Synthesis and photo-thermal property of alginate/gold nanorod composite spheres

Houru ZHOU, Jing ZHANG, Aili WEI, Song CHEN*

College of Materials Science and Engineering, Taiyuan University of Technology, Taiyuan 030024, China
E-mail: chensong2009@126.com

Abstract: Gold nanorods (GNRs) have received considerable attention in the development of novel photo-thermal materials because of their unique optical property. In this paper, alginate/GNR composite microspheres were synthesized through emulsification of the aqueous alginate/GNR mixture in the paraffin oil via a water/oil emulsion technique followed by cross-linking process in the solution of CaCl$_2$. Microstructure and near-infrared (NIR) responsive photo-thermal property of the resultant composite spheres were investigated. SEM observations showed that the composite spheres were spherical in morphology and had the diameter of 5-40 μm. XRD patterns showed that the typical diffraction bands of GNRs were observed at 38° and 44° in the composite spheres. Under the 808 nm-NIR irradiation, the composite spheres were NIR-responsive and the temperature of the aqueous suspension of the composite spheres increased from 28°C to 39°C. It was found that their photo-thermal property could be well adjusted through controlling the content of GNRs in the composite spheres and irradiation time.

1. Introduction
Recently, there is an increasing interest in the development of the near-infrared (NIR) responsive materials in photo-thermal therapy [1-2]. Gold nanorods (GNRs) are one type of the typical NIR responsive materials as they show strong localized surface plasmon resonance in the visible and NIR regions due to the anisotropic structure [3]. They easily convert the energy of NIR light to the heat energy, which has been utilized for killing the cancer cells [3]. Moreover, NIR light could penetrate the living tissues without significantly adverse effect [4]. Therefore, GNRs have been extensively combined with other types of materials to produce the NIR-responsive composite materials such as GNR-polymer composite spheres [5], GNR-apatite composite spheres [6], and GNR-lipid composite nanofibers [7]. In particular, the GNR-based composite spheres are more attractive as they can be delivered into the targeted tissues via an injection route with the minimum tissue invasion [6].

Alginate is one type of the natural biopolymers and shows excellent biocompatibility and biodegradability [8]. Compared with other types of biopolymers such as collagen and chitosan, alginate has a strong affinity to the divalent metal ions such as Ca$^{2+}$ and Mg$^{2+}$ and could be easily stabilized with those metal ions [8-9]. Therefore, alginate-based materials are extensively cross-linked with Ca ions and have attracted considerable attention in the biomedical fields such as drug delivery system [9], cell encapsulation [10], and tissue regeneration [11]. Few studies have employed the synthesis and application of alginate/GNR composites. For example, Mitamura et al. prepared the alginate/GNR hydrogels [12], while Jo et al. evaluated the photon to thermal response of a single patterned alginate/GNR composite hydrogel [13]. However, the synthesis and photo-thermal
examination of alginate/GNR composite spheres have not been addressed.

In this study, the alginate/GNR composite spheres were synthesized and their microstructure and photo-thermal property were evaluated. The photo-thermal property of the as-synthesized composite spheres was discussed in term of the content of GNRs.

2. Materials and Methods

2.1 Synthesis of GNRs

GNRs were synthesized according to the method described in our previous study [6]. Briefly, 5 mL of CTAB solution (0.2 mol/L), 5 mL of HAuCl₄ (0.5 mmol/L) and 600 μL of NaBH₄ (0.01 mol/L) were mixed in a 50 mL-flask and kept stirring at room temperature for 2 min to produce the gold seed solution. To prepare GNRs, 50 mL of CTAB solution (0.2 mol/L), 2.6 mL of AgNO₃ (4 mmol/L), 50 mL of HAuCl₄ (1 mmol/L), 0.8 mL of HCl (1 mol/L), 0.7 mL of ascorbic acid solution (0.0788 mol/L), and 0.12 mL of gold seed solution were mixed in a 200 mL-flask and kept stirring at room temperature for 2 min and placed at room temperature for 12 h. The resultant GNRs were collected by centrifugation at 12,000 rpm for 10 min, washed with water twice, and finally re-suspended in water.

2.2 Synthesis of alginate/gold nanorod composite spheres

Alginate/GNR composite spheres were synthesized using sodium alginate (SA) and GNRs as starting materials via an emulsion technique (Figure 1). SA and SA/GNR mixture were applied for synthesis of SA spheres and SA/GNR composite spheres, respectively. 5 mL of SA solution (2%, w/v) containing GNRs with different content of 0, 0.026%, 0.052% and 0.104% were added to 20 mL of paraffin oil containing surfactants consisting of 1 mL of Span-80 and 0.3 mL of Tween-80 and kept stirring at room temperature for 30 min to produce the emulsion. After that, 3 mL of 8% CaCl₂ (w/v) were added to the emulsion for cross-linking of the composite spheres. After 2 h of agitation, the emulsion was added to 50 mL of 2% (w/v) CaCl₂ solution for a further cross-linking of the composite spheres. After 2 h, the resultant composite spheres were collected by centrifugation at 3000 rpm for 10 min, washed with ethanol and water, and finally freeze-dried.

2.3 Characterizations

Size and morphology of the samples were observed with a scanning electron microscope (SEM, JEOL,
Japan). Crystalline structure of the samples was indentified with an X-ray diffractometer (Rigaku, Japan). Ultraviolet-visible (UV–vis) spectra of the samples were scanned with a UV-8000S spectrophotometer (Shanghai Metash, China).

2.4 Photo-thermal Property
To examine the NIR-responsive photo-thermal performance, 20 mg of composite microspheres were suspended in 2 mL of phosphate buffer saline (PBS, 7.4) held in a 5-mL eppendorf tube and irradiated with an 808 nm NIR laser (2 W). The distance between solution and NIR probe was fixed at 5 cm. The temperature of the samples was monitored with a digital thermometer.

3. Results and Discussion
GNRs were synthesized via the conventional CTAB-mediated seed growth method [14]. UV spectrum of the GNR suspension was shown in Figure 2a. It is clearly observed that GNRs presented two typical adsorption bands at 512 nm and 821 nm. In general, the former was assigned to the transverse localized surface plasmon resonance, while the latter was assigned to longitudinal localized surface plasmon resonance. The presence of the band at 821 nm indicated that GNRs had the NIR-responsive and might show photo-thermal property under the NIR irradiation. To further confirm the formation of the GNR, size and morphology of GNRs were analyzed with a TEM measurement shown in Figure 2b. It is clearly observed that GNRs presented the typical rod-like morphology and their size dimension was 78±15 nm in length and 17±2 nm in width.

To produce SA/GNR composite spheres, the SA/GNA aqueous mixture was emulsified in the paraffin and then treated with Ca ions [8-11]. Size and morphology of the resultant samples were shown in Figure 3. Despite the presence of GNRs, both types of spheres were spherical in shape and had a similar size range of 5-40 μm, indicating that the SA spheres and SA/GNR composite spheres were successfully synthesized by means of emulsion technique and Ca cross-linking process.

Figure 2 (a) UV spectrum and (b) TEM image of GNR.
To further confirm the formation of SA/GNR composite spheres, the crystalline structure of SA spheres and SA/GNR composite spheres were shown in Figure 4. SA spheres had no any diffraction bands and showed typical amorphous structure. SA/GNR composite spheres had two diffraction bands at 38° and 44°, which were normally assigned to GNRs [6]. The former was assigned to (111) reflection plane, while the latter was assigned to (200) reflection plane. In contrast, the presence of GNRs further confirmed the formation of SA/GNR composite spheres.

It has been reported that GNRs and their derivatives show the excellent NIR-responsive photo-thermal properties [6]. From the above results, it has been confirmed that the SA/GNR composite spheres were successfully synthesized. The presence of GNRs implied that the as-synthesized composite spheres were NIR-responsive. To confirm the photo-thermal property, the composite spheres were irradiated with an 808 nm NIR light. Figure 5 shows temperature curve of the aqueous suspension of the SA/GNR composite spheres with the GNR content of 0, 0.026%, 0.052% and 0.104% under the irradiation of 808 nm NIR light. It was clearly observed that the temperature
change of the composite spheres was strongly correlated with the content of GNR and the irradiation time. No significant change in temperature for the composite spheres was observed in the absence of the GNRs. After combination of GNRs, the temperature for the composite spheres was increased from 28°C to 39°C as the content of GNRs was increased from 0.026% to 0.104%. Also, the temperature was gradually increased with increasing the irradiation time. These results indicate that the present composite spheres presented NIR-responsive photo-thermal property and their photo-thermal property could be well controlled through adjustment of GNR content and NIR irradiation time.

Figure 5 Temperature curve of the aqueous suspension of the SA/GNR composite spheres with the GNR content of 0, 0.026%, 0.052% and 0.104% under the irradiation of 808 nm NIR light.

4. Conclusions

In this study, the alginate/GNR composite spheres with the size range of 5-40 μm were synthesized via an emulsion technique and showed a controllable NIR-responsive photo-thermal property.

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