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Highly Stable, Water-Soluble CdSe/ZnS/CdS/ZnS Quantum Dots with Additional SiO$_2$ shell

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Abstract

Quantum dots (QDs) are fluorescent nanocrystals extensively used today in research and applications. They attract much interest due to the high photostability and fluorescence quantum yields close to 100%. The best QDs are made by synthesis in organic media, and they have to be transferred into aqueous solutions if biomedical applications are concerned. An advanced method for rendering QDs water-soluble is to coat them with hydrophilic SiO$_2$-layer. However, growing a silica shell with a predetermined thickness is a problem, because uncertain values of the molar extinction coefficients (ε) of core/shell QDs made it impossible to calculate precise yields of the chemical reactions involved. Here we suggest an approach to solving this problem by constructing the structural models of *per se* and silica-coated QDs followed by measuring ε in a course of the QD synthesis, thus carrying out precise quantitative reactions. Proceeding in such a way, we prepared the CdSe/ZnS/CdS/ZnS QDs with the structure predicted by the model and coated by silica shell. Prepared QDs are characterized by a narrow size distribution and the same fluorescence parameters as the original QDs in the organic medium. Developed approach permitted efficient QDs water-solubilisation and preparation of stable nanoparticles for plethora of biomedical applications.

Keywords: Quantum dots, QD, silica shell, core-shell.

1. Introduction

The semiconductor nanocrystals called quantum dots (QDs) are used as fluorescent labels in a growing number of practical biomedical applications and research. This is related to their unique properties that give them advantages over organic dyes

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traditionally used for this purpose. First, QDs are more photostable than organic flu-orophores [1], which provides a more precise detection of a weak fluorescent signal under the conditions of a long exposure or multiple accumulation. In addition, the use of QDs widens the possible range of simultaneous detection of several biomarkers, because QDs has narrow photoluminescence (PL) peaks with a half-width-at-half-maximum of 20–35 nm. Furthermore, unlike organic dyes, QDs with different PL bands can be excited with a single source in the blue spectral region. Finally, the PL quantum yields of some QDs are almost as high as 100% [2].

The main obstacle for wider use of QDs in biomedical practice is that the best QDs, in terms of their morphology and PL characteristics, are obtained by synthesis in organic media, yielding nanocrystals with a hydrophobic surface. Since most biomedical applications deal with aqueous media, QDs used there should be made water-soluble by means of special procedures, which often entail the side effects of decreased PL quantum yield and/or nanoparticles colloidal stability.

Two methods of QD hydrophilization are commonly used. The first one deals with a ligand exchange on the QD-surface thus replacing the original hydrophobic ligands with their hydrophilic analogues, e.g., thioglycolic acid, dihydrolipoic acid, cysteine, or more complex substances, bifunctional polyethylene glycol derivatives [3]. The advantage of this method is that the modification is easy to carry out and control. A major drawback, however, is that organic ligands are tethered to the QD surface by relatively weak or labile disulfide (S–S) or ionic Zn^{2+}-S^{2-} bonds, which various external factors may break. As a result, ligands may desorb and the colloids aggregate.

The other method is to coat the QDs with an additional hydrophilic shell of silica (SiO_2) [4] to attain a more robust passivation of the surface. This approach would prevent both the diffusion of toxic heavy metals from QD interior to the medium and the loss of colloidal stability because of ligand desorption. In addition, SiO_2 is low-toxic and is widely used in medicine [5, 6]. However, obtaining the optimal combination of the QD PL emission characteristics, colloidal stability, and capacity for penetrating into cells requires strict control of the synthesized silica shell, which is usually difficult. The main problem is that the precise amount of the core/shell (e.g., CdSe/ZnS) QDs in the solution should be known to calculate the reactions, whereas the reference molar extinction coefficients commonly used for this purpose have been reported only for the CdSe cores [7, 8]. Application of the same values to CdSe/ZnS QDs leads to large calculation errors and incorrect thicknesses of the shells grown.

In the present study, we demonstrate the growth of a SiO_2 shell with predetermined parameters on CdSe/ZnS/CdS/ZnS core/multishell (CdSe/MS) QDs [9]. The accuracy of

the procedure is ensured by two main factors. First, the molar extinction coefficient of a given QD sample is precisely measured during the synthesis of the original CdSe/MS QDs. Second, structural models are constructed for the CdSe/MS QDs themselves and the silica-coated QDs, which are used for precise calculation of the reactions. Developed procedure have been used to fabricate CdSe/MS/SiO$_2$ QDs with an outer silica shell of ~5 nm. The results demonstrate the precision and accuracy of the calculations and the possibility of obtaining stable, water-soluble QDs with a thin SiO$_2$ shell.

2. Materials and Methods

2.1. Chemicals

Cadmium oxide (99.5%, powder), 2-ethylhexanoic acid (2-EHA, 99%), 1-octadecene (ODE, technical grade, 90%), oleylamine (OLA, technical grade, 70%), hexadecylamine (technical grade, 90%), trioctylamine (TOA, 98%), trioctylphisphine (TOP, technical grade, 97%), selenium powder (powder, 100 mesh, 99.5%), zinc oxide (puriss, 99–100%), thiourea (TU, ACS Reagent, >99%), triethylene glycol dimethyl ether (TEGDME, 99%), dioctyl sulfosuccinate sodium salt (AOT, 98%, powder), (3-aminopropyl)-triethoxysilane (APTES, >98.0%), hexane (99%), sodium hydroxide (>98%, powder), tetraethoxysilane (TEOS, >99,0%), and ethanol (>99.8%) were purchased from Sigma-Aldrich. n-Hexadecylphosphonic acid (97%) was from PlasmaChem GmbH. Methyl acetate (MeOAc, 99%) was from Acros Organics; methanol (>99.5%) and cyclohexane were purchased from the local supplier Ekos-1. All reagents were used as received without purification. We used Milli-Q deionized water (18.2 M$\Omega \times$ cm) for preparation of buffer solutions and dissolution of QDs.

2.2. Synthesis of CdSe/MS quantum dots

Synthesis of CdSe/MS "core/multishell" QDs with an emission peak at 610 nm was performed as reported in Ref. [9]. Briefly, 3.5-nm CdSe cores were synthesized by the hot injection method using n-hexadecylphosphonic acid as a capping ligand. After isolation and purification of CdSe nanocrystals from a crude solution, an aliquot containing 100 nmol of the core QDs was transferred into a shell-growth solution, and alternating ZnS/CdS/ZnS monolayers were deposited using the SILAR technique [10]. After shell deposition was complete, the reaction mixture was cooled down to room temperature, and an aliquot was taken to measure the molar extinction coefficient

(ε) of the core/multishell QDs. The ε value at the first exciton absorption peak was calculated as

$$\varepsilon \left(\frac{1}{M \times cm} \right) = \frac{A}{c_i \times \frac{V_i}{V_f} \times l} \times \frac{V_{solv} + V_{al}}{V_{al}}, \qquad (1)$$

where A is the absorbance at the first exciton absorption peak, V_i and V_f are the reaction mixture volumes before and after deposition of the multishell, respectively, l is the optical path (1 cm), and V_{solv} and V_{al} are the volumes of the solvent used for dilution of the aliquot and the aliquot itself, respectively. The measurement was performed in triplicate to minimize the error resulting from the difficulty of taking an exact aliquot of the viscous reaction solution.

2.3. Precise coating of CdSe/MS quantum dots with a SiO$_2$ shell

The technique for growing the SiO$_2$ shell, sketched in Figure 1, is based on the approach reported in Ref. [4]. A 4.62×10^{-8} mol aliquot of the synthesized CdSe/MS QDs was dissolved in 5 ml of cyclohexane, and 7.5 μl of MPTMS and 1.07 g of AOT preliminarily dissolved in 12 ml of cyclohexane were added. The mixture was stirred at 1000 rpm for 45 min. After that, 685 μl of TEOS was introduced dropwise, 230 μl of 0.02 M NaOH (pH 9–10) was added, and the mixture was left for two days. At the next step, 60 μl of APTES and 15 μl of 0.02 M NaOH were added, and the mixture was stirred at 930 rpm for 1 h. Then, cyclohexane was distilled out, 50 ml of methanol and 50 ml of ethanol were added, and, after stirring at 930 rpm for 10 min, the mixture was centrifuged at 3000 rpm. The pellet was dissolved in ~50 ml of methanol, 40 mg of succindialdehyde was added, and the mixture was stirred for 24 h. After that, it was centrifuged, the pellet was dissolved in 40 ml of ethanol, the solution was stirred for 10 min and then centrifuged again. The resultant pellet was dissolved in 25 ml of 0.01 M NaOH.
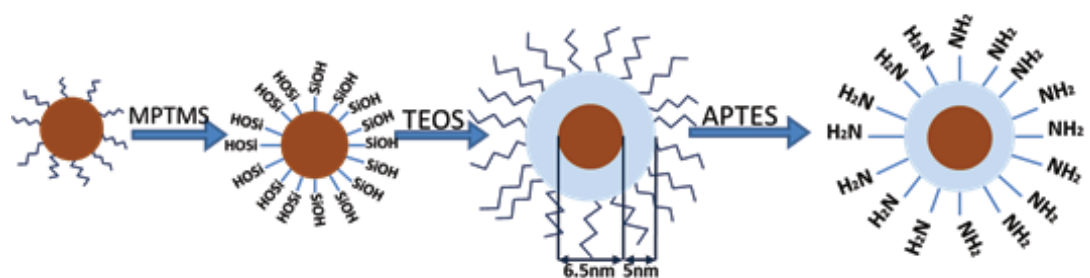

Figure 1: Schematics of the SiO$_2$ shell growth.

3. Results and Discussion

We used CdSe/ZnS/CdS/ZnS core/multishell QDs whose molar extinction coefficient was measured during their synthesis in an organic medium. This allowed us to precisely determine the number of QDs in the reaction mixture using the Beer–Lambert–Bouguer law and, hence, to accurately calculate the silica shell growth reaction using TEOS as a SiO$_2$ precursor. To calculate the necessary amounts of reagents at each step of the synthesis, we constructed a structural model of a spherical quantum dot 6.5 nm in diameter with a 5-nm silica shell. The model was used to precisely calculate the amounts of the reagents (TEOS, MPTMS, APTES, and succinic anhydride) required for modifying the QD surface. The amount of the TEOS silica precursor for growing a silica shell of a specified thickness was calculated as

$$V_{TEOS} = \frac{4}{3}\pi \times \left(\frac{d_1{}^3}{4} - \frac{d_0{}^3}{4} \right) \times N \times \frac{\rho_{SiO2}}{\rho_{TEOS}} \times \frac{M_{TEOS}}{M_{SiO2}}. \tag{2}$$

This equation was derived from the above geometrical considerations. Here, d_0 and d_1 are the nanoparticle diameters before and after the silica shell growth, respectively; ρ_{SiO_2} and ρ_{TEOS} are the SiO$_2$ and TEOS densities, respectively; M_{SiO2} and M_{TEOS} are the SiO$_2$ and TEOS molar weights, respectively; and N is the number of QDs introduced into the reaction.
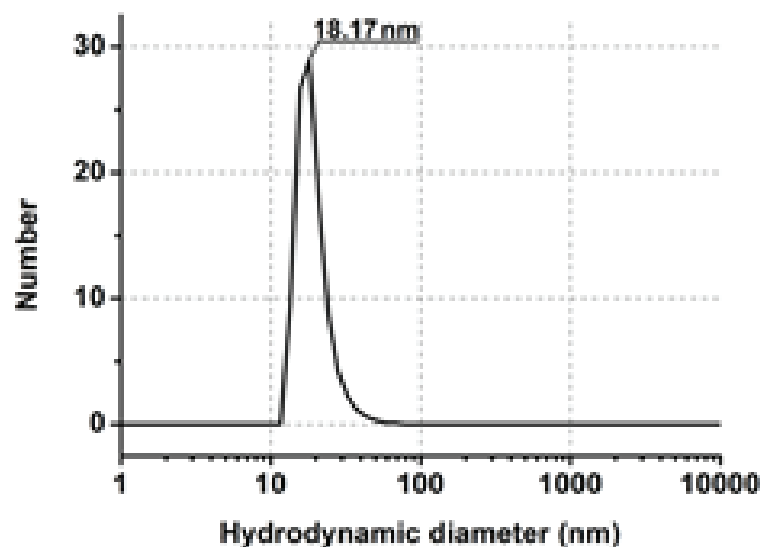

Figure 2: Hydrodynamic size distribution of silica-coated QDs.

The fabricated silica-coated QDs were analyzed by the dynamic light scattering technique. Figure 2 shows the hydrodynamic size distribution of the CdSe/MS/SiO$_2$ nanoparticles in an aqueous medium. As seen from these data, we obtained a QD

sample with a maximum at 18.17 nm and narrow size distribution. This value is well agreed with the computational model predicting a diameter of 16.5 nm.

Figure 3 shows the absorption and PL spectra of the QDs before and after silica coating. It is evident from these plots that the additional SiO_2 shell did not substantially modify the QD optical properties. However, it did cause some decrease in the PL quantum yield, which was 60% before silica coating and 38.1% after it. In the course of the shell growth, this change was visually discernible at the very first stage of the reactions, when the alkaline catalyzer was added after the QD surface was treated with MPTMS. Afterwards, as the SiO_2 layer was grown over MPTMS, the QD PL was gradually restored.
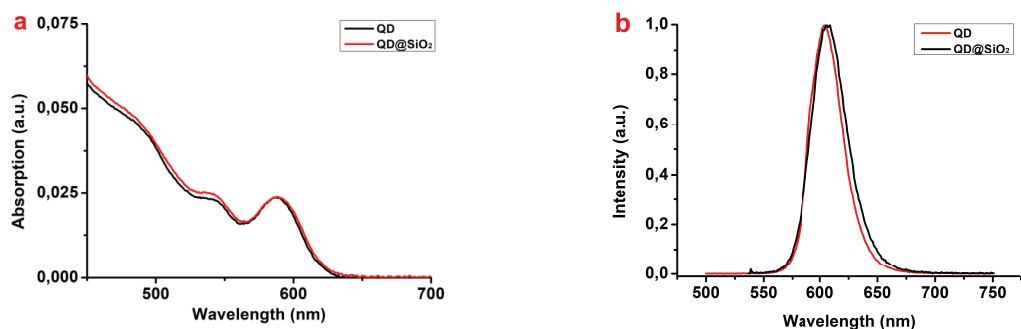

Figure 3: The quantum dots (QDs) optical properties before and after silica coating.

Absorption and photolumineascence spectra of QDs are shown on the panel (a) and (b), respectively.

We have further studied the morphology of the fabricated $CdSe/MS/SiO_2$ QDs using transmission electron microscopy (Figure 4). As seen in the microphotographs, the particles were spherical, and each QD had a SiO_2 shell, each shell containing only one QD. It is seen, however, that the nanoparticles aggregated, forming cross-links. We believe that this was because, first, the microphotographs were made long after the SiO_2 shell was grown and, second, the sample preparation for microscopy was accompanied by strong etching of the SiO_2 shell with the alkaline in which the QDs were dissolved after the silica coating.

4. Conclusion

In this paper, we have demonstrated that a SiO_2 shell of a predetermined thickness can be grown over CdSe/ZnS/CdS/ZnS core-multishell QDs thus producing a water-soluble nanoparticle with a known diameter. The synthesized water-soluble nanoparticles
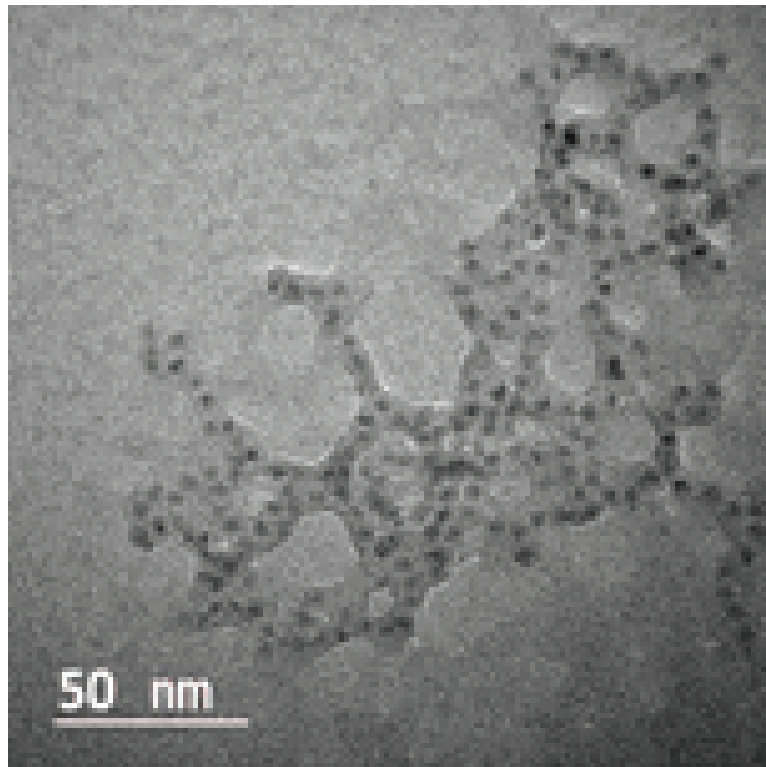
Figure 4: A transmission electron microscopic image of the silica-coated quantum dots.

have advanced PL properties, which remain basically unchanged after the silica coating. Suggested approach significantly extends the possible QDs biomedical applications such as early tumor diagnosis and imaging through the highly sensitive multiplexed fluorescent detection of cancer biomarkers.

Acknowledgments

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