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Optimization of DNA/lipid complex microencapsulation into liposome by reverse-evaporation method

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Background and Aims: Cationic liposomes represent the most commonly used gene delivery carrier. Cationic lipids form condensed complexes with negatively charged DNA results in DNA protection and facilitate intra-cellular delivery in-vitro; however, these carriers are unstable in blood and are rapidly eliminated in-vivo. Microencapsulation of DNA-cationic lipid complexes in neutral phospholipid bilayers can overcome these problems. In this study several factors were evaluated in preparation of optimized DNA encapsulated particles with appropriate size and encapsulation efficiency.
Methods: preparation of DNA-lipid complex was based on Bligh and Dyer extractions, using different DNA/lipid ratios ranging from 1 to 7. By this method DNA is drawn into organic phase in association with the cationic lipid. Different compositions of neutral lipids such as cholesterol, PEG-PE and DPPC with different neutral/total lipid mole ratios (0-40% cholesterol and 0-4% PEG-PE) were added to the organic phase (chloroform or chloroform-ether mixture). Double-distilled H2O was added and the emulsions were formed by different oil/water ratios (3, 4.5,6). After being vortexed and sonicated, the organic phase was evaporated by rotary evaporator until a gel phase was reached. Then, gel broke into liposomal dispersion by vortexing and buffer addition. The particles were characterized by Stewart lipid recovery assay, ethidium bromide dye exclusion assay and laser light scattering. The optimization was performed based on Taguchi design and the optimum condition regarding responses (mean size and encapsulation efficiency) was determined.
Results and Conclusions: The liposomes with the lipid composition of PEG-PE (2-4%) and cholesterol (20%) had sizes of 400-450 nm. Extrusion was performed to reduce the size (about 200 nm) and homogenize the particles. The encapsulation efficiencies were 75-90% in the formulations with DNA/lipid ratios of 3.5 to 7 and oil/water ratio of 6. The stability of the particle in heparin sulfate supplemented medium is under investigation.

Keywords: Liposome; DNA; Microencapsulation