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Improved drug delivery and therapeutic efficacy of PEgylated liposomal doxorubicin by targeting anti-HER2 peptide in murine breast tumor model

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Statement of the Problem: The most common chemotherapy regimens for treating cancer is based on the application of nonspecific cytotoxic substances which can induce toxic side effects. Targeted cancer therapy is a powerful therapeutic strategy to management of cancer. HER2 as an anticancer target has long been studied. Its overexpression plays an important role in the pathogenesis and progressiveness of breast and other cancers.

Methodology & Theoretical Orientation: To establish efficient and reliable drug delivery to HER2-overexpressing cells, the authors of this study have developed anti-HER2 (ErbB2) peptide-liposomal formulations of doxorubicin (DOX) by an engineered breast tumor targeting peptide ligand, AHNP, Anti-HER2/neu peptide, (FCDGFYACYADV) with three glycine amino acids as spacer before its original sequencing. Towards this goal, PEGylated liposome doxorubicin (PLD) bearing different ligand densities of AHNP was prepared and characterized for their size, zeta potential and peptide conjugation. The AHNP functionalization and density effects on breast tumor cell uptake, selective cytotoxicity, prevention of tumor growth and the tissue biodistribution of encapsulated DOX were studied in mice bearing TUBO breast cancer tumor model.

Findings: The findings demonstrated that increasing the ligand density of AHNP increases cytotoxicity and cell-uptake in SKBR3 and TUBO cells which overexpress HER2 but not in MDA-MB-231with low HER2 expression profile. The anticancer activity was also superior for targeted liposomal DOX with more AHNP densities. Conclusion & Significance: This experiment displayed the great potential of AHNP as a targeting moiety on the liposome surface and emphasized the significance of adjusting density of ligand to maximize the targeting capability of the nano drug delivery systems. Overall, the results showed that optimum AHNP density functionalization of PLD can significantly improve selectivity and the therapeutic index of liposomal DOX in the treatment of HER2 positive breast cancer and merits further investigation.

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