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

Production and evaluation of nanostructured lipid carriers containing retinoic acid conjugate for targeted delivery of 5-FU in colorectal cancers

J. Varshosaz[1], F. Hassanzadeh[2], H. Sadeghi[2], S. Andalib[1,*]

[1]*Department of Pharmaceutics, School of Pharmacy, Isfahan University of Medical Sciences*
[2]*Department of Medicinal Chemistry, School of Pharmacy, Isfahan University of Medical Sciences*

Background and Aims: The aim of the present study was to reduce 5-FU side effects by targeted nanostructured lipid carriers (NLCs) to LDL receptors over expressed in colorectal carcinoma and also use of a new synthesized conjugate of retinoic acid as a cytotoxic agent.
Methods: Retinoic acid- octadecylamine conjugate was prepared using (dicyclohexyl carbodiimide) DCC and (N-hydroxy succinimide) NHS as the reactive agents under the nitrogen atmosphere. This conjugate was then used for preparation of NLCs by emulsification-solvent evaporation method. The effect of the lipid type (cholesterol, cholestryl stearate), lipid percent (54.5-64.5%) , oil type (oleic acid,octanol) and oil percent (15-25%) on particle size, loading efficiency, zeta potential and release efficiency over 20 h were studied. At last the best formulation was selected for its cytotoxic effect on HT29 human colon cancer cell line.
Results: According to the Design Expert program the optimized formulation contained 54.5% cholesterol, 25% oleic acid, 10% PEG 40 stearate, 10% of the synthesized derivative i.e., retinoic acid-octadecylamine, 0.5% lecithin and 20 mg of 5-FU was chosen. The size of these NLCs was 105.8 nm, zeta potential -25.1 mv, loading efficiency 38% and release of 5-FU during 20 h was 37%. Cholesterol NLCs containing 5-FU and the conjugate of retinoic acid showed cell survival of about one fifth of free 5-FU and the NLCs without retinoic acid conjugate showed about half cytotoxicity respect to free 5-FU that showed 46% cell viability.
Conclusions: The presence of retinoic acid conjugate along with 5-FU loaded in cholesterol NLCs targeted to LDL receptors can enhance cellular cytotoxicity of 5-FU. So that when 5-FU was loaded in the NLCs containing retinoic acid conjugate, the cytotoxicity was nearly 2 fold of NLCs just loaded with 5-FU and more than 5 fold of free 5-FU in human colon cancer cells (HT29) significantly.

Keywords: 5-FU; Retinoic acid; Targeted NLCs; Colorectal cancer; Cytotoxicity; HT29 cell line