FUNCTIONALIZED GOLD NANOROD CORE-MESOPOROUS SILICA SHELL NANODEVICES WITH CONTROLLED RELEASE OF ANTICANCER DRUG

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INTRODUCTION: Gold nanorods (AuNRs) can find many biomedical applications including photothermal therapy [1]. AuNRs are normally coated with cetyltrimethyl ammonium bromide (CTAB) when synthesized via seed-mediated growth, resulting in cytotoxicity and low stability which hinder their medical applications. Coating silica on AuNRs may solve the problem and also makes it possible to conjugate targeting ligands to AuNRs [2]. But the shape and thickness control and functionalization of silica shell are the challenges. The reported methods for coating silica often lack reproducibility and also require precise control of CTAB concentration in AuNR stock solution [3]. This investigation developed a facile method to make folic acid modified AuNR core-mesoporous silica shell (AuNR@mSiO2) nanodevices for anti-cancer applications.

MATERIALS AND METHODS: AuNRs were synthesized by a modified seed-mediated growth method using binary surfactants. To form mesoporous silica shell on AuNRs, highly diluted tetraethyl orthosilicate (TEOS) in ethanol was the precursor and surfactants adsorbed on AuNR surface were used. Different amounts of TEOS/ethanol solution and CTAB were investigated for forming silica shell. To functionalize the surface of AuNR@mSiO2 nanoparticles (NPs) with amino groups, NPs were refluxed in boiled ethanol containing (3-aminopropyl) triethoxysilane (APTES). Folic acid was then conjugated to amino groups on silica shell. After removal of CTAB via refluxing in NH3NO3 and ethanol solution, doxorubicin hydrochloride (DOX, anticancer drug) was loaded into mesopores of NPs. Drug release behaviours were studied.

RESULTS AND DISCUSSION: There are problems for the seed-mediated growth of AuNRs using surfactant CTAB. To improve the uniformity and tune their surface plasmon resonance wavelength, binary surfactants could be used [4]. This investigation used a binary surfactant (sodium oleate and CTAB) in the growth solution to tune the

dimensions of AuNRs. The synthesized AuNRs showed high uniformity with 70 nm in length and 25 nm in diameter with negligible impurities (e.g. spheres) (Fig.1a). Previous studies hardly obtained a highly uniform silica coating and proper thickness [5]. In this investigation, a modified method was used. Also, through optimizing the process and concentration of reactants and surfactants, AuNR@mSiO2 NPs had a uniform and controllable thickness for the silica coating (Fig.1b). Mesopores in this coating were observed under TEM. After silica coating, the maximum longitudinal SPR wavelength red-shifted slightly but was still in the near-infrared region. Upon laser irradiation, AuNR@mSiO2 suspensions exhibited temperature increases (Fig.2a) due to the photothermal effect of AuNR core. Drug release from AuNR@mSiO2 was studied at different temperatures with or without laser irradiation. Under laser irradiation, drug release was promoted due to enhanced diffusion of drugs caused by temperature increase (Fig.2b).

CONCLUSION: A facile three-step method was developed to fabricate folic acid modified AuNR core-mesoporous silica shell (AuNR@mSiO2) NPs as multifunctional nanodevice for anti-cancer applications. The synthesized AuNRs were uniform in size and shape and the mesoporous silica shell formed on AuNRs was also uniform. The anti-cancer drug could be stored in the mesopores of the silica coating. It could be released in a controlled manner at the body temperature or under laser irradiation.

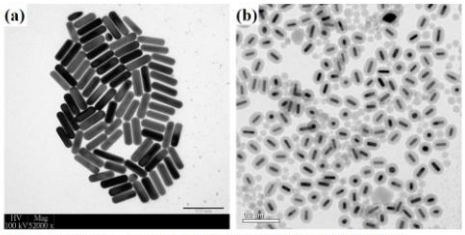

Fig. 1. TEM images of (a) AuNRs and (b) AuNR@mSiO$_2$ nanoparticles.

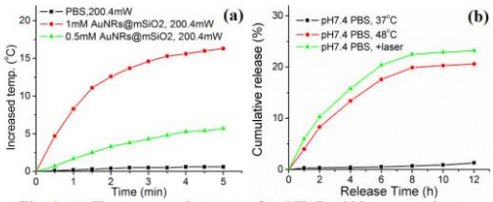

Fig. 2. (a) Temperature increase of AuNR@$mSiO_2$ suspensions upon laser irradiation; (b) Drug release curves of AuNR@$mSiO_2$ at different temperature with or without laser irradiation.

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