Colloidal gold nanoparticle formation derived from self-assembled supramolecular structure of cyclodextrin/Au salt complex†

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We present a novel procedure for the formation of colloidal gold nanoparticles (AuNPs) derived from the supramolecular self-assembled structure of a cyclodextrin (CD)/Au salt complex (SCA) without the necessity for additional reducing or stabilizing agents. The SCA served as a solid template for the formation of gold seeds by solid-state thermal treatment within the confining environment of the α-CD, i.e., the matrix of the SCA. Subsequently, thermally treated SCA, denoted as T-SCA, was placed (without further treatment) into an aqueous medium and gold seeds were nucleated for the formation of α-CD-stabilized AuNPs at room temperature. The surface topology of SCA, as revealed by field-emission scanning electron microscopy (FE-SEM), consisted of flaky plate-like structures. Wide angle X-ray diffraction (WXRD) revealed that the surface topology of SCA resulted from a transformation in the crystalline structure of α-CD from the cage-type to the hexagonally ordered channel-type. The structure transformation on the surface of SCA was attributed to the nucleated self-assembly of surface α-CD molecules by Au salt. From combined FE-SEM, energy-dispersed X-ray spectroscopy (EDXS), WXRD and differential scanning calorimetry (DSC) results, it was concluded that the thermal treatment of SCA led to the formation of gold seeds, attributed to the reduction and aggregation of some Au salt molecules, confined within the interface between the cage-type and channel type structure of the SCA. After placement of T-SCA into an aqueous solution, the growth and stabilization of AuNPs by α-CD were verified by UV-vis spectroscopy. The formation of AuNPs by this novel method, can be considered a one step seed-mediated growth process. The resulting AuNPs are spherical in morphology, narrowly size distributed and possesses excellent stability. Furthermore, the AuNPs size is tunable by simply controlling water content during nanoparticle growth.

Introduction

Since the pioneering work of Faraday,1 the synthesis and study of gold nanoparticles (AuNPs) have been of great scientific interest due to their unique optical properties2–4 and wide range of applicability in catalysis,5–6 chemical sensing,7–9 and photonics.10,11 Additionally, AuNPs find use in biotechnology applications ranging from biolabeling12,13 to cancer diagnostics14 to targeted drug delivery.15 For example, Mirkin and co-workers16 have reported the use of DNA-functionalized AuNPs as colorimetric sensors for the detection of biological targets. El-Sayed et al.17,18 have demonstrated that antibody-conjugated AuNPs are useful probes for living cells due to the sensitivity of their plasmon resonance band in the visible near-IR region. Furthermore, AuNPs in the size range 2–4 nm have been shown to successfully deliver photo-sensitizer drugs to cancer cells,19 and that active targeting can be achieved by decorating AuNPs with receptors to investigate their specific cellular uptake.20,21

Owing to the demand of AuNPs, simple and widely applicable preparation methods are desirable that allows for the facile control of the size, shape and dispersion of AuNPs.22 A general route to preparing AuNPs is the reduction of Au salt by various methods (e.g., wet chemical reduction, thermolysis, femtosecond laser ablation, UV irradiation, ultrasonolysis, radiolysis, etc.) in the presence of the appropriate stabilizer (e.g., thiol ligands, surfactants, polymers, etc.), or templates (dendrimer, microemulsion, micelle, reverse micelle, membrane, solid surface, polyelectrolyte, etc.).23 Above all, greater effort has been devoted to the synthesis of AuNPs using solution phase wet chemical reduction methods.

A common wet chemical approach for the synthesis of AuNPs is by the citrate reduction of Au salt in aqueous media under boiling conditions (so-called “Turkevich and Frens method”),

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resulting in 10–100 nm size AuNPs with a relatively narrow size distribution.24,25 Another common wet chemical method for the synthesis of AuNPs is seed-mediated growth.26,27 In seeding-growth methods, very small AuNPs are first prepared and subsequently used as seeds (nucleation centers) for the growth of larger size AuNPs (5–200 nm). On the other hand, a two-phase reaction, developed by Brust and co-workers,28 has been extensively investigated to produce very small AuNPs (1–5 nm) with a narrow size distribution. The reaction utilizes a borohydride reducing agent, a phase-transfer reagent and an alkylthiol stabilizer in a biphasic organic solvent–water system to produce AuNPs. Since its discovery, the Brust method has been widely employed to produce AuNPs, and due to its versatility numerous reducing agents29–36 and capping agents30–32,37–42 together with different preparation techniques43–47 have been used to extend the method. Despite the numerous synthetic methods currently available to produce AuNPs, as partially highlighted above, the ever increasing utility of AuNPs as the enabling material for the successful realization of new technologies continues to motivate new approaches for AuNP development. Furthermore, these new approaches should be facile and environmentally benign when compared to current methods.48

Here, we present a novel procedure for the formation of colloidal gold nanoparticles derived from the supramolecular self-assembly of a cyclodextrin (CD)/Au salt complex without the necessity for additional reducing and stabilizing agents. The resulting AuNPs are spherical in morphology, narrowly size distributed and possesses excellent stability. Furthermore, the AuNPs size is tunable by simply controlling water content during the reaction.

Gold nanoparticles were prepared from an assembly of unmodified α-CD containing Au salt molecules, herein denoted as SCA. The SCA served as a solid template for the formation of gold seeds by solid-state thermal treatment within the confining environment of the α-CD self-assembled structure. Subsequently, the thermally treated SCA, herein denoted as T-SCA, was placed (without further treatment) into an aqueous medium and gold seeds were nucleated for the formation of α-CD-stabilized AuNPs at room temperature. Fig. 1 illustrates a schematic for the mechanism of AuNP formation. An advantage of the current process, in comparison to other popular methods of AuNP formation, is that Au salt was reduced and stabilized in an aqueous medium by α-CD, a bio-derived and compatible molecule, without the additional usage of harmful and non-biocompatible reducing/stabilizing agents. Additionally, AuNPs capped with α-CD molecules make them tremendously attractive for applications ranging from sensors involving host–guest molecular recognition to the delivery of hydrophobic therapeutic molecules combined with the simultaneous molecular level imaging capabilities of the AuNPs. The simplicity and low environmental impact of the current process to produce α-CD-stabilized AuNPs make it attractive for large-scale production.

Results and discussion

From a practical viewpoint the procedure for colloidal AuNP formation is straightforward. The SCA was prepared by mixing unmodified α-CD into an Au salt/tetrahydrofuran (THF) solution. The mixture was allowed to stand for 48 h at room temperature, and then collected and rinsed with THF. The resulting material was a yellowish powder, which indicated the presence of Au salt within the α-CD self-assembled complex. The SCA was then thermally treated at 363 K for 10 h resulting in a yellowish-brown powder, which suggested the formation of nanometre-sized gold seeds confined within the α-CD complex.49 Placement of the T-SCA in deionized water resulted in a burgundy red solution, an indication of well-dispersed AuNP formation in the aqueous solution without the need of additional ingredients.

Fig. 2 shows SEM images of unmodified α-CD, THF-treated α-CD and SCA. Whereas unmodified α-CD exhibited no noticeable surface topology, THF-treated α-CD exhibited micron-sized flakes atop the surface (see Fig. 2b). THF caused the self-assembly reorganization of surface α-CD molecules, even

Fig. 1 Schematic illustration for the mechanism of colloidal AuNP formation derived from self-assembled supramolecular structure of α-CD/Au salt complex.
though THF is a poor solvent for \( \alpha\)-CD.\(^{50}\) Thus, we believe that THF induced the assembly of surface \( \alpha\)-CD molecules into flaky plate-like structures, which could then be exploited as a solid-state template for the production of gold seeds. Similar to the THF-treated \( \alpha\)-CD, the surface of the SCA was also covered with micron-sized flaky plate-like structures (see Fig. 2c). However, one noticeable difference between the morphologies of THF-treated \( \alpha\)-CD and the SCA was the shape and orientation of the surface structures. For the SCA, surface structures appeared hexagonally shaped and layered, while for THF-treated \( \alpha\)-CD, they appeared irregular in shape and disordered. In addition, from inductively coupled plasma atomic emission spectroscopy (ICP-AES) measurements, it was confirmed that Au atoms were present at a concentration of \( \text{ca. } 3.20 \times 10^4 \text{ ppm} \) within the SCA. Field-emission scanning electron microscopy (FE-SEM) equipped with energy dispersed X-ray spectroscopy (EDXS) distinctly showed that Au atoms were predominantly present in regions of the SCA exhibiting plate-like structures atop the surface (see Fig. S1 in the ESI†). These results suggested that Au salt molecules were immobilized around the ordered flaky plate-like regions of the SCA, or in other words, the ordered flake-like surface topology of the SCA may be attributed to the presence of Au salt during the self-assembly of \( \alpha\)-CD molecules in THF.

We obtained further information about the morphology of the solid-state template, SCA, for the formation of AuNPs via wide-angle X-ray diffraction (WXRD) measurements. As shown in Fig. 3a, unmodified \( \alpha\)-CD exhibited characteristic peaks of a cage-type crystalline structure, consistent with previous studies.\(^{51,52}\) The diffraction trace of THF-treated \( \alpha\)-CD (see Fig. 3b) resembled that of natural \( \alpha\)-CD, although slight indications of a structural transformation was evident. In contrast, the diffraction trace of SCA (see Fig. 3c) showed new peaks at \( 2\theta = 12.9^\circ (110), 19.6^\circ (210) \) and \( 22.4^\circ (300) \), in addition to the drastically reduced peaks corresponding to the cage-type crystalline structure of \( \alpha\)-CD. (Additional WXRD scans are available in Fig. S2 of the ESI†.) Hence, it is understood that the self-assembly and morphological change of the SCA were accompanied by a transformation of the crystalline structure of \( \alpha\)-CD from the cage-type to the hexagonally well-ordered channel-type.\(^{53-56}\) As THF-treated \( \alpha\)-CD does not exhibit the characteristic peaks of the channel-type structure, we put forth the notion that during the molecular self-assembly process of \( \alpha\)-CD molecules in THF, Au salt may act as a nucleus to initiate the arrangement of \( \alpha\)-CD into the hexagonally ordered channel structure, i.e., nucleated self-assembly, resulting in the observed flaky plate-like layered morphology. Due to the limited compatibility between \( \alpha\)-CD and THF, nucleated self-assembly

![Fig. 2](image2.png)

**Fig. 2** The morphological images of (a) unmodified \( \alpha\)-CD, (b) THF-treated \( \alpha\)-CD and (c) SCA visualized by FE-SEM. Insets: (b) image of THF-treated \( \alpha\)-CD powder, (c) image of SCA powder and magnified SEM image of SCA.

![Fig. 3](image3.png)

**Fig. 3** WXRD patterns of (a) unmodified \( \alpha\)-CD, (b) THF-treated \( \alpha\)-CD, (c) SCA and (d) T-SCA.
was expected to occur primarily at the surface of \( \alpha\)-CD aggregates.

The self-assembled aggregate of \( \alpha\)-CD containing Au salt, i.e., the SCA, served as a solid-state template for the formation of Au seeds geometrically confined within the \( \alpha\)-CD self-assembled matrix. Solid-state thermal treatment of the yellowish SCA powder (see Fig. 2c inset) led to a yellow/brown powder (see Fig. 4a inset), an indication of thermal nucleation for the formation of gold seeds.\(^\text{49}\) As expected from the color change, the WXRD pattern of T-SCA (see Fig. 3d and S2 in the ESI†) was comparatively different from that of SCA. It was observed that the peaks corresponding to the cage-type structure of \( \alpha\)-CD either considerably decreased (2\( \theta \) = 14.3\(^\circ\)) or disappeared (2\( \theta \) = 12\(^\circ\) and 21.6\(^\circ\)) in T-SCA, while the characteristic peaks for the channel-type crystalline structure (2\( \theta \) = 19.6\(^\circ\) and 22.4\(^\circ\)) were still present. In addition, the peaks of T-SCA broadened. The results suggested that the disruption (or breaking) of the cage-type crystalline structure was attributed to the formation of Au seeds in T-SCA due to the reduction of Au salt molecules during thermal treatment. In fact, we hypothesize that SCA is composed of two regions with different crystalline structures. In the interior of SCA, the complex had a cage-type structure (natural structure of \( \alpha\)-CD), i.e., the structure was not affected by the THF/Au salt solution, whereas for the exterior of SCA, the complex had an ordered flaky plate-like layer morphology with channel-type structure due to THF/Au salt solution induced reorganization of the surface of SCA. The disruption of the cage structure meant that Au salt molecules were positioned in between the cage-type and channel-type structure and that Au seed formation took place at the interface between the two phases. Furthermore, the results strongly implied that Au salt molecules led to the nucleated self-assembly of \( \alpha\)-CD molecules into the ordered flakes structure in SCA. (We note, that the flaky plate-like layers were not the result of an inclusion complex between \( \alpha\)-CD and Au salt, as morphological defects such as torsion, bending or cracking by the growth of Au seeds were not observed in T-SCA (see Fig. 4a).) Furthermore, no diffraction peaks corresponding to the face-centered cubic (fcc) structure of typical Au metal were observed after thermal treatment of SCA, T-SCA (see Fig. S3 in the ESI†), and DSC data showed that the complete transformation of Au salt into the bulk Au metal in the solid matrix occurred after 28 h of thermal annealing at 363 K (see Fig. 4b). Combined, these findings support the hypothesis that some Au salt molecules were reduced during the thermal treatment, and that reduced Au atoms aggregated to form Au seeds within T-SCA; or in other words, Au seeds geometrically nano-confined within the \( \alpha\)-CD solid template. Thus, after 10 h of thermal annealing, the time used in the current study, it is thought to be that both Au seeds and Au salt molecules coexisted within the T-SCA.

To form AuNPs, T-SCA was placed in deionized water at room temperature. As shown in Fig. 5, the aqueous solution changed color from light purple to burgundy red with increasing time, indicating the formation of well-dispersed AuNPs.\(^\text{24,26,27,57}\)

![Fig. 4](image) (a) SEM image of T-SCA and (b) DSC plots of THF-treated \( \alpha\)-CD and SCA as a function of time at 363 K. Inset: (a) image of T-SCA powder.

![Fig. 5](image) Time-variant photo-images and UV-vis spectra of T-SCA aqueous solution.
We confirmed that just mixing \( \alpha\text{-CD} \) and Au salt into water does not lead to the formation of \( \text{AuNPs} \) (see Fig. S4 in the ESI†). Furthermore, the addition of \( \text{SCA} \) into water at room temperature led to black precipitate and not \( \text{AuNPs} \) (see Fig. S5 in the ESI†). Combined, the observations reveal that the presence of Au seeds in \( \text{T-SCA} \), formed during solid-state thermal annealing, played a key role for the formation of \( \text{AuNPs} \) by acting as nucleation sites for \( \text{AuNP} \) growth.

As expected from the change in color of the \( \text{T-SCA} \) solution, the strong and broad surface plasmon resonance (SPR) band, a marker of well-dispersed \( \text{AuNPs} \), developed and shifted to lower wavelengths with time after water addition to \( \text{T-SCA} \) (see Fig. 5). Furthermore, the 220 nm band decreased with time, and the 280 nm band increased with time. The 220 nm band can be assigned to the charge transfer of the \( \text{AuCl}_4^- \), and the 280 nm band can be assigned to the lone pair interaction of \( \alpha\text{-CD} \) hydroxyl groups with the Au surface.\(^{58-61}\) The UV-vis spectra indicated that the reduction of \( \text{AuCl}_4^- \) and subsequent stabilization of the growing intermediate nucleation Au species by \( \alpha\text{-CD} \) occurred in the aqueous solution. Therefore, the mechanism for \( \text{AuNP} \) formation may be explained as follows: when \( \text{T-SCA} \) was placed in water, Au seeds confined within the solid-state template were first stabilized by \( \alpha\text{-CD} \) molecules, and subsequently, the stabilized Au seeds formed the nucleation burst structure with the unreduced Au salt molecules. At this time, Au seeds served as nucleation centers for \( \text{AuNP} \) formation, and \( \alpha\text{-CD} \) molecules served to reduce and stabilize the growing intermediate nucleating Au seeds into \( \alpha\text{-CD} \)-stabilized \( \text{AuNPs} \), as schematically illustrated in Fig. 6. The proposed mechanism of \( \text{AuNP} \) formation is similar to seed-mediated nucleation and growth in which smaller metal nanoparticles serve as nucleation centers for the growth of larger nanoparticles. Seed growth methods are multi-step wet chemical process typically requiring the additional use of organic and reducing additives. Additionally, an outside source of Au salt is necessary for nanoparticle growth. In the current scheme, the growth process is one step and requires no outside Au salt source. Furthermore, the reducing and stabilizing agent, \( \alpha\text{-CD} \), is a green material.

Interestingly, the size of the \( \text{AuNPs} \) could be simply controlled by manipulating the amount of water in the reaction medium. To control the size of \( \text{AuNPs} \), \( \text{T-SCA} \) was placed in 5, 10 and 15 mL of deionized water. As shown in Fig. 7, size-controllable \( \text{AuNP} \) formation was achieved by adjusting the volume of the aqueous reaction medium, a greater aqueous volume led to smaller

\( \text{AuNPs} \) and smaller particle size distribution. The quantitative mean sizes for \( \text{AuNPs} \) in 5, 10 and 15 mL of water, as determined by dynamic light scattering (DLS), were ca. 19.1 (±5.5), 16.9 (±4.0) and 12.4 (±1.2) nm, respectively, which were in good agreement with the TEM results. The decrease in \( \text{AuNP} \) size and size distribution with increasing water amount likely arose from the greater dispersion of Au seeds and Au salt in aqueous medium (so-called “loosen nucleation burst structure”), although the driving force of size variation is not fully understood. In addition, the \( \alpha\text{-CD} \)-stabilized \( \text{AuNPs} \) were highly stable and showed no signs of aggregation after a shelf-life greater than 6 months. Varying process parameters, \( \text{e.g.} \), control of the ratio

![Fig. 6](image1.png)  
**Fig. 6** Schematic illustration of the proposed mechanism for \( \text{AuNP} \) formation in water.

![Fig. 7](image2.png)  
**Fig. 7** TEM images and size distributions estimated from DLS of \( \text{T-SCA} \) aqueous solution with (a) 5 mL, (b) 10 mL and (c) 15 mL of water addition.
between α-CD and Au salt in the complex, employment of other cyclodextrins, e.g., β-CD and γ-CD, and process conditions, e.g., thermal annealing time, temperature and agitation, may provide more precise control for the size and shape of AuNPs. These studies are currently underway.

Conclusions

We have developed a new approach for the formation of AuNPs derived from a self-assembled supramolecular structure of the CD/Au salt complex. The process is facile and requires no additive reducing or stabilizing agents. Au seeds are formed by the solid-state thermal treatment of Au salt in the confined interface between the cage-type and channel-type structure of α-CD solid state template. Nanoparticle nucleation and growth takes place in an aqueous solution at room temperature via seed-mediated growth without the necessity for additional reducing or stabilizing agents. Resulting AuNPs are stabilized with α-CD, a bio-friendly molecule that may participate in host–guest interactions with foreign guest molecules; thus, making the α-CD-stabilized AuNPs attractive for applications ranging from nanosensors to delivery agents; and as nanoparticles possesses facile tunable surface chemistry based on host–guest interactions.

Experimental

Materials

α-Cyclodextrin (α-CD) and hydrochloroauric acid trihydrate (HAuCl₄·3H₂O, 99.9%) were purchased from Aldrich Chemical Co. Tetrahydrofuran (THF, HPLC) was supplied from Acros Organics. All materials were used as received without any additional purification.

Preparation of the self-assembled α-CD/Au salt complex and AuNP synthesis

150 mg of α-CD was first added in 0.3 mL of hydrochloroauric acid trihydrate solution (0.254 M in THF). The mixture was allowed to stand for 48 h at room temperature, and collected and rinsed with THF. The yellowish powder, which indicates the presence of Au salt in α-CD molecules, was obtained after drying and denoted as SCA (self-assembly of α-CD/Au salt). The SCA was thermally treated at 363 K for 10 h and the resulting powder (denoted as T-SCA) had a yellowish-brown color, indicating nucleation of Au salt. Then, 5, 10 and 15 mL of deionized water were individually added to 10 mg of T-SCA and the color of aqueous solution changed to burgundy red.

Characterization

The surface morphologies of unmodified α-CD, THF-treated α-CD, SCA and T-SCA were visualized by field-emission scanning electron microscopy (FE-SEM, XL30 FEG-SEM). The FE-SEM samples were coated with a thin conductive Ir layer (thickness: 5 nm) prior to observation. The content of Au in SCA was measured by inductively coupled plasma atomic emission spectroscopy (ICP-AES, Optima-4300 DV) with argon plasma source (6000 K), and the sample was analyzed three times and averaged. The position of Au atom in SCA was verified by using FE-SEM equipped with energy dispensed X-ray spectroscopy (Oxford EDXS operated with Quanta FE-ESEM) under low vacuum (0.9 Torr) without coating of conductive layer. Wide-angle X-ray diffraction (WXRD) patterns were obtained at room temperature on a Bruker D8 Discover diffractometer with a Cu Kα radiation source (wavelength = 0.154 nm). The supplied voltage and current were set to 40 kV and 40 mA, respectively. Powder samples were mounted using a plain microscope slide and scanned at a rate of 2θ = 3° min⁻¹ between 3 and 80°. To evaluate the thermal reduction time of Au salt in SCA, differential scanning calorimetry (DSC) analysis was performed using a TA DSC Q2000 under N₂ flow at 363 K as a function of time without removal of thermal history. The progress of AuNP formation was followed by UV-vis absorption spectrometry (Agilent UV-Visible ChemStation, Model 8453) in the range of 200–800 nm with 1 nm resolution. Quartz cuvettes with a 1 cm optical length were used. The transmission electron microscopy (TEM) images (Philips CM100 TEM, 100 keV) were taken of the direct sampling of the AuNPs solution on carbon-coated copper grids. Resulting micrographs were obtained at magnification of x340 000. The mean size of AuNPs was measured with a dynamic light scattering (DLS) method using a Brookhaven Instruments BI-200SM, consisted of a double-pumped continuous Nd:YAG laser (wavelength 532 nm, 100 mW) and photomultiplier. Measurements were performed at a 90° angle for 3 min and repeated a minimum of three times per sample. The measured time correlation functions were analyzed by autocorrelation using the method of the cumulants, providing an average value of the intensity-average particle size and particle polydispersity index (PDI). Intensity-average and number-average particle size distributions were calculated using the Laplace inversion program, CONTIN.

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