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Upconversion Nanoparticle-Mediated Carbon Monoxide Prodrug Delivery System for Cancer Therapy

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Abstract : Gas therapy is still at an early stage of research and development. Even though most gasotransmitters have proven their therapeutic potential, their handling, delivery, and controlled release have been extremely challenging. This research work employs a versatile nanosystem that is capable of delivering a gasotransmitter in the form of a photo-responsive carbon monoxide-releasing molecule (CORM) for targeted cancer therapy. The therapeutic action was mediated by upconversion nanoparticles (UCNPs) designed to transfer bio-friendly low energy near-infrared (NIR) light to ultraviolet (UV) light capable of triggering carbon monoxide (CO) from a water-soluble amphiphilic manganese carbonyl complex CORM incorporated into a carefully designed lipid drug delivery system. Herein, gaseous CO that plays a role as a gasotransmitter with cytotoxic and homeostatic properties was investigated to instigate cellular apoptosis. After successfully synthesizing the drug delivery system, the ability of the system to encapsulate and mediate the sustained release of CO after light excitation was demonstrated. CO fluorescence probe (COFP) was successfully employed to determine the in vitro drug release profile upon NIR light irradiation. The uptake of nanoparticles enhanced by folates and its receptor interaction was also studied for cellular uptake purposes. The anticancer potential of the final lipid nanoparticle Lipid/UCNPs/CORM/FA (LUCF) was also determined by cell viability assay. Intracellular CO release and a subsequent therapeutic action involving ROS production, mitochondrial damage, and CO production was also evaluated. In all, this current project aims to use in vitro studies to determine the potency and efficiency of a NIR-mediated CORM prodrug delivery system.

Keywords : carbon monoxide-releasing molecule, upconversion nanoparticles, site-specific delivery, amphiphilic manganese carbonyl complex, prodrug delivery system.
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