Brain-targeted image-guided drug delivery for HIV treatment

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Introduction

Antiretroviral therapies (ART) for human immunodeficiency virus (HIV) can reduce viral load significantly in plasma and other bodily fluids. However, the ultimate goal of eradicating HIV has not been attained due to limited accessibility of antiretroviral drugs to some locations and the existence of reservoirs. The brain is one of those sanctuary sites, and antiretroviral drugs show low effectiveness in central nervous system (CNS) penetration, primarily because of the Blood–Brain Barrier (BBB) [1]. Nanoparticle based-drug delivery systems have shown to improve the efficiency of brain delivery by active targeting, which includes magnetic targeting and cell-specific targeting through selective ligands. Among various nanoparticles, inorganic nanoparticles show promising properties for image-guided drug delivery, which enables efficient and accurate treatment by combining drug delivery and non-invasive imaging by a selective nanoformulation. In this project, we will develop near infrared (NIR)-responsive magneto-plasmonic nanostars (MPNS) bound with antiretroviral drug for image-guided drug delivery to the brain and on demand controlled release of antiretroviral drug using NIR. MPNS possess magnetic and plasmonic properties in a single nano-structure. This integration gives great potential for MR-guided drug delivery with enhanced BBB transmigration and NIR controlled drug release.

Experimental

We synthesized NIR-responsive MPNS with magnetic nanoparticle-core and gold-shell by a two-step process. First, magnetic nanoparticles (MagNPs) were synthesized by co-precipitation of Fe^{2+} and Fe^{3+} in an alkaline solution, followed by gold coating of MagNPs by citrate reduction [9]. MagNPs and sodium citrate were used as seeds and a reducing agent for Au^{3+} ions, respectively. The spherical core-shell nanoparticles with the surface plasmon resonance (SPR) peak in the visible wavelength were synthesized in this step. In the second step, the morphology of the spherical core-shell nanoparticles was modified to star shape to adjust SPR within the NIR wavelength. An antiretroviral drug tenofovir disoproxil fumarate (TDF) was bound on MPNS after mixing for 1h at room temperature. NIR triggered release study of TDF was conducted by applying an external NIR light using a continuous wave laser (808 nm, 950 mW). The TDF release was evaluated by measuring TDF concentration using a UV-visible spectrometer (UV-vis).

Results and Discussion

Successful synthesis of MPNS with magnetic core and gold shell structure was confirmed in our previous study. The star-shape structure of the nanoparticles and the existence of magnetic and plasmonic properties were confirmed by observing the nanoparticles using a transmission electron microscope (TEM) and measuring their properties. MR property of MPNS was also evaluated by using 4.7T MRI system (Agilent 4.7T) at AMRIS. Due to the surface plasmon resonance (SPR), the synthesized MPNS absorbed lights within NIR wavelength, which resulted in heat generation of MPNS. We evaluated the drug release profile induced by this NIR stimulation. The release of TDF was confirmed as fast as 5 min, and increased by extending the exposure time up to 30 min (Fig.1).

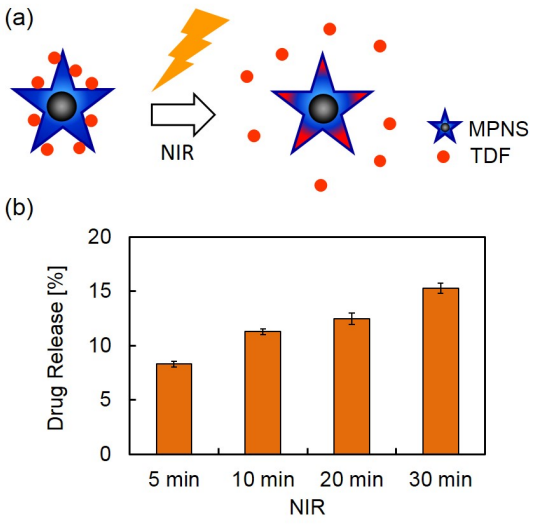

Fig.1 (a) Schematic illustration of NIR induced controlled release of antiretroviral drug from a magneto-plasmonic nanostars. (b) Drug release rate from the nanostars after NIR exposure for 5-30 min.

Conclusions

Successful synthesis of MPNS with magnetic nanoparticle-core and gold shell was confirmed. The time dependent drug release was observed by NIR stimulation.

Acknowledgements

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References

[1] Varatharajan et al, Antiviral. Res. **82**, 99–109 (2009).