Dendrimer-based Nanoparticles with Dual-Modality Imaging for Atherosclerosis

Huari Kou, Da Huang, Hu Yang*

Linda and Bipin Doshi Department of Chemical and Biochemical Engineering, Missouri University of Science and Technology, Rolla, MO 65401, United States; *huyang@mst.edu

Statement of Purpose: Cardiovascular disease has been one of the leading causes of death worldwide. Early detection and targeting therapy play an essential role in atherosclerosis progress.[1] Multifunctional nanoparticles possessing diagnostic and therapeutic capabilities are desired for diagnosing and treating atherosclerosis.[2] In this work, we designed and synthesized dendrimer-based nanoparticles with dual-modality imaging for both NIR and PET imaging for atherosclerosis diagnosis and therapy.

Materials: DAB-core PAMAM dendrimer generation 5 (G5) was purchased from NanoSynthons (Mt Pleasant, MI). $Cu(NO_3)_2$ and $NaBH_4$ were purchased from Sigma-Aldrich (St. Louis, MO). PEG-Mannose was purchased from Ruixi (Xi'an, China). IRDye 800CW NHS Ester was from LI-COR.

Method: 1) IRDye 800CW and Cu nanoparticle labeled G5: G5 and $Cu(NO_3)_2$ solution were mixed under stirring. After 1 hour, excessive $NaBH_4$ solution was added into the mixture to reduce copper ions. Then, IRDye 800CW NHS Ester was mixed with the solution. After dialysis, IRDye 800CW and Cu nanoparticle labeled G5 could be obtained. 2) G5 gel nanoparticle: As shown in Figure 1(a), the flash nano-precipitation method was conducted to synthesize G5 gel nanoparticle. In this step, NHS Ester cross linker was dissolved in acetone, while G5 with copper nanoparticles and 800CW dye was dissolved in DI water. The other two solutions were DI water. All solutions were mixed at a speed of 40 mL/min. 3) PEG-Mannose modified G5 gel nanoparticle: PEG-Mannose NHS Ester aqueous solution was mixed with G5 gel nanoparticle and purified via dialysis.

Characterization: UV-Visible spectrum was used to analyze the copper reduction process. And Zeta sizer was applied to detect the size distribution of nanoparticles. NIR response of nanoparticle material was tested by animal imager with 745nm excitation and 810 nm emission. TEM and SEM were applied to characterize the morphology of nanoparticles.

Results: The formation of copper nanoparticles was verified by the UV-Visible spectra. As shown in Figure 1(b), a peak around 570 nm disappeared after reduction, corresponding to the reduction of copper ion to copper metal.[3] The size distribution of different samples is displayed in Figure 1(c). G5 dendrimer size was about 7 nm. And it increased to 140 nm after reacting with a cross-linker reactant. The nanoparticle size was about 170 nm after conjugating with PEG-Mannose. The resulting nanoparticles were tested under an animal imager for their NIR imaging capability assessment. The nanoparticles in suspension exhibited good response to NIR irradiation with a low NIR dye concentration of about 40 nmol/mL.

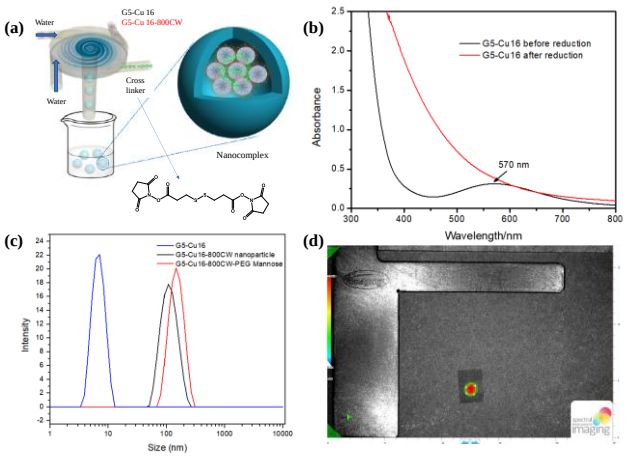

Figure 1. (a) Illustration of flash nano-precipitation method; (b) UV spectra for G5-Cu16 complex before and after reduction; (c) Size distribution of different samples; (d) NIR image of G5-Cu16-800CW nanoparticle.

Conclusions: This well-designed nanoparticle complex can be readily used in PET imaging by substituting copper with its radioactive counterpart. We will test PET imaging in the near future. This nanoparticle can be further functionalized with different groups for targeted atherosclerosis diagnosis via NIR and PET imaging. Meanwhile, it can also act as a vehicle for drug delivery.

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Reference:

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