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Nonionic alginate-functionalized up-conversion nanoparticles for enhancing NIR-imaging and targeted delivery of Doxorubicin to KB cancer cells

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A novel nano-carrier with great biocompatibility, imaging functionality and drug delivery ability has been developed. In this work, the carrier poly (ethylene glycol) bis (amine)-modified alginate (Al-NH-PEG-NH2) with folate (FA) as the targeting molecule (Al-NH-PEG-NH-FA) were synthesized to act as functionalizing agents for UCNPs. The synthesized polymer enhanced the stability, biocompatibility and up-conversion luminescent intensity (20-fold) of the UCNPs compared to bare UCNPs. The UCNP-Al-NH-PEG-NH-FA nano-carrier enabled the specific targeting of folate receptor-positive KB cells, as confirmed via *in vitro* near infrared (NIR) imaging. The anticancer drug doxorubicin (DOX) was loaded onto the nano-carrier with high drug loading efficacy (81.2%) then the pH-responsive drug releasing ability was measured. The release of DOX from the nano-carrier was pH dependent and the release rate was much faster at a lower pH (pH=5) than at a higher pH (pH=7.2). The *in vitro* evaluation of KB cells demonstrated that the DOX-loaded UCNP-Al-NH-PEG-NH-FA provided a sustained intracellular DOX release and a prolonged DOX accumulation in the nucleus, resulting in a prolonged therapeutic efficacy. Additionally, the DOX-loaded UCNP-Al-NH-PEG-NH-FA showed higher cytotoxicity towards the KB cells than free DOX. Thus, the biocompatible nonionic alginate-functionalized UCNPs hold substantial potential to be further developed as effective NIR imaging agents and drug-delivery carriers.

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