New drug development

A POWERFUL DRUG-DELIVERY SYSTEM IN REDUCING CARDIO-TOXICITY OF TRASTUZUMAB: A BIO-DISTRIBUTION STUDY USING 99mTc RADIOLABELING TECHNIQUE

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Objective: The research work is based on the concept of targeted drug delivery of Trastuzumab, a monoclonal antibody against breast cancer, using PEGylated liposomes. Almost one-third cases of breast cancers are associated with over-expression of human epidermal growth factor receptor 2 (HER2). Trastuzumab acts by interfering with HER-2 receptors in the breast. However, HER-2 pathway plays a significant role in heart too, where it is involved in the regulation of normal cellular metabolism, growth and survival. The most significant toxicity associated with trastuzumab is cardiomyopathy ranging from subclinical decreases in left ventricular ejection fraction (LVEF) to cardiac failure manifesting as congestive heart failure (CHF). The risk is greatest when administered concurrently with anthracyclines. Inhibition of HER-2 receptors in the breast is desirable for its therapeutic benefit but their blockage in the heart is related to its associated cardio-toxicity.

Methods: Trastuzumab was incorporated into PEGylated liposomes by lipid-layer hydration technique using different ratios of lipids. Accordingly, the formulation with maximum entrapment of the drug was selected to investigate the biodistribution of trastuzumab loaded liposomes and compared to free trastuzumab in rats xenografted with human MCF-7 breast cancer cell lines. For the purpose of biodistribution study, trastuzumab was radiolabelled with 99mTc.

Results: Percent entrapment efficiency (%EE) of the liposomes was found to be 65.7 ± 4.6%. The labelling efficiency was almost same upto 1 h after incubation for trastuzumab and liposomes. Less than 2% to 8% radioactivity was dissociated after 6 hours incubation in the saline which indicates the suitability of the complex for its in vivo use. Results of biodistribution revealed that in the case of 99mTc-liposomes, the radioactivity present in the cancerous breast was more at all the time points compared to other organs.

Conclusion: PEGylated liposomes can definitely serve as a potential tool to overcome the cardiomyopathy associated to trastuzumab. Retention time of liposomes is less at the heart due to lymphatic drainage and at that time too, the drug is shielded by lipid barrier.

Disclosure: All authors have declared no conflicts of interest.