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OCTREOTIDE CONJUGATED DUAL LOADED NANOPARTICLES OF TOPOTECAN AND THYMOQUINONE FOR TARGETING BREAST CANCER: FORMULATION, CHARACTERIZATION AND IN VIVO CYTOTOXICITY ASSESSMENT

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Effective cancer therapy by an anticancer drug relies on its ability to reach the diseased site in its most active form and target multiple cancer hallmarks. However, the insufficiency of the classical anticancer drugs to target multiple pathways of cancer progression and the inability of the conventional delivery systems to carry the payload to the tumor site results in severe side effects and sub-optimal outcome necessitating the exploration of traditional medicine and measures to improve targeted delivery to treat this highly complex disease. The current study aims at utilizing octreotide as the targeting ligand for decorating the PLGA nanoparticle system incorporating a natural bioactive thymoquinone with a well-established anticancer drug, topotecan, to target the somatostatin receptors overexpressed in breast cancer. Topotecan and thymoquinone loaded nanoparticles (TP-TY NPs) were formulated by double emulsion solvent evaporation and decorated with octreotide by carbodiimide chemical conjugation. The optimized particles were the characterized in terms of particle size, zeta potential, reconstitution time, entrapment and loading efficiency. The optimized particles were then evaluated by ex-vivo cytotoxicity analysis in MCF-7, followed by in vivo analysis in Ehrlich ascites tumor model. The optimized Oct-TP-TY NPs had a particles size and polydispersity index of 245.7±3.5 and 0.204±0.18 respectively, zeta potential of -1.08 mV and reconstituted in less than 15 seconds. % loading and entrapment efficiency was 37±1.2 and 2.8±0.65 respectively for topotecan and 62.2±1.2 and 6.2±0.5 respectively for thymoquinone. The decorated particles showed a significantly lower IC50 (1.9±0.4 ug/ml) as compared to its undecorated counterpart (3.5±1.5 ug/ml) or free drug solution (16.1±1.8 ug/ml). This was further supported by higher cellular uptake of the former. Finally, Oct-TP-TY NPs resulted in marked tumor regression as compared to TP-TY NPs and free drug solution with no or minimal detrimental effect on the haematological profile. In conclusion, the biological evaluation generated proof of evidence in support of the current research.

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