Preparation, Characterization and Evaluation of Liposomes Containing Lapatinib

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Abstract: Lapatinib is a lipophilic reversible dual tyrosin kinase inhibitor which acts by binding to ATP-Binding site of the EGFR and HER2 receptors. Phase 1 and 2 clinical trials have established the role of lapatinib in the treatment of refractory metastatic breast cancer. Commercial formulation of lapatinib is an oral tablet with limited absorption and different side effects such as gastrointestinal problems which can be managed by changing the route of administration. Intravenous injection is the preferred pathway which can improve the bioavailability of this agent. Liposomes are a group of interesting carriers with the ability to incorporating the significant amount of lipophilic agents. The objective of the present study is developing a liposomal formulation for intravenous administration of lapatinib. Different formulations with different drug and phospholipid contents were prepared by thin film layer hydration method. DPPC and EPC in combination with cholesterol were examined for developing the optimum formulation. Size and zeta potential were determined by Malvern zetasizer. MTT assay against SK-BR3 cell line was studied for determining the cytotoxicity of the optimum formulation. Cellular uptake was studied by confocal microscopy and flow cytometry analysis. In vivo biodistribution of this formulation is under investigation. The encapsulation efficiency of different formulations were in the range of 9% to 96.7%. The average particle size of the optimized formulation was 120 nm. Uptake studied showed the superior penetration of the liposomal formulation in comparison to the free fluorescent probe solution. The MTT assay showed the superior cytotoxicity of the liposomal formulation against bare drug. This study presents a liposomal formulation capable of incorporating the satisfactory amount of lapatinib with the ability of improving its characteristics and cytotoxicity against SK-BR3 cell line.

Keyword: Lapatinib; Nanoliposome; Metastatic breast cancer