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Development of Methylene Blue Embedded Gold Nanorod@Silica Nanocomposites as Cancer Theranostic Platform

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Extended Abstract

Recently, gold nanorods (GNRs) have drawn much attention for biomedical applications due to their excellent plasmonic property and biocompatibility. Especially, surface-enhanced Raman scattering (SERS) technology based on GNRs has been recognized as an alternative to quantum dot-based fluorescence imaging method because GNRs can induce not only enhancement of the Raman signal by a factor of $10^8 \sim 10^{14}$ but also little photobleaching effect. Moreover, the longitudinal plasmonic response of GNRs can be rapidly converted into thermal energy as a result of lattice oscillation through electron–phonon coupling. This photothermal conversion of the plasmonic response of GNRs could offer an extraordinary therapeutic approach for various malignant and nonmalignant diseases. Consequently, GNRs have potential in terms of developing theranostics without complicated nanostructures. However, photothermal therapy may sometimes fail to completely annihilate solid tumors because it can trigger a cytoprotective pathway in cancer cells in response to physicochemical stresses, e.g., the expression of heat-shock proteins (HSPs). The surviving cancer cells could exhibit thermo-tolerance and chemotherapy resistance and thus become more difficult to eradicate. Therefore, development of a complementary therapeutic method based on the GNR system is strongly recommended to achieve increasing anticancer efficacy. Photodynamic therapy (PDT) is another photon-induced therapeutic method that uses a photosensitizer, but one of the major drawbacks in current PDT therapy is caused by resonant light wavelengths below 700 nm and the difficulty in preparing a water-soluble photosensitizer due to the hydrophobic structure of the photosensitizer. Methylene blue (MB) is not only a water-soluble phenothiazine photosensitizer with a high quantum yield of singlet oxygen ($^1O_2$) generation ($\phi_\Delta \sim 0.5$), but it is also a popular cationic dye for histological and bacteriologic staining owing to its prominent blue color. In addition, MB is very useful as an FDA-approved drug to treat methemoglobinemia, as an antimicrobial agent for treating urinary tract infections, and as an anti-parasitic agent for treating malaria infection. Additionally, recent studies have suggested that MB could be used as an antagonist against heat-shock response gene expression in cancer cells. From an economic point of view, its low price also facilitates its use in practical applications.

In the current work, we demonstrate MB-loaded GNR@SiO_2 (MB-GNR@SiO_2) core@shell nanoparticles as a theranostic platform for SERS cancer imaging and a near infrared (NIR) light-induced synergistic cancer therapy combining PDT and photothermal therapy. Raman enhancement factor was approximately 3.0×10^{10} and this SERS performance was enough to detect a single cancer cell. Unlike conventional PDT techniques, one of the most promising advantages of the present MB-GNR@SiO_2 nanoparticles is the photosensitizing response of the incorporated MB molecules *via* the NIR light through plasmonic electron transfer from the GNRs. Therefore, the cancer-killing efficacy of the present MB-GNR@SiO_2 nanocomposites could be significantly enhanced as compared to that of bare GNRs. We believe that the present study provides empirical evidence to substantiate the promising potential of MB-GNR@SiO_2 nanoparticles to significantly advance the field of cancer theranostics.