Research in Pharmaceutical Sciences, 2012;7(5)
School of Pharmacy and Pharmaceutical Sciences
Isfahan University of Medical Sciences

Antitumor efficacy of RGD-targeted liposomes containing doxorubicin in mice bearing C-26 colon carcinoma

M. Amin*, A. Badiee, M. Jaafari

Nanotechnology Research Center, Biotechnology Research Center, School of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran

Drug therapy for the treatment of tumors is often limited by a narrow therapeutic index. One approach that overcomes this limitation is the active targeting of tumors with particulate drug carriers containing chemotherapeutic drugs among which nanoliposomes are of the most promising delivery vehicles. The derivatization of nano-sized drug loaded liposomes with a ligand leads to the selective targeting of the particulate to selected areas in body, thereby focusing drug delivery. RGD peptides targeting integrins are promising ligands for the generation of vascular targeting agents. The aim of this study was to evaluate antitumor and biodistribution behavior of stealth RGD-targeted liposomes containing doxorubicin (Dox) in mice bearing c26 colon carcinoma. Nanoliposomes consisted of HSPC, cholesterol, mPEG2000-DSPE were prepared by thin film method plus extrusion. Dox were remotely loaded using ammonium sulfate gradient. RGD peptides were attached to the distal end of maleimide functionalized mPEG2000-DSPE. RGD peptides were consisted of 3 cyclic RGD based peptides (RGD1-Lip-Dox, RGD2-Lip-Dox, RGD3-Lip-Dox) and a cyclic RAD peptide (RAD-Lip-Dox) as negative control.

All preparations and CaelyxTM were compared with respect to their in vitro uptake and their in vivo biodistribution, therapeutic efficacy and side effects in mice bearing c26 colon carcinoma. Biodistribution studies indicated that although RGD-Lip-Dox preparations clear from the blood faster compared to CaelyxTM, no significant differences were observed in tumor accumulation of RGD1-Lip-Dox and CaelyxTM. However, RGD3-Lip-Dox was accumulated in tumor significantly more than CaelyxTM. The interaction of RGD-Lip-Dox preparations with HUVEC cells, were also evaluated in different incubation times. Median survival times indicated a better survival in mice received RGD3-Lip-Dox. Among different RGD modified liposomes.

Results obtained in this study indicated that RGD3-Lip-Dox preparation confers promising pharmacokinetic and antitumor activity in comparison with other RGD-modified liposomes.

Keywords: Liposome; Integrins; RGD peptides; Solid tumor; Doxorubicin