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Physicochemical and Biological Characterization of 1,2-Dialkoylamidopropane-Based Lipoplexes for Gene Delivery

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Abstract : Cationic lipid-mediated delivery of nucleic acids represents an exciting approach for developing therapeutically realistic gene medicines. Elucidation of the molecular and formulation requirements for efficient lipofection is a prerequisite to enhance the biological activity of such delivery systems. To this end, the in vitro lipofection activity of the ionizable asymmetric 1,2-dialkoylamidopropane-based derivatives bearing single primary amine group as the cationic head group was evaluated. The electrostatic interactions of these cationic lipids with plasmid DNA in physiologically relevant medium were investigated by means of gel electrophoresis retardation and Eth-Br quenching assays. The effect of the presence of the helper lipid on these interactions was evaluated. The physicochemical properties of these lipids in terms of bilayer fluidity and extent of ionization were investigated using fluorescence anisotropy and surface potential techniques, respectively. The results showed that only the active lipid, 1,2lmp[5], existed in a liquid crystalline state at physiological temperature. Moreover, the extent of ionization of this lipid in assemblies was significantly higher that it's saturated analogues. Inclusion of the helper lipid DOPE improved the encapsulation and association between 1,2lmp[5] and plasmid DNA, which was reflected by the significant boost of lipofection activity of the 1,2lmp[5]/DOPE formulation as compared to the lipid alone. In conclusion, membrane fluidity and sufficient protonation of ionizable cationic lipid are required for efficient association and encapsulation of plasmid DNA and promoting improved in vitro lipofection activity.

Keywords : cationic lipids, gene delivery, lipofection, membrane fluidity, helper lipids, surface potential
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