Sci. Bull. (2016) 61(4):282–291
DOI 10.1007/s11434-016-1009-y

www.scibull.com
www.springer.com/scp

Article

Chemistry

High-yield preparation of robust gold nanoshells on silica nanorattles with good biocompatiblity

Changhui Fu · Chaofeng He · Longfei Tan · Shunhao Wang · Lu Shang · Linlin Li · Xianwei Meng · Huiyu Liu

Received: 6 November 2015 / Revised: 8 December 2015 / Accepted: 28 December 2015 / Published online: 30 January 2016

Abstract Although gold nanoshells are widely considered as one of the promising photothermal nanomaterials used for biomedicine, the high cost, low yield and poor stability severely limit their potential application in clinical trials. Herein, robust gold nanoshells on silica nanorattles (GSNs) were easily prepared in a high yield by an improved seed-mediated method employing polyvinylpyrrolidone (PVP) as a stabilizing and capping agent. The present method is very simple, effective and reproducible and can well control the growth process of gold nanoshells. The as-prepared GSNs have a narrow size distribution (<10 % in standard deviation). Furthermore, the utilization rate of Au in the solution used for the growth of gold nanoshells increases by 70 % than that in previous method. The resultant GSNs have a good structural stability after placing over 6 months due to the protection of PVP. More importantly, in vivo and in vitro toxic studies indicate that the GSNs have good biocompatibility. We believe that our preparation method will remarkably promote the use of gold nanoshells for biomedicine.

Keywords Gold nanoshells · Silica nanorattles · Polyvinylpyrrolidone (PVP) · High yield · Biocompatibility

Changhui Fu, Chaofeng He and Longfei Tan contributed equally to this work.

Electronic supplementary material The online version of this article (doi:10.1007/s11434-016-1009-y) contains supplementary material, which is available to authorized users.

C. Fu · C. He · L. Tan · S. Wang · L. Shang · X. Meng (✉)
Laboratory of Controllable Preparation and Application of Nanomaterials, Technical Institute of Physics and Chemistry, Chinese Academy of Sciences, Beijing 100190, China
e-mail: mengxw@mail.ipc.ac.cn

S. Wang
University of Chinese Academy of Sciences, Beijing 100049, China

L. Li (✉)
Beijing Institute of Nanoenergy and Nanosystems, Chinese Academy of Sciences, Beijing 100083, China
e-mail: lilinlin@binn.cas.cn

L. Li
National Center for Nanoscience and Technology (NCNST), Beijing 100083, China

H. Liu (✉)
Beijing Key Laboratory of Bioprocess, College of Life Science and Technology, Beijing University of Chemical Technology, Beijing 100029, China
e-mail: liuhy@mail.buct.edu.cn

1 Introduction

Recently, near-infrared (NIR) light-absorbing nanomaterials, such as copper sulfide [1], graphene [2], gold nanorods [3] and gold nanoshells [4], have been widely studied for application in photothermal therapy of cancer. Particularly, gold nanoshells are one of the ideal photothermal transducers owing to its extremely high photothermal conversion efficiency and low toxicity [5, 6]. Halas and co-workers started nanoshell-based photothermal therapy and achieved the first clinical trial in 2010 (see http://www.nanospectra.com/index.html and Ref. [7]). Since then, many groups including us have reported the gold nanoshell-based "theranostics" used for personalized medicine and molecular imaging [8, 9]. However, the use of gold nanoshells in clinic is still limited by the complicated synthesis method and structural stability.

To date, gold nanoshells are often prepared by the widely used seed-mediated growth and the deposition–precipitation methods [10]. In the typical seed-mediated growth process, colloidal golds served as nucleation sites are firstly modified on the surface of silica, and then the Au nanoparticles grow gradually, forming a shell on the silica surface through a heterogeneous nucleation process. This method needs a low concentration of Au precursor to control the growth of gold nanoshells in a slow reaction rate because the growth process of nanoshells is kinetically controlled. Otherwise, the quick growth of gold nanoparticles through self-nucleation process greatly reduces the utilization of Au precursor [11]. In this case, it needs more time to prepare gold nanoshells with a certain particle size and completed shell layer due to the multi-steps process [12]. Furthermore, the growth process of nanoshells is highly sensitive to the functional groups on the silica surface [13], stirring rate [14], reaction pH [15] and surface chemistry of colloidal golds [16], thus making the poor batch-to-batch reproducibility of this method. For instance, the colloidal golds attached on SNs (named as gold seeds) prepared by different batches usually results in a great diversity in the shell morphology accompanied with different surface plasmon resonance (SPR) adsorptions. Furthermore, the gold nanoshells prepared in above methods often have a poor storage stability. For example, Zhang et al. [17] found that Au nanoparticles detached from gold nanoshells during the storage process, resulting in the loss of absorption in NIR region.

Therefore, a simple strategy with great improvement in the productivity, reproducibility and structural stability is desirable for the synthesis of gold nanoshells. We deem that the growth process of gold nanoshells can be kinetically controlled by using some organic surfactants in the reaction solution. The biopolymer polyvinylpyrrolidone (PVP) has been widely used as an effective capping agent for complexing and stabilizing Ag, Co and Au nanocrystals [14, 18]. Additionally, PVP is also often used as a shape-controlling agent to promote the highly anisotropic growth of nanocrystals with different shapes [19]. These works inspire us that PVP may be an effective capping agent for controlling the growth of gold nanoshells.

Herein, we develop a kinetic-controlled seed-mediated growth method for preparing uniform and robust gold nanoshells on hollow/mesoporous silica spheres (SNs) using PVP as a capping agent. In this method, PVP stabilizes Au monomer species and thus effectively suppresses the self-nucleation and growth of Au nanoparticles, resulting in more reduced Au atoms adhered onto the SNs for the growth of Au nanoshells. The utilization rate of Au by this method was improved by $\sim$70 % compared to that of the conventional seed growth method. The gold nanoshells obtained by using different batches of gold seeds have almost identical SPR absorption. Furthermore, the protection of PVP on the gold nanoshells effectively prevents Au nanoparticles from detachment and aggregation, thus making the GSNs have excellent structural and optical stabilities. More significantly, the preliminary study of the in vitro toxicity and in vivo toxicity of the GSNs demonstrates that no obvious toxicity was observed even at a high dose of 250 mg kg^{-1}, indicating that the GSNs prepared in this method have a good biocompatibility.

2 Experimental

2.1 Materials

Tetramethylolphosphonium chloride (THPC), potassium carbonate (K_2CO_3, 99 %), hydroxylamine hydrochloride ($NH_2OH{\cdot}HCl$) (99 %), chloroauric acid ($HAuCl_4$), PVP ($M_W = 36{,}000$), calcein-AM and propidium iodide (PI) were purchased from Sigma. All chemicals were used as received without further treatment.

2.2 Synthesis of PVP-GSNs

The multi-step syntheses of PVP-GSNs included the preparation of SNs and gold seeds. The experimental process about SNs and gold seeds in detail was shown in the supporting information. Afterward, 7.4 mL $HAuCl_4$ (1.54 wt%) aqueous solution (Fig. 1f, solution 1) was added to 400 mL K_2CO_3 solution (0.5 mg mL^{-1}). After stirring for 30 min, the color of the solution slowly changed from yellow to colorless, indicating the formation of $Au(OH)_4^-$ ions, as shown in Fig. 1f. Then, 0.6 g PVP was added to the above solution under vigorously stirring (Fig. 1f). Subsequently, 3.5 mL of gold seeds (2 mg mL^{-1}, 4:1) was added in solution 3. Finally, 10 mL $NH_2OH{\cdot}HCl$ (0.36 mmol) was injected to trigger the growth of gold nanoshells. Two minutes later, PVP-GSNs formed and were collected by centrifugation and washed with deionized water for three times. The PVP-GSNs were stored at 4 °C for further use.

2.3 Characterization

Transmission electron microscope (TEM, JEOL-2100F) was conducted to observe the formation process of GSNs, and UV–Vis–NIR spectrophotometer (JASCO-570) was carried out to determine the absorption spectra of the samples. Dynamic light scattering (DLS, Malvernzetasizer-3000HS) was used to measure the size distribution and zeta potentials. Inductive coupled plasma, (ICP-OES, IRIS Intrepid II XSP, Thermo Fisher) was performed to quantitatively measure the concentration of Au and Si.