Research in Pharmaceutical Sciences, 2012;7(5)
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Development of a novel in-situ forming liposomal hydrogel to release intact liposomes in mice

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Background and Aims: Liposomes have a great potential in providing controlled release and altering the pharmacokinetics of many drugs. However, rapid uptake of conventional liposomes by the reticuloendothelial systems (RES) is the main obstacle. To prolong the circulation of liposomes, a combination of liposomes and hydrogel was prepared and its biodistribution was studied.
Methods: Liposomes composed of DSPC:Chol:DOPE at molar ratio 50:45:5 were labeled with 99mTc complex of hexamethylpropyleneamineoxime (99mTc-HMPAO). As an in-situ forming hydrogel, chitosanglycerophosphate was used and gelation time was determined at different temperature. Four different formulations including 99mTc-HMPAO solution, hydrogel/99mTc-HMPAO, 99mTc-HMPAO liposomes and hydrogel/ 99mTc-HMPAO liposomes were injected into the mouse peritoneum. Mice were then sacrificed at different times and the percentage of injected dose per gram of tissue (% ID/g) were obtained.
Results: Results showed that free label left the peritoneum very rapidly in both solution and hydrogel forms, so that the activity was 2.5 and 3.8 (%ID) at 1 h, respectively. While these values for liposomes and liposomal hydrogel were 25.8 and 51.2 (%ID) and decreased to 1.9 and 19.2 after 24 h, respectively. Notably, blood profile of liposomal hydrogel showed a two phase profile regarding gel formation and a sustained blood activity. Free label had high activity in RES and GI tract in early hours and decreased by the time. Contrary, the accumulation of liposomes and liposomal hydrogel was increased in RES during 24 h in range of 1- 34.5 and 1.1- 35.1 (%ID/g), respectively.
Conclusions: A novel delivery system based on the integration of liposomes in hydrogel was developed to release intact liposomes in a sustained way.

Keywords: Radilabel liposome; In-situ forming liposomal hydrogel; Tissue distribution