A Novel Liposomal Formulation for Co-Delivery of Paclitaxel and Lapatinib

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Abstract:

Paclitaxel is one of the most promising anticancer agents, acts by stabilizing microtubules. Its clinical use is accompanied by problems including poor water solubility and frequent emergence of multidrug resistance (MDR). Taxol® is a commercial formulation of paclitaxel containing Cremophor EL® as the solubilizing agent. Cremophor causes severe hypersensitivity reactions. Another problem with paclitaxel is occurring MDR caused by increasing drug efflux via ATP-Binding superfamily. Lapatinib is a reversible dual tyrosine kinase inhibitor with inhibitory function against ATP-binding receptors, thus can sensitize resistant cancer cells to chemotherapeutic agents. Liposomes are carriers with attractive characteristics which convert them to ideal carriers for lipophilic drugs such as paclitaxel and lapatinib. Developing a novel liposomal formulation for co-delivery of paclitaxel and lapatinib for overcoming paclitaxel associated MDR. The D-optimal design was applied for optimizing the formulation prepared by thin film hydration method. The size distribution and zeta potential were determined by Malvern Zetasizer. The incorporation efficiency was determined by RP-HPLC. The TEM image was taken and MTT assay was studied against Sk-br-3 cells. The confocal microscopy and flowcytometry analysis was studied in T47D cells with applying the coumarin-6 as the fluorescent probe. The In vivo toxicity in Balb/c tumoral models is under evaluation. The optimized formulation had the incorporation efficiency of 42% and 89% for lapatinib and paclitaxel respectively. The MTT assay showed the superior toxicity of liposomal formulation in comparison to bare drugs. The confocal microscopy and flowcytometry analysis showed the better uptake of formulation after 8 hours in comparison to free coumarin. This study presents a novel liposomal formulation capable of co-encapsulating paclitaxel and lapatinib for overcoming paclitaxel associated MDR. In vitro studies showed the improved characteristics of paclitaxel and lapatinib after formulating in liposomal carriers.

Keyword: Paclitaxel; Lapatinib; Nanoliposome; Multi Drug Resistance