Ensembles of carboxymethylcyclodextrins on cationic liposomes as capacious nanocontainers for the hydrophobic molecules

Vladislava A. Pigareva, Darya A. Stepanova, Vasily V. Spiridonov and Andrey V. Sybachin

Lomonosov Moscow State University, Chemistry Department, Moscow, 119991, Russia

ABSTRACT: Spherical lipid bilayer vesicles - liposomes have been proved to be effective drug delivery vehicles. However, the capacity of the liposomal nanocontainer towards hydrophobic substances is strongly limited and very rare exceeds several percent. An increase in payload can be achieved by concentrating several liposomes in a small volume, for example, by electrostatic self-assembly on a polymer carrier. Alternative way is to modify the surface of the liposome with molecules with additional affinity to hydrophobic molecules. Carboxymethyl-cyclodextrins (CDs) are small biocompatible cyclic polysaccharides with the dimensions less than 1 nm. Structure of the inner moiety of CDs makes it possible to form host-guest complexes with aromatic fragments of bioactive molecules. Modification of the surface of the liposomes with CDs could significant improve the capacity of the liposomal nanocontainer towards hydrophobic molecules. We suggest using the liposomes formed by mixture of electroneutral dioleoylphosphatidylcholine (DOPC) and cationic dioleoyltrimethylammoniumpropane (DOTAP) lipids as a core for the adsorption of CDs. While carboxyl groups of CDs ensure electrostatic adsorption on the surface of lipid bilayer containing cationic groups additional stabilization of the complexes could be achieved by the hydrophobic interactions of CDs with bilayer. The interaction of liposomes with CDs was studied by means of laser microelectrophoresis and dynamic light-scattering. The composition of the complexes was studied using static light-scattering while the capacity of the complex nanocontainers towards hydrophobic molecules was studied by spectrophotometery using phenolphthalein and curcumin. The nanocontainers were visualized by atomic force microscopy and transmission electron microscopy. It was found that ceramide (CerPEG) should be used as a component of lipid membrane - modification of the surface of liposomes with PEG allows one to prevent the aggregation induced by the adsorption of the CDs. For the DOPC/DOTAP/CerPEG liposomes with diameter 50 nm it was found that several hundreds of the CDs could be adsorbed on their surface. It is important to stress that colloid stable systems could be formed using different ratio of the CDs to DOTAP molecules resulting liposomes with different surface charge from the EPM values 3.8 (μm/s)/(V/cm) to almost zero value. These resulting nanocontainers were demonstrated to be capable to adsorb hydrophobic molecules in the bilayer area of the liposomes and in CDs moieties drastically increasing liposomal payload.

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KEY WORDS: liposomes, carboxymethylcyclodextrins, nanocontainers, drug solubilization

References

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