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Assembly of functional gold nanoparticle on silica microsphere

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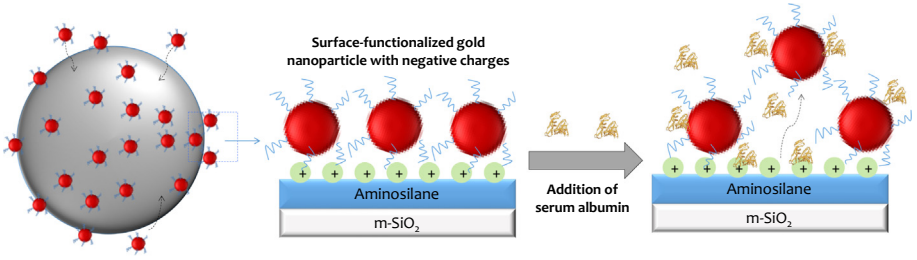
HIGHLIGHTS

- Methodology for gold nanoparticle on silica microsphere by an electrostatic-directed approach.
- Improved homogeneity and loading of gold on silica microsphere through control of surface properties.
- Binding and BSA-induced desorption of gold strongly correlated to molecular conjugation.

GRAPHICAL ABSTRACT



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ABSTRACT

We demonstrate a controlled synthesis of silica microsphere with the surface-decorated functional gold nanoparticles. Surface of silica microsphere was modified by 3-aminopropyltriethoxysilane and 3-ami nopropyldimethylethoxysilane to generate a positive electric field, by which the gold nanoparticles with the negative charges (unconjugated, thiolated polyethylene glycol functionalized with the traceable packing density and conformation) were able to be attracted to the silica microsphere. Results show that both the molecular conjugation on gold nanoparticle and the uniformity in the amino-silanization of silica microsphere influenced the loading and the homogeneity of gold nanoparticles on silica microsphere. The 3-aminopropyldimethylethoxysilane-functionalized silica microsphere provided an uniform field to attract gold nanoparticles. Increasing the ethanol content in aminosilane solution significantly improved the homogeneity and the loading of gold nanoparticles on the surface of silica microsphere. For the gold nanoparticle, increasing the molecular mass of polyethylene glycol yielded a greater homogeneity but a lower loading on silica microsphere. Bovine serum albumin induced the desorption of gold nanoparticles from silica microsphere, where the extent of desorption was suppressed by the presence of high-molecular mass polyethylene glycol on gold nanoparticles. This work provides the fundamental understanding for the synthesis of gold nanoparticle-silica microsphere constructs useful to the applications in chemo-radioactive therapeutics.

1. Introduction

Colloidal silica has shown to be attractive for a variety of applications in various emerging biotechnology [1–5]. Because of the advantageous properties including the high hydrophilicity, high mechanical stability, and the high biocompatibility, colloidal silica is one of the most promising candidates for the biomedical applications. Furthermore, the silane chemistry provides an effective route for the rational design. Through the surface engineering with different types of functional ligands via the silane chemistry, the efficiency of the colloidal silica in the targeting therapy can be effectively improved. Considering all types of colloidal silica exploited in the existing platforms, silica microsphere (m-SiO_2) satisfies the requirements of the targeting therapy. In principal,

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drugs molecules can be adsorbed onto the surface of m-SiO_2 or be encapsulated inside the m-SiO_2, delivered to the target, and then released at the specific sites of tumor cells [1–4,6,7]. The concept of using m-SiO_2 as a new vector to the existing therapeutics is attractive, since it can be used as a multi-functional carrier for drug delivery while avoiding the toxicity to healthy tissue.

Recently, utilizing the concept of nanotechnology to the existing m-SiO_2-based platform is popular in therapeutics. Through an assembly of functional nanoparticles (NPs) to m-SiO_2 (denoted as m-SiO_2-NP), we can combine the advantageous properties from both NP and m-SiO_2 to provide a synergetic effect in therapeutics [6]. Previous studies have used the hollow m-SiO_2 to encapsulate the functional NPs including the therapeutic proteins and quantum dots. Then the m-SiO_2-NP can be delivered to the specific sites of the human body where the therapeutics release [8]. In addition to the controlled release of drugs and genes, the m-SiO_2-NP construct can be used in vitro as contrast-enhancing agent for ultrasound imaging, or it can be used to enhance the optical limiting performance of nanoparticle dispersions [9].

In addition to the encapsulation method described previously, using a surface-engineering approach to decorate the surface of m-SiO_2 with NPs has also been utilized. The advantage is that this approach allows for the combination of the functionalities of NPs and the existing m-SiO_2-based biomedical platforms [10,11]. Regarding to the NPs for the biomedical applications, colloidal gold nanoparticles (AuNPs) are of particular interest due to its high biocompatibility and specific surface plasmon resonance (SPR) band, by which AuNP can be exploited for the hyperthermal treatment as a part of cancer therapy [12–14]. Recent advancements have been achieved such as the fabrication of an enzyme-mimic fluorescence nanosensor [10] and plasmon modulated light scattering-based bio-sensing techniques [15] through a combination of m-SiO_2 with the surface-bound AuNPs through a direct mixing of m-SiO_2 with Au colloids. The combination exhibits good features of selectivity and stability in the determination of the concentration of glucose in solution. The selective enhancement of the elastic light scattering signals was found through a combination of m-SiO_2 with a surface layer of AuNPs that induces both a shift in frequency and an increase in intensity for the resonant scattering peaks of m-SiO_2. The enhancement in the scattering intensity is controllable by using AuNPs, which allows for the real-time monitoring of the activities of live cells [15]. The therapeutic performance in bio-diagnostics and targeted drug delivery can be improved, showing that the construct can be designed to achieve a target cell-specific uptake for the efficient therapy. However, an obvious challenge is to uniformly deposit AuNP onto the m-SiO_2 with a desired loading and structural stability. Hence understanding the mechanism of AuNP deposition onto the m-SiO_2 through surface functionalization is critically important.

In this work, we propose an electrostatic-directed approach as a viable strategy for the assembly of m-SiO_2–AuNP construct. As depicted in Fig. 1, the electrostatic interaction was created on the surface of the aminosilane-modified, positively-charged m-SiO_2, by which the functional AuNPs with a net negative charge can be attracted to the surface of m-SiO_2. Due to the charge repulsion from the deposited AuNPs, the unbound AuNPs can be attracted to an unoccupied location to create a homogenous deposition pattern on the surface of m-SiO_2. By adopting a further surface functionalization via ligand conjugation, we expect to provide a control to the surface properties of AuNPs, and thus the functionality of the m-SiO_2–AuNPs can be enhanced. As a test bed, we use m-SiO_2 with a diameter of 40 μm which can be used to partially embolize the small arterial vessels supplying the tumor and also deliver intense radiation and potent drug molecules locally to destroy the tumor cells in the liver tumor cell treatment (i.e., typically 10–100 μm in diameter) [16–18]. Biomedically-interested [19–23] unconjugated AuNPs (i.e., citrate-stabilized) and partially-PEGylated AuNPs with different molecular mass (M_m) were employed to be deposited on the surface of m-SiO_2. The aminosilanes (3-Aminopropypl)triethoxysilane (APTES) and 3 -Aminopropyldimethylethoxysilane (APDMES) are chosen as representative silanes, both of which have shown to be useful for the biocompatible surface modifications [24–27]. We evaluate the structure stability of m-SiO_2–AuNP by using bovine serum albumin (BSA) as a test plasma protein, and we monitor the change of AuNP deposition on the m-SiO_2 after the interaction with BSA. Our objective is to provide a generic approach to electrostatically assemble the m-SiO_2–AuNP constructs in aqueous solution and to shed light on the surface chemistry of m-SiO_2 and AuNPs and the relationship to the structural stability of the m-SiO_2–AuNP after the subsequent interaction with proteins in the media.

2. Materials and methods

2.1. Materials

Powders of silica microspheres (m-SiO_2, nominally 37–40 μm in diameter) were obtained from Cospheric Inc. (Santa Barbara, CA, USA). Nominally 60 nm citrate-stabilized Au colloids were purchased from BBI Solutions (Cardiff, UK). (3-Aminopropypl)triethoxysilane (APTES, 98%) was supplied by Alfa Aesar (Heysham, USA). 3-Aminopropyldimethylethoxysilane (APDMES, 92%) was from Gelest Inc. (Morrisville, USA). SH-PEGs with M_m = 800 g/mol (SH-PEG800. Polydispersity index = 1.1) and M_m = 6000 g/mol (SH-PEG6K. Polydispersity index = 1.1), bovine serum albumin (BSA. >98%), and ammonium acetate (AmAc. >98%) were purchased from Sigma–Aldrich (St. Louis, MO, USA). SiO_2 nanopowders (HDK® N20) was obtained from Wacker (Munchen, Germany). Ethanol (⩾99.8%, Sigma–Aldrich, St. Louis, MO, USA) and biological grade 18.2 MΩ cm deionized (DI) water (Millipore, Billerica, MA, USA) was used for preparation of solutions.

2.2. Preparations of silanized m-SiO_2, surface-PEGylated AuNP, and m-SiO_2–AuNP

Aminosilane solution (110 μL, 0.35 mol/L) was prepared by using a mixture of ethanol and DI water as solvent. m-SiO_2 colloids (110 μL, 0.01 g/ml) were added to the solution and reacted for 2 h. After reaction, both the unbound and the weakly-bound silane molecules were removed through the solvent replacement.

The PEGylation of AuNP was performed by using SH-PEG with a concentration of 4 μmol/L to react with Au colloids for at least 12 h. Former studies have shown that the thiol–Au chemistry provide an effective route to graft the ligands onto the surface of AuNP [23,28,29]. In this study we adopt the mechanism to PEGylate the Au surface through the thiol–Au bond. After reaction, the unbound SH-PEG molecules were removed from the system, and then 50 μL of the Au colloids was directly mixed with ≈5 μL of silanized m-SiO_2 colloids and reacted for 1 h. Finally the solvent of Au colloids was replaced with equal volume of DI water for storage and the subsequent analysis. The ionic strength was controlled by using the 2 mmol/L of sodium chloride or AmAc aqueous solution as the solvent.

2.3. Characterization methods

2.3.1. Scanning electron microscopy (SEM)

The field-emission SEM (Hitachi SU8010, Hitachi, Japan, operated at 10 kV) was employed to characterize the morphology and primary diameter of m-SiO_2 and AuNP. The estimated resolution was ≈1 nm. Samples of m-SiO_2 and m-SiO_2–AuNP were