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Trastuzumab Decorated Bioadhesive Nanoparticles for Targeted Breast Cancer Therapy

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Abstract : Brest cancer, up-regulated with human epidermal growth factor receptor type-2 (HER-2) led to the concept of developing HER-2 targeted anticancer therapeutics. Docetaxel-loaded D-α-tocopherol polyethylene glycol succinate 1000 conjugated chitosan (TPGS-g-chitosan) nanoparticles were prepared with or without Trastuzumab decoration. The particle size and entrapment efficiency of conventional, non-targeted and targeted nanoparticles were found to be in the range of 126-186 nm and 74-78% respectively. In-vitro, MDA-MB-231 cells showed that docetaxel-loaded non-targeted and HER-2 receptor targeted TPGS-g-chitosan nanoparticles have enhanced the cellular uptake and cytotoxicity with a promising bioadhesion property, in comparison to conventional nanoparticles. The IC50 values of non-targeted and targeted nanoparticles from cytotoxic assay were found to be 43 and 223 folds higher than DocelTM. The in-vivo pharmacokinetic study showed 2.33, and 2.82-fold enhancement in relative bioavailability of docetaxel for non-targeted and HER-2 receptor targeted nanoparticles, respectively than DocelTM, and after i.v administration, non-targeted and targeted nanoparticle achieved 3.48 and 5.94 times prolonged half-life in comparison to DocelTM. The area under the curve (AUC), relative bioavailability (FR) and mean residence time (MRT) were found to be higher for non-targeted and targeted nanoparticles compared to DocelTM. Further, histopathology results of non-targeted and targeted nanoparticles showed less toxicity on vital organs such as lungs, liver, and kidney compared to DocelTM.

Keywords : breast cancer, HER-2 receptor, targeted nanomedicine, chitosan, TPGS
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