SYNTHESIS AND CHARACTERISTICS OF CORE-SHELL AND MULTISHELL STRUCTURED NANOPARTICLES FOR ANTICANCER APPLICATIONS

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INTRODUCTION: In developing new theranostics, core-shell and multishell structured composite nanoparticles (NPs) are of great interest because they not only provide functions based on properties of the core but also generate new functions such as combined cancer therapies[1]. Gold NPs (AuNPs) have been extensively investigated for theranostics. Compared to spherical AuNPs, gold nanorods (AuNRs) have major advantages for cancer detection and treatment[2]. Mesoporous silica NPs are often used as drug carriers due to their rich mesopores. It is also shown that surface enhanced Raman scattering (SERS) is highly sensitive to the AuNP nanostructure[3]. This study investigated the synthesis and properties of AuNP capped AuNR core-mesoporous silica shell (AuNR@mSiO2@Au) composite NPs.

MATERIALS AND METHODS: Core-shell structured AuNR@mSiO2@Au NPs were synthesized using a three-step process. First, AuNRs were synthesized using a seed-mediated growth method with binary surfactants. Secondly, AuNR@mSiO2 NPs were made using a sol-gel and surfactant-removal method while mesopores in silica shell were loaded with doxorubicin hydrochloride (DOX, anticancer drug). Thirdly, AuNPs with a diameter of ~5 nm were assembled on the surface of AuNR@mSiO2 NPs to obtain AuNR@mSiO2@Au NPs with the core@shell@shell structure. For cancer detection, R6G (rhodamine 6G, a Raman reporter) was embedded in NPs. Drug loading and release for this nanodevice were studied. The SERS activity of NPs was measured using Raman spectroscopy.

RESULTS AND DISCUSSION: As-synthesized AuNRs showed a monodispersed morphology with a diameter of 20 nm and length of 75 nm. Core-shell structured AuNR@mSiO2 NPs were made with the thickness of the silica shell around 25 nm. After removal of the template (surfactants adsorbed on the surface of AuNR), the mesoporous structure of the silica shell was created on AuNRs (Fig. 1a). Fig.1b shows AuNR@mSiO2@Au NPs formed. Many AuNPs (5 nm in diameter) were deposited on the surface of AuNR@mSiO2 NPs. These AuNPs generated a lot of hotspots which would enable high sensitivity in SERS signals. Fig. 2a exhibits SERS curves. The intensity of Raman signals of R6G were significantly enhanced when it was embedded in AuNR@mSiO2@Au NPs, even at very low R6G concentration (10-5M). The photothermal effect arising from the AuNR core of AuNR@mSiO2@Au NPs was also

studied. When irradiated with a 780 nm laser, AuNR@mSiO2@Au immediately converted light to heat to increase the temperature of AuNR@mSiO2 suspensions. Temperature increase was up to 5℃ even at low laser intensity and with low NP concentration. Drug release from AuNR@mSiO2@Au was studied at 37℃ with and without laser irradiation. Under laser irradiation, the DOX release was much faster and in much larger quantity (Fig. 2b).

CONCLUSION: Core-shell and multishell structured AuNR@mSiO2@Au composite NPs could be successfully produced using a three-step process. These NPs are promising new theranostics for cancer detection and treatment. AuNPs on the outer surface of NPs would provide high-sensitivity SERS signals while AuNR core could provide the photothermal effect. Furthermore, the anti-cancer drug could be stored in mesopores of silica shell and released in a controlled manner.

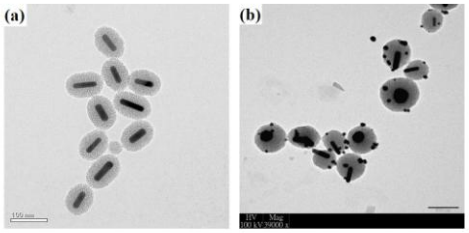

Fig. 1. TEM images of (a) AuNR@$mSiO_2$ nanoparticles and (b) AuNR@$mSiO_2$@Au nanoparticles.

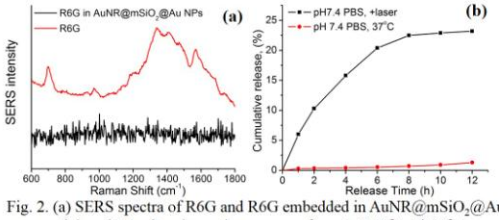

Fig. 2. (a) SERS spectra of R6G and R6G embedded in AuNR@$mSiO_2$@Au nanoparticles; (b) In vitro drug release curves from AuNR@$mSiO_2$@Au nanoparticles at 37°C with or without laser irradiation.

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