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Ag_2Te quantum dots with compact surface coatings of multivalent polymers: Ambient one-pot aqueous synthesis and the second near-infrared bioimaging

Min Yang[a], Rijun Gui[a,b,*], Hui Jin[a,b], Zonghua Wang[a,**], Feifei Zhang[a], Jianfei Xia[a], Sai Bi[a], Yanzhi Xia[a]

[a] Collaborative Innovation Center for Marine Biomass Fiber, Materials and Textiles of Shandong Province, Shandong Sino-Japanese Center for Collaborative Research of Carbon Nanomaterials, Laboratory of Fiber Materials and Modern Textiles, The Growing Base for State Key Laboratory, College of Chemical Science and Engineering, Qingdao University, Qingdao 266071, Shandong, PR China

[b] Department of Chemistry, School of Chemistry and Chemical Engineering, Shanghai Jiao Tong University, Shanghai 200240, PR China

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ABSTRACT

In this study, we described a facile ambient one-pot aqueous synthesis of fluorescent Ag_2Te quantum dots (QDs) adopting multivalent polymers (poly(maleic anhydride) homopolymers) as stabilizers. In experiments, Ag_2Te QDs were synthesized *via* a stepwise addition of the stabilizers, precursors ($AgNO_3/Na_2TeO_3$) and promoters ($NaBH_4/N_2H_4\cdot H_2O$) in ambient one-pot aqueous solution. By regulating the compositions of raw materials, water-dispersed Ag_2Te QDs (3.8–4.7 nm) were achieved and exhibited tunable photoluminescence (PL) emission (995–1068 nm) in the second near-infrared (NIR-II) region, accompanying with the minimized surface coating thickness (1.5–1.9 nm). Such compact coating of multivalent polymers promoted PL emission of Ag_2Te QDs, so showing high PL quantum yields (PLQYs: 13.1–15.2%). In addition to compact sizes and high PLQYs, experimental results testified that the Ag_2Te QDs demonstrated high photo-/colloidal stability and ultralow cytotoxicity, which implied their promising applications, especially serving as an effective nanoprobe for bioimaging in the NIR-II biological window.

1. Introduction

Silver chalcogenide colloidal semiconductor nanocrystals, also termed as Ag_2X (X = S, Se and Te) quantum dots (QDs), are ideal materials for low-toxicity and near-infrared (NIR) emissive QDs because Ag_2X QDs have narrow bandgaps (0.9–1.1, 0.15 and 0.67 eV for Ag_2S, Ag_2Se and Ag_2Te bulk, respectively) [1–3]. Ag-based binary QDs with NIR emission have potential applications in the biomedical field, especially used for *in vivo* imaging based upon their good biocompatibility [4,5]. Compared with imaging applications of cells and live animals in traditional NIR region (NIR-I, 700–950 nm), bioimaging in the second NIR region (NIR-II, 1.0–1.4 μm) is much appealing due to much lower albedo, endogenous autofluorescence and markedly improved signal-to-noise [6]. Bioimaging in the NIR-II region possesses negligible scattering, maximal penetration depth and high feature fidelity [7–9].

As for silver chalcogenide family, Ag_2Te is a little explored member in comparison with Ag_2S and Ag_2Se. Ag_2Te has high electron mobility and low thermal conductivity, indicating its thermoelectric applications [10]. In previous literatures, a variety of Ag_2Te nano-wires/tubes/rods/particles have been reported [11–14], however few efforts have referred to luminescent Ag_2Te QDs that could be further developed as promising materials for imaging in NIR-II biological window. Zhou et al. developed a solvothermal approach to prepare sulfur doped Ag_2Te nanoparticles in order to achieve desired electrical resistivity, but no photoluminescence (PL) of products was observed [15]. Liu et al. employed a rapid injection of trioctylphosphine-Te into the mixture of Ag-dodecanethiol and 4-*tert*-butyltoluene to prepare Ag_2Te nanocrystals, which showed NIR absorption and photoconductive response [16]. For applications in biosystems, hydrophobic Ag_2Te nanomaterials prepared in organic solvents should be treated by ligand exchange and

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* Corresponding author at: Qingdao University, College of Chemical Science and Engineering, Qingdao 266071, Shandong, China. Tel.: +86 532 85950873; fax: +86 532 85950873.

** Corresponding author. Tel.: +86 532 85950873; fax: +86 532 85950873.

E-mail addresses: guirijun@qdu.edu.cn (R. Gui), wangzonghua@qdu.edu.cn (Z. Wang).

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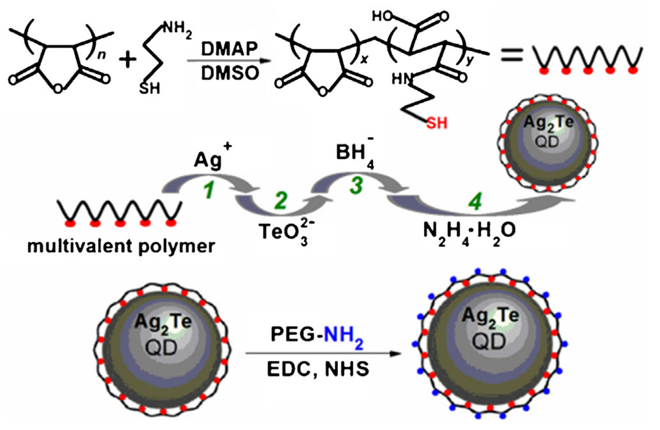

Scheme 1. Schematic illustration of the preparation procedures of multivalent polymers and the surface functionalized Ag_2Te QDs.

surface modification to gain hydrophilic products. Recently, Chen et al. reported the cation-exchange between Ag^+ and firstly prepared CdTe QDs in aqueous solution, which facilitated the preparation of NIR-II emissive Ag_2Te QDs [17]. This cation-exchange method was relatively complicated, referring to two separated synthesis steps. In addition, the cation-exchange process probably induced surface traps around QDs and therefore partly resulted in a lower PLQY ($\leq$2.1%), which was unfavorable for further biomedical applications of the resulting QDs.

As established, hydrodynamic sizes of QDs are pivotal for their intracellular imaging. A bulky size can lead to limited diffusion of QDs inside cytoplasm and probably compromises the molecular binding [18]. Therefore, great researches about the compact surface coatings for QDs have been reported in succession, while the QDs maintained bright luminescence and high photo-/colloidal stability [18–26]. Especially, considerable efforts have focused on the minimization of QDs in size through replacing capping ligands with long alkyl chains (ligand exchange reactions). Small hydrophilic capping ligands can dramatically reduce the surface coating thickness, but these resulting QDs demonstrate a lower colloidal stability and a reduced brightness [20–26]. To address these problems of stability and brightness (quantum yields, QYs), different multidentate polymers (thiols-based ligands) have been developed to minimize hydrodynamic sizes of QDs [22–30]. Until most recently, there is no report on direct ambient synthesis of QDs, using multivalent polymer ligands (with multiple thiols pendant groups) as stabilizers. Multivalent polymers possess similar molecular structures to multidentate polymers, indicating some similar functions. On this account, multivalent polymers when used for stabilizers in the QDs preparation could not only minimize hydrodynamic sizes of QDs, but also could conquer colloidal stability, photobleaching and brightness of QDs [30,31]. Thus, multivalent polymers are responsible for excellent physicochemical properties and satisfactory photo-/colloidal stability. High PLQYs of QDs stabilized by the polymers would be expected.

Herein, we put forward an ambient one-pot synthesis to prepare NIR-II emissive Ag_2Te QDs in aqueous solution at room temperature (Scheme 1). Poly(maleic anhydride)-*graft*-cysteamine (PMAC, typical multivalent polymers) were utilized as stabilizers to synthesize surface compactly coating Ag_2Te QDs that would be expected to exhibit combined advantages, including small hydrodynamic sizes, excellent stabilities, high PLQYs, strong resistances to photobleaching, *etc.* In aqueous solution of PMAC, $AgNO_3$ was added, followed by a stepwise addition of Na_2TeO_3 and $NaBH_4$ under stirring. Afterward, $N_2H_4{\cdot}H_2O$ was injected into the mixed solution with continuously stirring for a preset period to generate PMAC-stabilized Ag_2Te QDs. By adjusting the compositions of different raw materials, surface compact Ag_2Te QDs were achieved and exhibited tunable PL emission (in NIR-II region) and high PLQYs. Furthermore, the surface coupling of Ag_2Te QDs with NH_2-terminated poly(ethylene glycol) (PEG-NH_2) would efficiently promote the water solubility and biocompatibility of surface functionalized Ag_2Te QDs, which suggested their potentials for applications, particularly serving as efficient nanoprobes for NIR-II PL bioimaging at the level of single molecule or single nanoparticle.

2. Materials and methods

2.1. Chemicals and materials

Multivalent polymers (PMAC) were synthesized, based upon the reaction of poly(maleic anhydride) (~5 kDa) with cysteamine [31]. Approximately 40% of maleic anhydride groups were chemically modified, which facilitated the strong binding affinity of PMAC (each polymer chain contains ~20 of active thiols groups) with the surface of QDs (more relevant details are available in Supplementary data, Part S1 and Fig. S1). $AgNO_3$ (99.9%), Na_2TeO_3 (98%), $NaBH_4$ (96%), $N_2H_4{\cdot}H_2O$ (85%), bovine serum albumin (BSA, ~66.7 kDa) and indocyanine green (ICG, 75%) were purchased from Aldrich. Other chemicals obtained from Shanghai Reagent Corp. can be utilized directly as received without any further purification. Deionized water was utilized throughout. Phosphate buffered saline (PBS, Na_2HPO_4 and NaH_2PO_4) solutions were utilized in experiments. Notably, all experiments were performed in compliance with the relevant laws and institutional guidelines, and the institutional committees have approved the experiments.

2.2. Preparation of PMAC-stabilized Ag_2Te QDs

Typically, for the Sample **No. 4** (as listed in Table 1), 5 mL of $AgNO_3$ (0.5 mmol L^{-1}) aqueous solution was added into a conical flask containing 5 mL of PMAC (1 mmol L^{-1}) aqueous solution. Afterward, Na_2TeO_3 (0.25 mmol L^{-1}), $NaBH_4$ (0.05 mg mL^{-1}) and $N_2H_4{\cdot}H_2O$ (5 mol L^{-1}) aqueous solutions (each 5 mL) were added in sequence under stirring. The resulting mixture was stirred at room temperature to allow the QDs growth. After continuous reaction for 2 h, the QDs with NIR-II PL emission were obtained. A longer reaction time (3 h) only caused a slight emission variation (<5 nm). By regulating the compositions of raw materials (PMAC/$AgNO_3$/Na_2TeO_3/$NaBH_4$/$N_2H_4{\cdot}H_2O$), different sized Ag_2Te QDs were achieved and demonstrated tunable PL emission in the NIR-II region. The reaction solution was collected by adding acetone and then centrifugated. These resultant precipitates (*i.e.* Ag_2Te QDs) were repeatedly washed with ethanol and water, followed by drying the precipitates in vacuum at room temperature, and finally re-dispersing them in water for subsequent experiments.

2.3. Characterization

PL emission spectra were recorded on a FLSP 920 (Edinburgh Instruments) fluorescence spectrophotometer with a Xenon lamp (190–1100 nm) used for excitation and UV–vis absorption spectra were measured using a UV-2450 (Shimadzu) spectrophotometer. TEM images and energy diffraction X-ray (EDX) spectra were obtained with a JEOL JEM-1400 TEM (JEOL) operating at 120 kV of acceleration voltage. High-resolution transmission electron microscopy (HRTEM) images were acquired with an H-600 (Hitachi) TEM operating at an acceleration voltage of 200 kV. Powder X-ray diffraction (XRD, Siemens) patterns were obtained with wide-angle X-ray scattering, using a D5005 X-ray powder diffractometer equipped with graphite monochromatized Cu K_α radiation (λ = 1.54056 Å). Hydrodynamic sizes were measured by dynamic light scattering apparatus (DLS, Malven Instruments). Imaging of