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Publication date:
2019

Document Version
Publisher's PDF, also known as Version of record

Citation (APA):
Lipid-conjugated cargo can desorb from lipid-based particles in biological environment
Controlling the degree of desorption through particle design

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Introduction
The application of lipid-based particles as drug-carriers in drug delivery systems has during the last decade shown great promise. However, it is important to be aware of the inherent lipid dynamics in biological environments, which can cause the lipidated cargo to desorb from the particles. Desorption of lipid-conjugated drugs could lead to severe off-target side-effect, while desorption of lipid-conjugated fluorophores could lead to misinterpretation of fluorescence-based uptake studies.

We employed a simple size-exclusion chromatography (SEC) based method to study the degree of fluorophore desorption. Using two types of lipid-based particles, i.e. liposomes and reconstituted high-density lipoproteins (rHDL), we show that the degree of desorption can be minimized by the compositional design of the particles.

Method

The liposomes were incubated 24 hours at 37 °C in human plasma, before separation of plasma components and liposomes by SEC (using a Sepharose CL-4B column). The fluorescence from the collected fractions was used to quantify the degree of desorption.

The liposomes were incubated for 2 hours at 37 °C in FBS. The components were separated by SEC (using a Superdex 200 Increase 10/300 GL column). The fluorescence from the collected fractions was used to quantify the degree of desorption.

The rHDL was incubated for 2 hours at 37 °C in FBS. The components were separated by SEC (using lipid/peptide ratio of 1:7). 1 mol% fluorophore was incorporated in each rHDL formulation.

The effect of fluorophore type, protein/peptide type and lipid composition on the degree of desorption was studied.

Fluorescence intensity [kcps]

Retention volume [mL]

The composition of the rHDL affects the degree of desorption

Fluorophore desorption from rHDL

Effect of protein / peptide

Effect of lipid composition

Effect of fluorophore type

Fluorophore desorption from liposomes

The fluorophore type and lipid composition of the liposomes affect the degree of desorption

The degree of fluorophore desorption was quantified using both saturated liposomes (DSPC:cholesterol:DPPE-PEG2000 56.6:38.2:5.2) and unsaturated liposomes (POPC:cholesterol:DPPE-PEG2000 56.6:38.2:5.2) containing 0.1 mol% fluorophore.

Conclusions
Lipid-conjugated cargo can desorb from lipid-based particles in biological environments, as we have illustrated by quantifying the desorption of lipid-conjugated fluorophores from both liposomes and rHDL. This can have severe consequences for drug delivery systems using lipid-based particles, however, we show how the degree of desorption can be controlled through compositional design of the particles. We encourage researches to use the simple SEC-based method to evaluate the compositional stability of lipid-based particles for drug delivery.

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References