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Sequential Release of Dual Drugs Using Thermo-Sensitive Hydrogel for Tumor Vascular Inhibition and to Enhance the Efficacy of Chemotherapy

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Abstract : The tumor microenvironment affects the therapeutic outcomes of cancer disease. In a malignant tumor, overexpression of vascular endothelial growth factor (VEGF) provokes the production of pathologic vascular networks. This results in a hostile tumor environment that hinders anti-cancer drug activities and profoundly fuels tumor progression. In this study, we develop a strategy of sequential sustain release of the anti-angiogenic drug: Bevacizumab(BVZ), and anti-cancer drug: Doxorubicin(DOX) which had a synergistic effect on cancer treatment. Poly (D, L-Lactide)- Poly (ethylene glycol) –Poly (D, L-Lactide) (PDLLA-PEG-PDLLA) thermo-sensitive hydrogel was used as a vehicle for local delivery of drugs in a single platform. The in vitro release profiles of the drugs were investigated and confirmed a relatively rapid release of BVZ (73.56 ± 1.39%) followed by Dox (61.21 ± 0.62%) for a prolonged period. The cytotoxicity test revealed that the copolymer exhibited negligible cytotoxicity up to 2.5 mg ml-1 concentration on HaCaT and HeLa cells. The in vivo study on Hela xenograft nude mice verified that hydrogel co-loaded with BVZ and DOX displayed the highest tumor suppression efficacy for up to 36 days with pronounce anti-angiogenic effect of BVZ and with no noticeable damage on vital organs. Therefore, localized co-delivery of anti-angiogenic drug and anti-cancer drugs by the hydrogel system may be a promising approach for enhanced chemotherapeutic efficacy in cancer treatment.

Keywords : anti-angiogenesis, chemotherapy, controlled release, thermo-sensitive hydrogel
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