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Preparation of oligodeoxynucleotide encapsulated cationic liposomes and release study with models of cellular membranes

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Abstract:

Cationic liposomes are used for cellular delivery of antisense oligodeoxynucleotide (AsODN), where release of encapsulated AsODN is mainly controlled by endocytosis and fusion mechanisms. In this investigation, it was tried to model such a release process that is difficult to evaluate in cell culture. For this purpose, an AsODN model (against protein kinase C-α) was encapsulated in a DODAP-containing cationic liposome and evaluated for size, zeta-potential, encapsulation and ODN stability. Vesicular models of outer layer and total plasma membranes and early and late endosomal membranes were developed, based on lipid content and pH, using ether injection method. ODN release was determined by the fluorescence dequenching of encapsulated FITC-ODN. Zeta potential, size and ODN encapsulation efficiency of the prepared liposomes were -2.49 ± 7.15 mV, 108.4 nm and 73% respectively. ODN protection was 3-4 times more than that of conventional liposome/ODN complexation method. There was a correlation between model concentration and percent of ODN release. At 7.5 µM, the percent of released ODN was 76% for the cholesterol-free model of the late endosome and 16% for the early endosomal membrane; while the release was less than 11% for the models of plasma membrane. ODN release increased with temperature in the range of 4-37◦C for the late endosomal model, but not for others, possibly due to their high cholesterol contents or acidic pH. The interaction was fast and completed within 5 minutes and didn't change in the range of 5-60 minutes. Our data are in agreement with published cell culture studies and reveal that cell-liposomes interaction can be modeled by lamellar membranes.

Keywords:

Gene delivery ، Antisense oligonucleotide ، Cationic liposomes ، Model membrane

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