J|A|C|S COMMUNICATIONS

Published on Web 10/13/2009

Mechanical Capping of Silica Nanotubes for Encapsulation of Molecules

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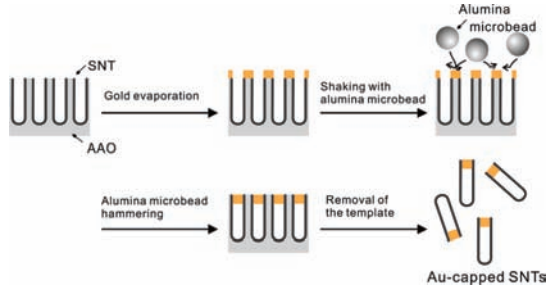
Recently, multifunctional silica nanotubes (SNTs) are being widely used for many biomedical applications due to their structural benefits such as distinctive inner and outer surfaces which can be functionalized differentially.[1−5] Controlling the structure of the open end of SNTs is crucial to control drug/gene uptake and the release rate for the development of an elaborate drug/gene delivery system and to fabricate multifunctional SNTs containing desired functional molecules or NPs inside of SNTs.[6] Capping of SNTs would be the easiest approach to control the open end's geometry of SNTs and has been achieved using chemical reactions such as imine bond formation with polymer nanoparticles[7] or a Au growth reaction selectively at the open ends of SNTs.[8] However, the chemical capping methods limit the availability of possible cargo molecules due to the issue of chemical compatibility between cargo molecules (e.g., drug, gene, or other functional molecule) and the capping chemical reaction.

In this paper, we describe a general capping method of SNTs using an alumina microbead hammering treatment, which can be used to encapsulate functional molecules into SNTs without chemical linkers or chemical reactions. Scheme 1 shows a schematic diagram for the preparation of Au-capped SNTs. First, SNTs were prepared in the pores of a homemade nanoporous anodic aluminum oxide (AAO) template using a surface sol−gel (SSG) method.[8,9] SSG enables highly uniform control of the wall thickness of SNTs with the accuracy of less than 1 nm by the controlling number of SSG cycles.

Scheme 1. Schematic Diagram for the Preparation of Au-Cap Using Alumina Microbead Hammering Treatment[a]



[a] Ag and PLGA were also used as capping materials (see Figure 2B and 2C).

A gold layer (72-nm thickness) was deposited onto the SNT-grown AAO template using Au evaporation. The resulting template was then transferred into a 1.5 mL microtube filled with alumina microbeads and was treated with alumina microbead hammering by shaking vigorously in a microtube vortex for 10 min up to 72 h at the maximum speed (Vortex Genie 2).[10] Figure 1 shows SEM images of SNT-grown AAO with a Au layer on the top before and after microbead hammering treatment for 48 h, respectively.

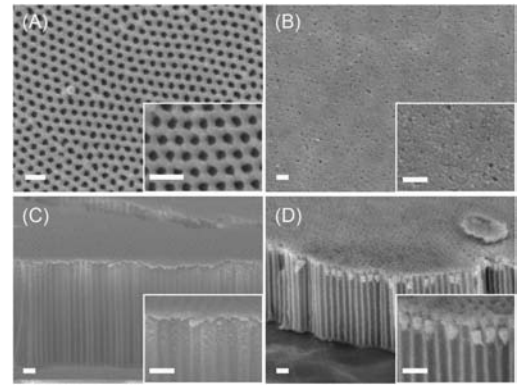


Figure 1. Top-view (A, B) and side-view (C, D) SEM images of SNT-grown AAO templates before (A, C) and after (B, D) alumina microbead hammering treatment of Au evaporated SNT-AAO surface. Scale bars are 200 nm.

As seen in Figure 1A, although the pore diameter decreases after the Au deposition compared to the SNT-grown AAO without a Au layer (Figure S1), the pores still remain open. However, after 48 h of the hammering treatment with alumina microbeads, most of the pores were closed, indicating that the gold layer located on the AAO surface was flattened down by the hammering action of the alumina microbeads and was inserted into the open entrance part of the SNTs (Figure 1B). This result can be clearly seen in the side-view SEM images of the sample. Before the hammering treatment (Figure 1C), it seems that the continuous gold layer is placed on the top of the SNT-grown AAO template with measurable thickness. In contrast, after the hammering treatment, independent cylinder-shaped gold caps are found near the open ends of the nanotubes (Figure 1D). For the control experiment carried out with SNT-grown AAO without a gold layer, no such nanostructure was found at the open ends of the SNTs after the alumina microbead hammering treatment. Figure 2A shows transmission electron microscopy (TEM) images of free-standing SNTs liberated from the AAO template, which reveals that the Au cap was successfully fabricated at the open end of the SNTs.

The success of this strategy lies in the right control of the hardness of the materials used in this experiment, including gold, alumina, and silica. Otherwise, unwanted damage to the nanostructure during the hammering process may occur. Gold is a malleable metal, so that we can expect that its shape can be easily changed

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10.1021/ja905485s CCC: $40.75

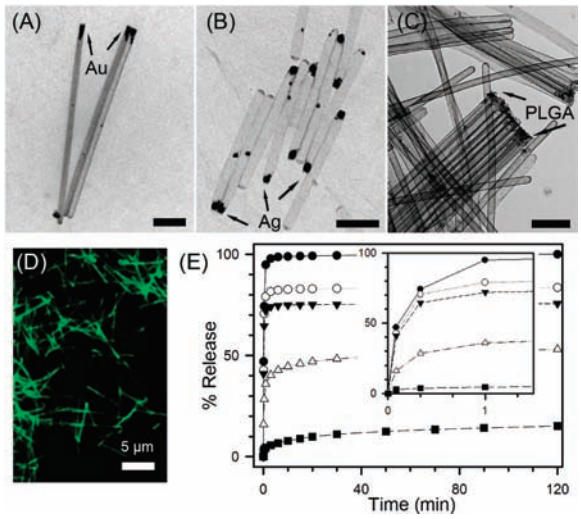

Figure 2. TEM images of capped SNTs with Au (A), Ag (B), and PLGA (C) after liberation from AAO template. Fluorescence microscope image of fluorescein-encapsulated SNTs (D). Scale bars are 500 nm, if not specified. (E) In vitro release of fluorescein from SNTs hammered with alumina microbeads for the given time: 0 min (●), 2 min (○), 10 min (▼), 6 h (Δ), and 2 d (■).

by mechanical contact with hammering materials harder than gold. Considering all these factors, alumina microbeads were selected as the hammering material because the alumina microbead is composed of the same material as AAO. According to Mohs hardness scale,[11] alumina (ca. 9) is a harder material than Au and SiO_2 (ca. 7). As a consequence, the gold layer could be selectively reformed into the Au cap by the hammering treatment, while SNT-grown AAO remained unaffected.

When it comes to the availability of capping materials, the advantage of our capping method is apparent because any material with appropriate malleability like Au can be employed as the capping material. Figure 2B shows TEM images of SNTs with silver caps prepared by the same method used for the Au caps. Not only inorganic metals but also organic polymers can serve as the caps for SNTs. Figure 2C shows TEM images of SNTs with polylactic-co-glycolic acid (PLGA) prepared by the hammering treatment. Unlike Au and Ag caps, biodegradable polymer caps such as PLGA can serve as reversible capping agents that respond to the surrounding conditions, which is highly required for drug/gene delivery.

Another advantage of our capping method is that functional materials can be easily encapsulated inside the SNT without surface immobilization or chemical reaction. This means functional materials do not need to be derivatized to have chemically reactive groups such as amine, carboxylic acid, etc. to be attached to the surface through covalent bonds. For a proof-of-concept experiment, we encapsulated organic fluorescent dyes, fluorescein, and Rhodamine B as model cargo molecules. As seen in Scheme S1, before the hammering treatment, SNT-grown AAO was immersed in a dye solution and dried in the air. Then the same processes as mentioned above were performed under darkness. Figures 2D and S3 show the fluorescence microscope images of the resulting SNTs with fluorescein and Rhodamine B inside, respectively.

To investigate the dependence of capping efficiency on hammering treatment times, we performed dye release tests with fluorescein-encapsulated Au-capped SNTs while the SNTs were embedded in the pores of the template (see Supporting Information). Assuming that the maximum amount of fluorescein equals the amount of fluorescein released from the SNTs without the hammering treatment, as seen in Figure 2E, the saturation values of the amounts of dyes released from the hammering-treated SNTs decrease with respect to hammering time but always stay below 100%. This result seems to be caused not by the equal amount of partial release from every SNT but by the coexistence of fully capped SNTs and partially capped SNTs in the sample as we can see in SEM images of the template showing both the fully capped SNTs and partially capped SNTs (Figure S2B−D). These saturation values thus can be used to estimate the efficacy of our capping method. Therefore, we can conclude that at least a 2-d hammering time is required to obtain 85% fully capped SNTs because 15% dye release was observed from 2-d hammering treated SNTs. In addition, an experiment carried out with the free-standing Au-capped SNTs liberated from the templates after the release test revealed that the fluorescent intensity of the fluorescence active SNTs did not show any noticeable decrease after a 6-week incubation in water.

In conclusion, we successfully developed an efficient method that can be used to cap the open end of SNTs with various materials such as Au, Ag, and PLGA. This method employs deposition of desired capping materials onto the SNT-grown AAO and is followed by an alumina microbead hammering treatment. We also demonstrated that desired functional materials could be encapsulated inside SNTs without chemical linkers and safely stored for days. We believe that functional caps that are biodegradable will contribute to the advent of smart SNTs required for an ideal drug/gene delivery system.

Acknowledgment. This subject is supported by The Pioneer Research Program of the Korea Science and Engineering Foundation (KOSEF), by the Industrial Core Technology Development Program funded by the Ministry of Knowledge Economy (No. 10033183), and by the Kyungwon University Research Fund in 2009. This research was funded by a University System of Maryland Integrated Nanobio Seed Grant through the Maryland Department of Business and Economic Development and the National Institutes of Health (1R01DE019050) and partly supported by Korea Science and Engineering Foundation (KOSEF) grant funded by the Korean government (MEST, R31-2008-000-10071-0).

Supporting Information Available: Experimental details and detailed analysis of SEM images depending on hammering treatment time. This material is available free of charge via Internet at http://pubs.acs.org.

References

(1) Mitchell, D. T.; Lee, S. B.; Trofin, L.; Li, N. C.; Nevanen, T. K.; Soderlund, H.; Martin, C. R. *J. Am. Chem. Soc.* **2002**, *124*, 11864–11865.
(2) Chen, C.-C.; Liu, Y.-C.; Wu, C.-H.; Yeh, C.-C.; Su, M.-T.; Wu, Y.-C. *Adv. Mater.* **2005**, *17*, 404–407.
(3) (a) He, B.; Son, S. J.; Lee, S. B. *Langmuir* **2006**, *22*, 8263–8265. (b) He, B.; Son, S. J.; Lee, S. B. *Anal. Chem.* **2007**, *79*, 5257–5263.
(4) Buyukserin, F.; Medley, C. D.; Mota, M. O.; Kececi, K.; Rogers, R. R.; Tan, W.; Martin, C. R. *Nanomed.* **2008**, *3*, 283–292.
(5) Nan, A.; Bai, X.; Son, S. J.; Lee, S. B.; Ghandehari, H. *Nano Lett.* **2008**, *8*, 2150–2154.
(6) Hillebrenner, H.; Buyukserin, F.; Stewart, J. D.; Martin, C. R. *Nanomed.* **2006**, *1*, 39–50.
(7) Hillebrenner, H.; Buyukserin, F.; Kang, M.; Mota, M. O.; Stewart, J. D.; Martin, C. R. *J. Am. Chem. Soc.* **2006**, *128*, 4236–4237.
(8) Son, S. J.; Lee, S. B. *J. Am. Chem. Soc.* **2006**, *128*, 15974–15975.
(9) Kovtyukhova, N. I.; Mallouk, T. E.; Mayer, T. S. *Adv. Mater.* **2003**, *15*, 780–785.
(10) Iwasaki, T.; Satoh, M.; Koga, T. *Powder Technol.* **2001**, *121*, 239–248.
(11) Lide, D. R. *CRC handbook of chemistry and physics*, 76th ed.; CRC Press: Boca Raton, FL, 1995; pp 12−191.

JA905485S