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Self-assembled pectin-conjugated multi-arm-polyethylene glycol nanoparticles loading dihydroartemisinin for anticancer combination therapy

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Single-drug therapy for cancer is greatly hampered by its poor water-solubility, difficulties in controlling and predicting the drug release, and non-specific delivery to the target tissue that limited to the clinical application. In order to overcome these limitations, a novel self-assembled nanoparticle platform based on pectin-multi-arm-polyethylene glycol-dihydroartemisinin conjugate (Pec-Multiarm-PEG-DHA) was first presented. This conjugate was synthesized by introducing hydrophobic drugs dihydroartemisinin to hydrophilic polymer molecules eight-arm polyethylene glycol, and then was linked to pectin via ester linkages. Moreover, another anticancer drug hydroxycamptothecin (HCPT) was encapsulated into the self-assembled nanoparticles (Pec-Multiarm-PEG-DHA/HCPT NPs). The obtained nanoparticles possessed appropriate size (~ 85 nm), high drug-loaded efficiency (~9.12 wt% DHA), encapsulation efficiency (~ 12.11 wt% HCPT), good stability and pH-dependent. The time-dependent cytotoxic of the Pec-Multiarm-PEG-DHA/HCPT NPs was only 4% 4T1 cell and 2% MCF-1 cell survived after 72 h. Pec-Multiarm-PEG-DHA/HCPT NPs exhibited a higher cytotoxicity, longer blood retention time of free drug (8.0-fold DHA, 7.4-fold HCPT) and more effective cellular uptake than free drugs. 4T1 tumor-bearing mice treated with the nanoparticles also showed a 90.6% survival advantage in comparison with 15.5% free DHA and14.1% free HCPT. In addition, it is clearly an elaborate certification that nanoparticles could reduce the risk of hypersensitivity reactions substantially. Therefore, Pec-Multiarm-PEG-DHA/HCPT NPs is a promising potential for anticancer combination therapy.

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