a supramolecular approach for creating novel polymer nanocapsules based on polyrotaxane formation on the surface of gold nanoparticles (AuNPs). PEG chains grafted onto AuNPs threaded through multiple α-CD rings, forming a supramolecular outer layer composed of pseudopolyrotaxane columns perpendicular to the nanoparticle surface. Stoppering the ends of the polymer thread to confine α-CD onto the nanoparticle surface, cross-linking the α-CD rings and then removing the AuNP cores produced supramolecular nanocapsules with a shell consisting of α-CD polyrotaxane columns. The number of α-CD units making up the supramolecular nanocapsules may prove tunable, and the capsules may be novel nanomaterials for different applications.

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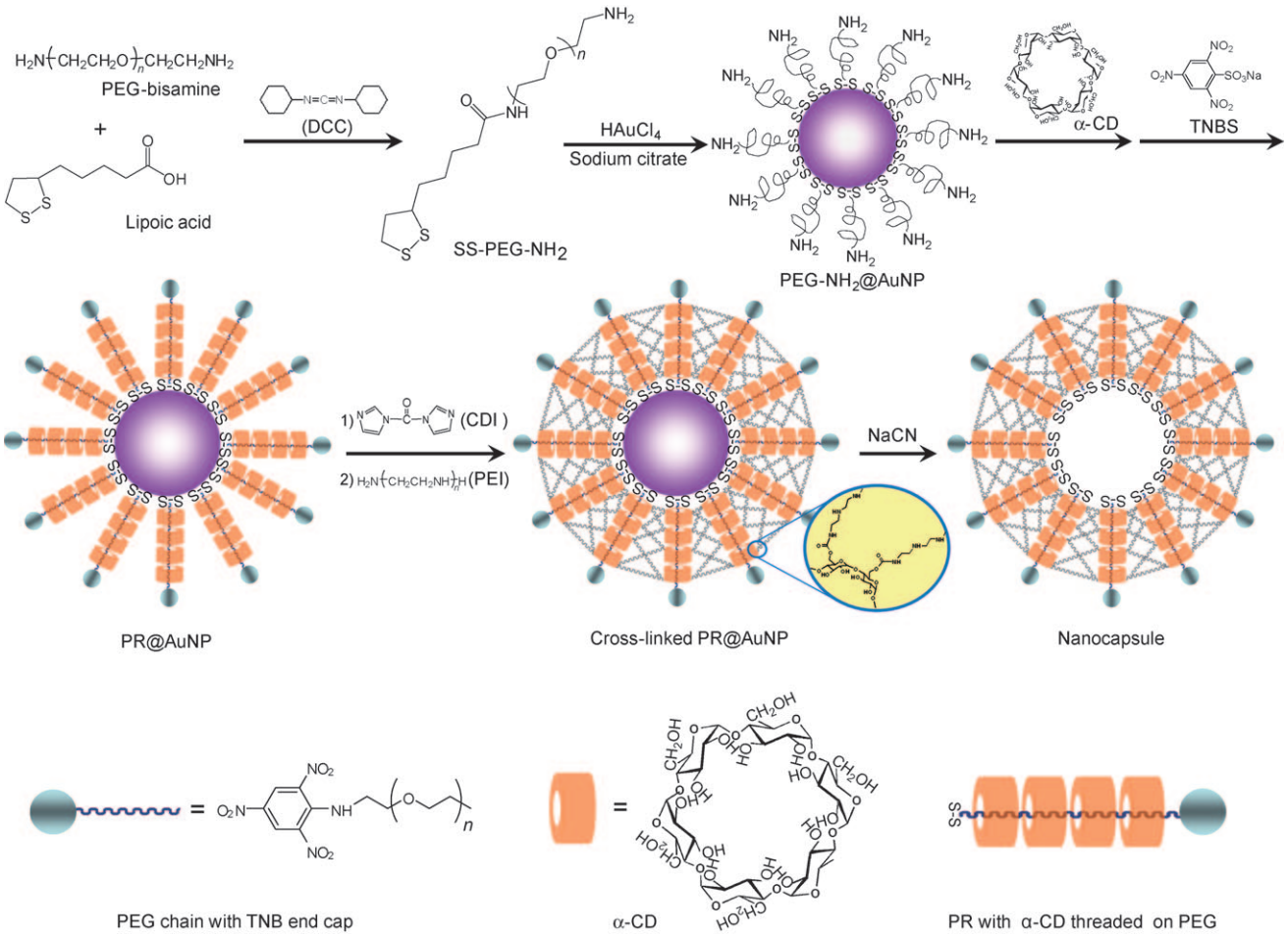
To commence the synthesis of the supramolecular nanocapsules (Scheme 1), PEG-bisamine, with a number-average molecular weight (M_n) of 2000 g mol^{-1}, was coupled with one molecule of lipoic acid to give PEG with disulfide group at one end and amino group at the other end (SS-PEG-NH_2). We synthesized AuNPs in the presence of SS-PEG-NH_2, giving AuNPs with PEG-monoamine affixed to the surface through disulfide anchors (PEG-NH_2@AuNP).[31] Mixing PEG-NH_2@AuNP with saturated α-CD aqueous solution resulted in formation of a pseudopolyrotaxane α-CD-PEG inclusion complex on the AuNP surfaces, which consisted of multiple α-CD rings threaded over the PEG chains grafted onto the AuNPs (see the Supporting Information for details). To block the end of the PEG chains and prevent the dethreading of α-CD, the terminal amino groups were treated with sodium 2,4,6-dinitrobenzenesulfonate (TNBS), to form a bulky stopper that is big enough to trap the threaded α-CD on the PEG chains, giving a polyrotaxane (PR) structure on the AuNP surfaces (PR@AuNP). PR@AuNP was not water-soluble, as was thecase for previuosly reported conventional PRs.[25] The many hydroxy groups incorporated in α-CD units were then activated with 1,1′-carbonyl diimidazole (CDI), and treated with branched polyethylenimine (PEI; M_n = 600 g mol^{-1}), forming cross-links between the polyrotaxane units. The cross-linked PR@AuNP was water-soluble as the PEI segments rendered the polyrotaxane shell more hydrophilic. However, it was not soluble in THF, because PEI is too hydrophilic to be dissolved in THF. Finally, the AuNP cores of the cross-linked PR@AuNP were removed by addition of 1.0 M NaCN solution, through conversion of Au^0 into $[Au(CN)_4]^-$ in the presence of oxygen in water,[32] which gave the target supramolecular nanocapsules consisting of cross-linked α-CD-based polyrotaxane shells.

UV/Vis spectroscopy was used to characterize the intermediate and final products during the synthesis procedures (Figure 1), because AuNPs have visible absorption[15] and the 2,4,6-trinitrobenzene (TNB) group has UV absorption. TNBS had no absorption at wavelengths greater than 500 nm (Figure 1a) and formed a yellowish solution. The UV/Vis spectrum of PEG-NH_2@AuNP had an absorption band with a maximum at around 530 nm, owing to the surface plasmon resonance of AuNPs (Figure 1b), which resulted in a violet-red color. After the formation of the supramolecular polyrotaxane shell around the AuNP cores, the cross-linked PR@AuNP continued to absorb at around 530 nm (Figure 1c), which was still a result of AuNP plasmon absorption. The cross-linked PR@AuNP gave an additional absorption band at around 420 nm owing to the TNB stopper group of the polyrotaxane (Figure 1c). The plasmon absorption band of the cross-linked PR@AuNP at 530 nm reflects isolated



Scheme 1. Synthesis of the supramolecular nanocapsules, including illustrations of the structures of the nanocapsules and precursors.

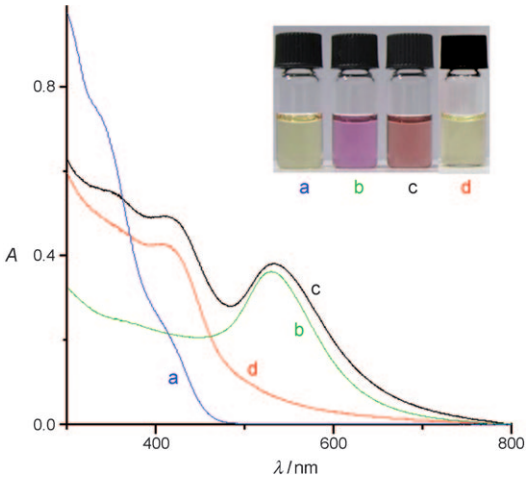


Figure 1. UV/Vis spectra and appearance (inset) of aqueous solutions of the nanocapsules and precursors: a) TNBS; b) PEG-NH_2@AuNP, c) cross-linked PR@AuNP; d) nanocapsules.

AuNP cores coated by a supramolecular polyrotaxane shell rather than multiple AuNPs entrapped within a supramolecular polyrotaxane shell. The cross-linked PR@AuNP solution had a reddish-brown color combining those of PEG-NH_2@AuNP and TNBS (Figure 1c). The removal of the AuNP cores and formation of supramolecular nanocapsules were monitored by changes in the UV/Vis spectrum. The AuNP etching process was followed by a loss of the Au plasmon absorbance at 530 nm. The nanocapsules showed no Au plasmon absorption at 530 nm, but the absorption band at around 420 nm, owing to the TNB stopper group, remained (Figure 1d). As a result, the nanocapsule solution was a yellowish color, similar to that of TNBS.

The ^{1}H NMR spectrum of PEG-NH_2@AuNP (Figure 2b) showed mainly the signal of the PEG units at around 3.6 ppm. In the spectrum of cross-linked PR@AuNP (Figure 2c), signals were detected corresponding to α-CD (Figure 2a), the PEI cross-linker segments, the threading PEG units, and the end capping TNB group, although these peaks were broadened because of the restriction of molecular motion by the cross-linking and chain interlocking. The spectrum of the supramolecular nanocapsule (Figure 2d) was similar to that of cross-linked PR@AuNP, since the nanocapsule only lacked the AuNP core.

The compositions of PEG-NH_2@AuNP and PR@AuNP were estimated using thermogravimetric analysis (see the Supporting Information). PEG-NH_2@AuNP underwent thermal decomposition up to a weight loss of 81%, owing to the decomposition of the PEG units. The remaining 19% arose

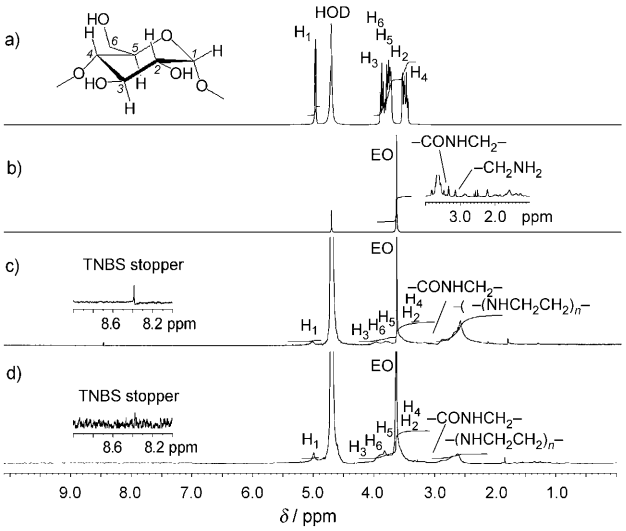


Figure 2. 400 MHz ^{1}H NMR spectra of the supramolecular nanocapsule in comparison with its precursors in D_2O: a) α-CD; b) PEG-NH_2@AuNP; c) cross-linked PR@AuNP; d) nanocapsule.

from the AuNP cores (15%) and a residue of PEG (4%). PR@AuNP underwent a two-step thermal degradation. The first step is mainly attributed to the decomposition of α-CD, and the second mainly to SS-PEG-NH_2. The remaining 13% corresponded to the AuNP cores (7%) and residues of α-CD and PEG (6%). Hence, it was estimated that PR@AuNP contained 77% α-CD, 14% PEG and 7% gold.

The AFM image of the cross-linked PR@AuNP particles deposited on a glass substrate (Figure 3a,c) indicates an average diameter of 49 nm and heights in the range of 15–22 nm (height analysis given in the Supporting Information). The polyrotaxane shell is soft, whereas the AuNP core is rigid. The larger diameter corresponds to the partially flattened geometry, while the height range correlates to the size of AuNP core. The supramolecular shell integrity of the nanocapsules was maintained after the removal of the AuNP cores (Figure 3b,d). The supramolecular nanocapsules appear to be flattened on the substrate, owing to the soft nature of the supramolecular shell, and to the sample–substrate interactions. A similar observation was reported for hollow nanoparticles of poly(*N*-isopropylacrylamide) synthesized through AuNP templates.[15] The hollow nature of the supramolecular nanocapsules is clear. The resultant supramolecular nanocapsules deposited on the substrate have outer and inner average diameters of 54 and 20 nm, respectively, giving an average shell thickness of 17 nm, which corresponds to the length of the α-CD-based polyrotaxanes formed on the AuNP surfaces.

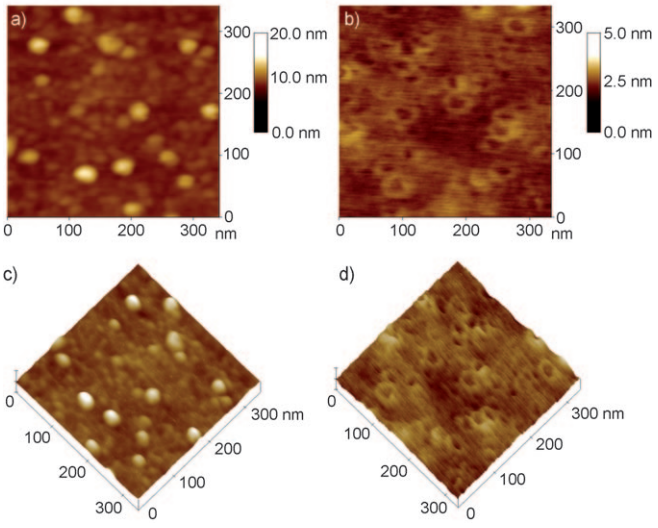


Figure 3. AFM images of the nanocapsules and cross-linked PR@AuNP: a) cross-linked PR@AuNP; b) nanocapsules; c) 3D rendering of AFM image of cross-linked PR@AuNP; d) 3D rendering of AFM image of nanocapsules.

The synthesis of monolayer spheres using thiolated β-CD directly anchored on AuNP surface, rather than by threading multiple CD units onto polymer chains,[33] resulted in shell thicknesses fixed to that of one β-CD molecule, which hindered the formation of robust hollow spheres, such as ours, which could be clearly observed under AFM. The monolayer-thick spheres instead appeared as solid dots under AFM.[33]

In summary, we have successfully developed a strategy to synthesize novel supramolecular nanocapsules based on polyrotaxane formation between α-CD and PEG anchored to AuNP surfaces, to our knowledge, the first case of such polyrotaxane formation on nanoparticles. Both the cavity size and the shell thickness of the supramolecular nanocapsules could be tuned with the size of the AuNP cores and the length of the α-CD-based polyrotaxane columns, respectively. The cyclodextrin shell of the supramolecular nanocapsules may be further modified to alter the functionality of the nanocapsules. For example, removal of the PEG threads may lead to spheres with porous shells, which can bind guest molecules.

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