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Fabrication of silica-coated gold nanorods and investigation of their property of photothermal conversion

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ABSTRACT

This study described the preparation of silica-coated Au nanorods (AuNR/SiO_2) in a colloidal solution, assessed their property of photothermal conversion, and investigated their ability to kill cancer cells using photothermal conversion. Au-seed nanoparticles were produced by reducing hydrogen tetrachloroaurate ($HAuCl_4$) with sodium borohydride ($NaBH_4$) in aqueous n-hexadecyltrimethylammonium bromide (CTAB) solution. AuNRs were then fabricated by reducing $HAuCl_4$ and silver nitrate ($AgNO_3$) with L-ascorbic acid in the aqueous CTAB solution in the presence of Au-seed nanoparticles. The as-prepared AuNRs were washed by a process composed mainly of centrifugation to remove the CTAB. The washed AuNRs were coated with silica by mixing the AuNR colloidal solution, an aqueous solution of (3-aminopropyl)trimethoxysilane, and tetraethylorthosilicate/ethanol solution with a water/ethanol solution. We found that the addition of AuNR/SiO_2 in water, in mice, and in a culture medium with cancer cells, followed by irradiation with a laser, cause an increase in temperature, demonstrating that AuNR/SiO_2 have the ability of photothermal conversion. In addition, the cancer cells in the culture medium were found to be killed due to the increase in temperature caused by the photothermal conversion.

1. Introduction

Hyperthermia has been used as a treatment method for providing heat energy to living cells. Electromagnetic waves such as lasers and microwaves are often used as heat sources. The use of radiosensitizers, agents that convert electromagnetic waves into heat energy, provides efficient hyperthermia.

Au nanoparticles exhibit surface plasmon resonance (SPR) absorption. A part of the absorbed energy derived from SPR is converted into heat energy. The wavelength of SPR is known to be dependent on the shape or aspect ratio of the nanoparticles [1–3]. Au nanoparticles with an aspect ratio of 1, or Au nanospheres, have an SPR band at wavelengths as short as ~500 nm due to the transverse oscillation of electrons. In contrast, Au nanoparticles with higher aspect ratios, or Au nanorods (AuNR), have an SPR band at wavelengths as high as 600–900 nm due to the longitudinal oscillation of electrons. This phenomenon causes a wider range of wavelengths of light to be available for photothermal conversion. Thus, the Au nanoparticles can be used as radiosensitizers that absorb light energy from a wide range of wavelengths—from visible to near infrared light.

Light with wavelengths between 650 and 900 nm has higher permeability in living bodies than light with wavelengths less than 650 nm or more than 900 nm; thus, the light with wavelengths from 650 to 900 nm is called the window of the living. Accordingly, the 650–900-nm light can provide optical energy to the probes inside living bodies more effectively than light with wavelengths below 650 nm or above 900 nm. This means that the temperature

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of diseased tissues close to the probe can be expected to be elevated upon irradiation with 650–900-nm light. Such a treatment would not inflict pain on the patients during hyperthermia. Infrared light has lower energy than visible light because of its longer wavelength. Because low-energy light would not damage any tissue other than the diseased tissues, infrared light would be suitable and safe for use a probe.

Metal ions released from metallic materials are toxic to tissues. Even Au is toxic to tissues, although its toxicity is lower than most metals. Coating the Au nanoparticles with materials inert to living tissues, such as silica, may provide a physical barrier between the living tissue and the Au core, thus reducing the toxicity of Au nanoparticles. Nanoparticles tend to aggregate, thus deteriorating their characteristic properties. Coating the nanoparticles with materials that are colloidally stable might help control the aggregation. Silica is a good candidate for a shell material because of the high colloidal stability of silica nanoparticles. Therefore, silica-coating of the Au nanoparticles could solve both the above problems.

Various techniques, based on sol-gel reaction, have been proposed for coating Au nanoparticles with silica [4–9]. Our research group had also studied silica-coating of Au nanoparticles using this method [10–15]. Most of these studies have been performed for coating silica on Au nanospheres. Silica-coating of AuNRs has also been performed by several research groups [16–20]. In most studies, the AuNRs are produced by simultaneous reduction of Ag ions and Au ions with a reducing reagent in an aqueous solution in the presence of a surfactant and Au-seed nanoparticles; n-hexadecyltrimethylammonium bromide (CTAB) is usually used as the surfactant. Thus, even if the AuNRs are washed repeatedly after incubation with CTAB, a large amount of CTAB remains on the surface. Since quaternary ammonium surfactants such as CTAB are harmful to cells, its presence in the nanoparticles has to be eliminated or reduced. However, the rod-like structure of AuNR has been known to collapse if all the CTAB is removed. Thus, it is necessary to remove an optimum amount of CTAB for successful silica-coating. The present study proposed a method for fabricating silica-coated AuNRs, in which the maximum amount of CTAB is removed from the AuNR colloid solution prior to silica-coating, so that the toxicity of the AuNR/SiO_2 nanoparticles can be minimized. We also investigated the property of thermal conversion, and the ability of AuNR/SiO_2 to kill cells by increasing the temperature, upon near-infrared laser irradiation.

2. Materials and methods

Details of materials and methods are explained in a Supplementary Material.

3. Results and discussion

3.1. Morphology of AuNRs and AuNR/SiO_2

A photograph of the AuNR colloid solution is shown in Fig. 1(a) (inset). The solution had a bluish purple color, which implied the presence of AuNRs. Neither precipitates nor flocculates were observed in the solution, which indicated that the AuNRs were colloidally stable. A TEM image of the AuNRs is shown in Fig. 1(a) (inset). Most nanoparticles had a rod-like structure, though a few spherical and oblong nanoparticles were also observed. The average lateral and longitudinal sizes were 20.2 ± 3.6 and 41.9 ± 5.7 nm, respectively. Fig. 1(a) also shows a Vis extinction spectrum of the AuNR colloidal solution. Two dominant peaks were detected at 516.0 and 683.0 nm and they were attributed to the SPR bands of AuNRs due to the transverse and longitudinal oscillations of electrons, respectively, thus confirming the production of AuNRs.

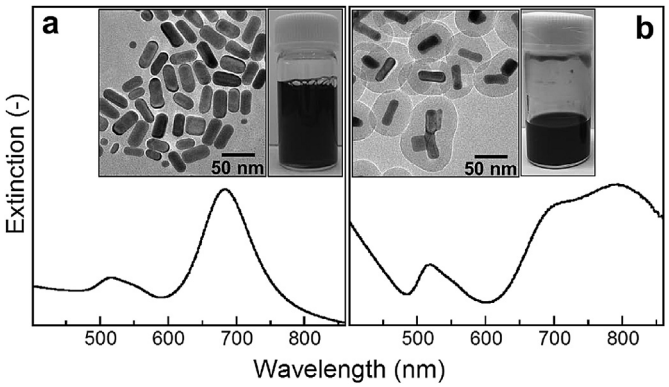

Fig. 1. Visible extinction spectra of (a) AuNRs and (b) AuNR/SiO_2. Insets show their colloid solutions and TEM images.

A photograph of the AuNR/SiO_2 nanoparticle colloid solution is shown in Fig. 1(b) (inset). The solution had a bluish purple color similar to that of the AuNRs, which implied that the rod-like structure of AuNR was not broken by the silica-coating process. Neither precipitates nor flocculates were observed in the solution, indicating that the colloidal stability of AuNRs was retained even after the silica-coating. A TEM image of the AuNR/SiO_2 is shown in Fig. 1(b) (inset). The AuNRs were successfully coated with silica shells, and the shell thickness was estimated to be 36.8 ± 7.3 nm. Some particles contained aggregates of AuNRs as cores. The hydrolysis of TEOS caused the generation of silanol groups, which increased the ionic strength of the solution. Increased ionic strength has been reported to compress the double layer of colloidal particles [21–23]. The generation of silanol groups therefore decreased the double-layer repulsion between the nanoparticles. The increased ionic strength was thus primarily responsible for the aggregation and growth of AuNRs in the present system. The aggregates were then coated with silica shells. It should be noted that the AuNRs generally aggregated at the tip of the AuNRs. As the AuNRs are formed via particle growth at their tips, the surface near the tips might have sites, on which molecules, clusters, nuclei, and fine particles are easily adsorbed. Accordingly, we speculated that these sites of the AuNRs approached the corresponding sites of other AuNRs, thus forming the aggregates. Fig. 1(b) shows a Vis extinction spectrum of the AuNR/SiO_2 colloidal solution. The SPR band formed due to the transverse oscillation of electrons was detected at 519.5 nm, while those formed due to the longitudinal oscillation of electrons was detected at 713.0 and 793.5 nm. The SPR band at 713.0 nm was attributed to the longitudinal oscillation of electrons because 713.0 nm was closer to 683.0 nm for the AuNRs. As the aspect ratio of Au nanoparticles increases, the wavelength of the SPR bands due to the longitudinal oscillation of their electrons also increases [1–3]. Thus, the detection of SPR bands at wavelengths as high as 793.5 nm implied that AuNRs with a high aspect ratio were produced in the present system. The TEM image (the inset of Fig. 1) revealed that some AuNRs were aggregated. This aggregation might have increased the apparent aspect ratio of AuNRs, which might have resulted in the detection of SPR bands at the higher wavelength.

3.2. Photothermal conversion of AuNR and AuNR/SiO_2 nanoparticle

Fig. 2(a) shows the temperature of the AuNR colloid solution as a function of the duration of laser-irradiation at various Au concentrations. At an Au concentration of 0 mM, the temperature increased to 40.6 °C in 1 min, and then increased slightly with time.

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