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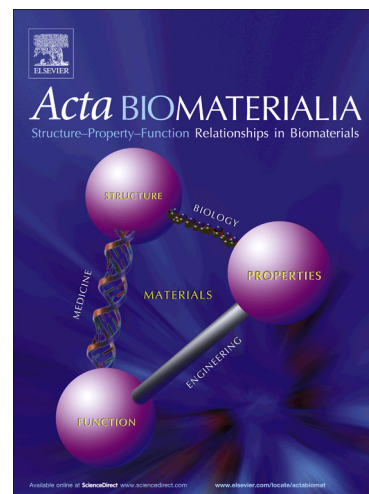
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# Effects of Sucrose Ester Structures on Liposome-Mediated Gene Delivery

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**ABSTRACT:** Sucrose esters (SEs) have great potential applications in gene delivery because of their low toxicity, excellent biocompatibility, and biodegradability. By using tripeptide-based lipid (CDO) as a model lipid and SEs as helper lipids, a series of liposomes were prepared. The SEs with hydrophilic–lipophilic balance (HLB) values of 1, 6, 11, or 16 and the fatty acids of laurate, stearate, or oleate were used in the liposomes. We investigated the effect of HLB values of SEs and fatty acid types on gene transfection efficiency and toxicity of liposomes. The results showed that transfection efficiencies of the liposomes containing SEs with HLB value of 6 were superior to other liposomes in HeLa, MCF-7, NCI-H460, and A549 tumor cells. For the same HLB value, liposomes of laurate SEs were preferable to transfect cells compared to SEs of stearate and oleate. The liposomes with SEs showed higher cellular uptake than liposome without SEs (LipoCDO). LipoL12-6/Luc-siRNA treatment on tumor-bearing mice exhibited about 60% *in vivo* gene silencing of luciferase, and LipoL12-6 could mediate IGF-1R siRNA to greatly inhibit tumor growth. Moreover, liposomes with SEs revealed remarkably low toxicity *in vitro* and *in vivo*. The illustration of SE structures on gene delivery will promote the use of SEs for clinical trials of liposomes.

**KEYWORDS:** *Cationic liposomes, Sucrose esters, Helper lipids, Gene delivery, Toxicity*

## 1. Introduction

Sucrose esters (SEs) are amphiphiles with sucrose as the hydrophilic group and fatty acids as the lipophilic group. As sucrose contains eight hydroxyl groups, compounds ranging from sucrose mono- to octa-fatty acid esters can be produced (Fig. 1) [1-3]. The most common fatty acids used in SEs are lauric, myristic, palmitic, stearic, oleic, behenic, and erucic acids. Through the variation in the type or number of the fatty acid groups, SEs with a wide range of HLB values can be obtained. Therefore, commercial SEs comprise mixtures with various degrees of esterification. In recent years, SEs have attracted much attention because of their biological activities including insecticidal [4], biodegradable [1,5], antitumor [6], and antimicrobial properties [7,8].

Cationic liposomes are composed of lipid constituents and can improve the gene delivery efficacy owing to their typical bilayer structure [9]. Helper lipids play a very important role during the formation of lipoplexes by combining cationic liposomes and genes, as they could determine the morphologies of lipoplexes [10]. In our previous report, we first incorporated a stearate SE as

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