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Improved Chemotherapeutic Efficacy Against Resistant Human Breast Cancer with Co-Delivery of Docetaxel and Nigella Sativa's Bioactive as a Cancer Targeted Nanomedicine

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Abstract

Multi-targeted chemotherapeutics combinations have received considerable interest in recent years for solid tumors chemotherapy. Here, we optimized low molecular weight chitosan (CS) grafted lipid nanocapsules (LNCs) (referred as CLNCs) for co-delivery of Docetaxel (DTX) and Thymoquinone (THQ) for treatment of drug resistant breast cancer. We first screened the size reduction techniques (homogenization vs ultrasonication) then 33-Box-Behnken design was employed to determine optimal conditions of the final LNCs with the desired quality attributes. Uncoated LNCs exhibited a particle size of 141.7±2.8nm (PdI: 0.17±0.02) with %EE of 66.1±3.5% and 85.3±3.1% for DTX and THQ, respectively. The CS functionalization of LNCs improved the uptake and endosomal escape effect and leads to significantly higher cytotoxicity against MCF-7 and triple negative (MDA-MB-231) breast cancer cells. Furthermore, enhanced anti-angiogenic effect was observed with DTX and THQ carrying CLNCs in Chick embryo choriallantoic membrane (CAM) assay.