Targeted delivery of anticancer drug with antiangiogenic dendrimers for effective cancer treatment

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Dendrimers are extensively being investigated in therapy of cancer. Recently poly-l-lysine (PLL) dendrimers have been reported to show antiangiogenic activity. In the present study, we report folic acid conjugated PLL dendrimers (FPLL) as an efficient carrier for model anticancer drug, doxorubicin hydrochloride (Dox), along with pH sensitive drug release, selective targeting to cancer cells, anticancer activity and antiangiogenic activity. In the in vitro release profile this nanoconjugate of Dox showed initial rapid release with gradual slow release. Further drug release was found to be pH sensitive with faster release at acidic pH. In the chick embryo chorioallantoic membrane (CAM) assay and tubule formation assay with human umbilical vein endothelial cells, (HUVEC) Dox-FPLL formulation showed the significant antiangiogenic activity. The ex vivo investigations with MCF-7 cancer cell lines showed enhanced cytotoxicity with Dox-FPLL with significantly enhanced intracellular uptake (p<0.001). The in vivo therapeutic potential of nanoconjugate was determined in MCF-7 breast cancer xenograft model in tumor-bearing mice. Dox-FPLL increased the concentration of Dox in tumor with superior anti-tumor activity in human breast cancer (MCF-7) tumor model. The formulation significantly prolonged survival as determined by Kaplan Meier survival analysis (p<0.001), further confirming the efficacy, safety and biocompatibility of formulation. Thus, the developed formulation based on dual attack on cancerous tissue could prove a promising strategy to treat a deadly ailment, Cancer.

Biography
Keerti Jain has completed her MPharm at the age of 26 years from Department of Pharmaceutical Sciences, Dr. H. S. Gour University, India. Presently, she is pursuing her Ph.D. in the supervision of Prof. N K Jain at Dr. H. S. Gour Central University, India. She has published more than 10 research articles, review articles and book chapters in reputed journals. She has published a review article entitled “Dendrimer toxicity: Let’s meet the challenge” in International Journal of Pharmaceutics, which was selected in top 25 articles of this Journal and gained more than 100 citations. One of her article has been published in reputed Journal Progress in Polymer Science with impact factor of 26.383.