Dual-Stimuli Responsive Nanomedicine for Cancer Therapy

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Chemotherapy is currently a prominent medical intervention for cancer. However, studies have shown various nonspecific detrimental effects to healthy cells and tissues during treatment. In order to overcome these side effects, we have designed dual-stimuli responsive nanoparticles: PEG-BA-ADA/CB[7]-PLA/SSPLA NPs. In our study, a chemotherapeutic drug paclitaxel (PTX) is encapsulated inside PEG-BA-ADA/CB[7]-PLA/SSPLA NPs. With polyethylene glycol (PEG) on the outer surface of NPs, PEG-BA-ADA/CB[7]-PLA/SSPLA NPs could efficiently accumulate near cancer cells attributed to long circulation and enhanced permeation retention (EPR) effects. The high ROS level external from the cancer cells would break down the ROS-responsive boronic acid ester bond (BA) so that the surface PEG will be removed. Without PEG, the NPs could retain inside the environment and be endocytosed by cancer cells. Intracellularly, the high level of GSH breaks down the disulfide bond within SSPLA (poly-l-lactic acid polymer crosslinked by disulfide bonds), leading to the release of the PTX. The efficient cellular uptake of PEG-BA-ADA/CB[7]-PLA/SSPLA NPs was shown in breast cancer cells (4T1), whereas much less NPs were taken up by healthy liver cells (A12). When treated with free PTX and PTX loaded PEG-BA-ADA/CB[7]-PLA/SSPLA NPs, the viability of 4T1 cells was reduced down to 34.88% and 18.90%, respectively. In a dramatic contrast, PTX loaded group exhibited minimal cytotoxicity against noncancerous A12 cells, maintaining 64.26% cellular viability. Evidently, the free PTX exhibited intrinsic, nonspecific cytotoxicity towards A12, with 25.85% cellular viability observed. PEG-BA-ADA/CB[7]-PLA/SSPLA NPs may offer a new drug delivery platform for highly selective cytotoxicity against cancer cells.

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