Surface Functionalization of Upconversion Nanoparticle for Biological Usage

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Abstract – Upconversion nanoparticle (UCNP) coated with uniform silica shells, which were further functionalized with poly(ethylene glycol) (PEG) and (3-aminopropyl)triethoxysilane (APTES), produces water dispersible core-shell structured UCNPs with average hydrodynamic size around 100 nm. The hydrothermal treatment to the particle stabilize amines of APTES on the surface of UCNPs. The stable and positive zeta potential also prove that the amines is successfully attached on the particle's surface, with good stability in colloidal solution. We also discovered that hydrothermal treatment temperature over 200 °C diminish the luminescence properties of UCNPs.

Index Terms – Upconversion, functionalization, silica, core-shell.

INTRODUCTION

Luminescence nanomaterials offer great potential for disease diagnose and even treatment. In biomedical field, they have been demonstrated to be useful in in vivo imaging and photodynamic therapy [1]. For the biological application mentioned above, utilization of upconversion luminescence (UCL) emission is favorable [2]. Upconversion luminescence is a process where low energy light is converted to higher energy light through sequential absorption of multiple photons from low power continuous wave near infrared (NIR) laser. Upconversion luminescence generates low auto-fluorescence and less damage to cells, it also has deeper penetration depth compare with ultraviolet (UV) and visible light excitation [3]. Ideal upconversion nanoparticle system not only should own multimodality for imaging and therapy purpose, but also, most importantly, should have stable colloidal stability in physiological buffer.

A sort of method to synthesize UCNPs have been evolved, three common methods usually used. They are co-precipitation [4], thermal decomposition [5], and hydro(solvo)thermal process [6]. Thermal decomposition is the best technique to obtain highly monodisperse UCNPs with highest luminescent quantum yield. In this method, rare earth (RE) trifluoroacetates are heated to attain thermal equilibrium in the presence of oleic acid and octadecene [7]. Here, oleic acid function as a stabilizing agent to terminate particle agglomeration, while octadecene behave as a high boiling point solvent. The oleic acid forms a coordinate bond to the surface of particles, hence the surface is very hydrophobic. UCNP prepared via thermal decomposition is well dispersed in organic solvents such as cyclohexane, but insoluble in aqueous solution.

If employed in biosciences, UCNPs have to be well dispersible in physiological solution. Furthermore, in order to make particles carrying bioeffectors, the surface of UCNPs has to be functionalized to facilitate bioconjugation of appropriate biomolecules. Such surface chemistry is expected to be versatile to immobilize proteins, nucleic acid oligomers, peptide, and drugs [8]. To fulfil these requirements, we hence studied the surface functionalization of upconversion nanoparticles for biological usage using detergent assisted silica coating followed by hydrothermal Stober process to install polyethylene glycol (PEG) and amine.

METHOD

A. Synthesis of $NaYF_4$ nanocrystals

$NaYF_4$ nanocrystal doped with lanthanide ion is synthesized by the previous protocol [5] with minor modification. UCNPs is synthesized by mixing corresponding amount of yttrium and lanthanide acetate hydrate in 60 mL 1-octadecene and 24 mL oleic acid. The solution was heated to 120 °C under vacuum with stirring to remove water and oxygen. The mixture was cooled down to room temperature and add 40 mL of methanol solution containing corresponding amount of ammonium fluoride and sodium hydroxide. The mixture was stirred and the temperature was increased to 80 °C for 30 minutes to evaporate methanol. After the methanol removal, the solution is heated at 310 °C under N_2 flow for 1 hour, then cooled down into room temperature. The nanoparticle was precipitated by adding ethanol to reaction mixture and washed with hexane. The UCNPs was re-dispersed and stored in cyclohexane.

B. Coating of silica on the nanocrystals

Silica coating is prepared by following previous protocol [9] with minor modification. The coating of silica on the nanocrystal is done by mixing 400 µL CO-520 and 50 mg $NaYF_4$ nanocrystal in 40 mL cyclohexane. The mixture is stirred for 10 min, then 1.6 ml CO-520 and 320 µl ammonia (wt 30%) was added. The container was sealed and sonicated for 20 min. After that, 160 µL TEOS were added into the solution, and the solution was stirred for overnight at speed of 500 rpm at room temperature. $NaYF_4$ @SiO_2 nanocrystals were precipitated by adding ethanol, and the nanocrystals were washed with ethanol/water (1:1 v/v) twice and then stored in ethanol.

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C. PEG and Amines Functionalization with hydrothermal treatment

PEG and Amines functionalization is done by following previous protocol [10] with modification. 20 mL ethanol containing 20 mg UCNP@Silica is mixed with 4 mL deionized water and 200 µL ammonium hydroxide. The mixture is stirred for 5 minutes, then 123 µL PEG-Silane$_{Mw500}$ and 47 µL APTES is added into the solution. The resulting solution is stirred at speed of 500 rpm for overnight. After that, the solution is degassed and purged with N_2 for 30 minutes, and then put inside the Teflon lined autoclave chamber. It is heated at 70 ºC, 100 ºC, and 200 ºC for 48h. The resulting nanoparticles is precipitated by centrifugation and washed with ethanol/water (1:1 v/v) twice and then stored in ethanol.

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