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TITLE

Dual Strategy for Treatment of Cancer Based on Development of Anti-Angiogenic Carrier for Anticancer Agent

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In this study poly(propylene) imine (PPI) dendrimers were conjugated peripherally with arginine to mimic the surface structure of an endogenous angiogenesis inhibitor endostatin. Simultaneously the developed surface engineered dendrimers were evaluated as site specific delivery vehicle for anticancer drug, doxorubicin hydrochloride. Synthesis of PPI dendrimers and conjugation of arginine to surface group was confirmed by FTIR, NMR and TEM. Doxorubicin was loaded by equilibrium dialysis method. The developed formulation showed the initial rapid release followed by sustained release characteristics in in vitro and in vivo studies. The formulation exhibited significant anti-angiogenic activity in the in vivo chick embryo chorioallantoic membrane (CAM) assay and selective uptake by cancer cells in the ex vivo cell uptake studies and in vivo biodistribution studies.

Endostatin inhibits angiogenesis by competing for heparan sulfate proteoglycan (HSPG) binding site, which act as co-receptors for some important angiogenic factors including bFGF. Endostatin demonstrates arginine clusters in its structure, which is responsible for binding to HSPG. Arginine conjugated dendrimers showed the anti-angiogenic activity by mimicking the surface structure of endostatin and exhibited the sustained and targeted delivery of anticancer drug owing to the nanometric nature of dendrimer.

Clinical evidences suggest that the combination of anti-angiogenic agents with chemotherapy resulted in synergistic anticancer effect. So the results of this study advocate that the developed formulation would prove as a promising strategy in the field of medicine for treatment of cancer as it will attack malignant tissue at two steps, inhibition of angiogenesis and destruction of proliferating cancer cells.

Biography

Ms. Keerti Jain has completed her M. Pharm. at the age of 26 years from Department of Pharmaceutical Sciences, Dr. H. S. Gour University, Sagar. Presently she is pursuing her Ph. D. in the supervision of Prof. N. K. Jain at Dr. H. S. Gour Central University, Sagar, India. She has published 2 papers in reputed journals. Keerti 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 20 citations in a short period of 28 April 2010 to 10 January 2012.