Synthesis and in vitro evaluation of carbamate-linked cationic lipids

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Abstract (300 word limit)

Cationic lipids are very promising for gene delivery, as they have the advantages of being easy to prepare, no immunogenicity and low toxicity. Since the first cationic lipid—DOTMA (N-[1-(2, 3-dioleoyloxy)propyl]-N,N,N-trimethylammonium chloride) was used for gene delivery, numerous cationic lipids with different structures have been synthesized and used for the delivery of nucleic acids into cells. Cationic lipids have three basic chemical functional domains: a hydrophilic headgroup, a hydrophobic domain, and a linker bond. The linker bond of cationic lipid was between the polar head group and the hydrophobic tail domain, whose nature could influence the stability and the biodegradability of liposomes. Cationic lipids containing carbamate linker have shown great interests as they are stable in the neutral pH condition but liable to acid-catalyzed hydrolysis under appropriate circumstances.

We designed and synthesized a series of carbamate-linked lipids bearing quaternary ammonium headgroup and identical length of hydrocarbon chains for in vitro gene delivery. The chemical structure of carbamate-linked lipids was confirmed by IR, ^{1}H NMR, ^{13}C NMR, and ESI-MS. The liposomes formed from carbamate-linked lipids and helper lipids (Chol or DOPE) could effectively bind and condense plasmid DNA into complex with proper size and zeta-potentials. And, the transfection efficiency and cell viability of some of carbamate-linked lipids was superior or parallel to that of two commercial transfection agents, Lipofectamine2000 and DOTAP. Therefore, the carbamate-linked cationic lipid might be a promising gene carrier that has high transfection efficiency as well as low cytotoxicity, and could be considered as carrier for gene delivery in vivo.

This research is financially supported by the National High-Tech Research and Development Program of China (863 Program, 2014AA020707), the National Natural Science Foundation of China (21503035, 21776044and 21606041), the Fundamental Research Funds for the Central Universities (DC201502020205 and DC201501076).

Image

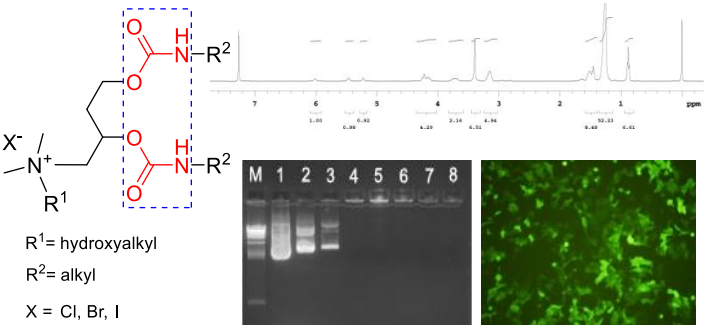


Figure 1. Chemical structure and characterization of carbamate-linked cationic lipids for gene delivery in vitro.



Biography (150 word limit)

Dr. Shubiao Zhang now is a distinguished professor at Dalian Minzu University and a doctor supervisor at Dalian Institute of Chemical Physics and Dalian University of Technology. He received his Ph.D. in applied chemistry at Dalian University of Technology in 2000, after that he worked as a post-doctoral fellow at Dymatic Chemical Inc for over 2 years. From then on he works as a teacher at Dalian Minzu University, and is involved in the study about non-viral vectors for gene delivery and bio-active materials. He leads many research programmes supported by Natural Science Foundation of China, Ministry of Science and Technology, Ministry of Education, Hoffmann La-Roche Ltd. and some domestic companies. He published over 100 peer-reviewed articles, among them over 30 were indexed by SCI, 20 by EI with the total cites of over 1000 times. He is a reviewer for many high quality peer-reviewed journals such as Journal of Controlled Release, and Bioconjucate Chemistry.

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