A simple add-and display method for immobilisation of cancer drug on his-tagged virus-like nanoparticles for controlled drug delivery

ABSTRACT

pH-responsive virus-like nanoparticles (VLNPs) hold promising potential as drug delivery systems for cancer therapy. In the present study, hepatitis B virus (HBV) VLNPs harbouring His-tags were used to display doxorubicin (DOX) via nitrilotriacetic acid (NTA) conjugation. The His-tags served as pH-responsive nanojoints which released DOX from VLNPs in a controlled manner. The His-tagged VLNPs conjugated non-covalently with NTA-DOX, and cross-linked with folic acid (FA) were able to specifically target and deliver the DOX into ovarian cancer cells via folate receptor (FR)-mediated endocytosis. The cytotoxicity and cellular uptake results revealed that the His-tagged VLNPs significantly increased the accumulation of DOX in the ovarian cancer cells and enhanced the uptake of DOX, which improved anti-tumour effects. This study demonstrated that NTA-DOX can be easily displayed on His-tagged VLNPs by a simple Add-and-Display step with high coupling efficiency and the drug was only released at low pH in a controlled manner. This approach facilitates specific attachment of any drug molecule on His-tagged VLNPs at the very mild conditions without changing the biological structure and native conformation of the VLNPs.