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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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Abstract

Effective cancer therapy by an anticancer drug relies on it's 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 -1.08mV 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 IC 50 (1.9±0.4ug/ml) as compared to its undecorated counterpart (3.5±1.5ug/ml) or free drug solution (16.1±1.8ug/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 combination of a synthetic and a natural bioactive in an octreotide decorated nanoparticle system for targeted breast cancer therapy.

Biography:

Dr. Devina Kakar is a Regulatory and Medical Affairs specialist in Tech Observer, Delhi, India. At present, she is working as a Project Manager and Medical Affairs scientist for an upcoming project in GSK Consumer Health, Gurgaon, India and has been acknowledged for leading the same. She did her M. Pharm in Quality Assurance and Ph.D. in Pharmaceutics from Jamia Hamdard, New Delhi, India, and was awarded with the AICTE and Senior Research Fellowship from ICMR during her post-graduation and Ph.D. respectively. Having worked for about 7 years in academic research in the domain of cancer nanomedicine, she has several articles to her credit. Taking forward her keen interest in medical writing, she is actively involved in several projects on regulatory as well as medical affairs.

Speaker Publications:

1. Topotecan–tamoxifen duple PLGA polymeric nanoparticles: investigation of in vitro, in vivo and cellular uptake potential; T Khuroo, D Verma, S Talegaonkar, S Padhi, AK Panda, Z Iqbal; International journal of pharmaceutics 473 (1-2), 384-394
2. Development and optimization of ketoconazole loaded nano-transfersomal gel for vaginal delivery using Box-Behnken design: In vitro, ex vivo characterization and antimicrobial …; S Singh, D Verma, MA Mirza, AK Das, MK Anwer, Y Sultana, ...; Journal of Drug Delivery Science and Technology 39, 95-103
3. A vaginal drug delivery model; MA Mirza, AK Panda, S Asif, D Verma, S Talegaonkar, N Manzoor, ...; Drug delivery 23 (8), 3123-3134

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