STUDY OF LIPID-COPOLYMER SYSTEMS BY CRYO-TEM AND DLS

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Introduction

Self-assembled structures of lipids and polymers, i.e. cubosomes, hexosomes or chimeric liposomes have increased research interest because of their potential to serve as biocompatible carriers in drug delivery systems, to increase drug solubilisation and allow to control the release of the payload [1]. The most popular structures reported in recent years are glyceryl monooleate (GMO) and phytantriol (PHYT) stabilized by PEO_{99}-PPO_{67}-PEO_{99} triblock copolymer (P407) [1,2].
In this work the formulation of aggregated structures of lipids (e.g. GMO, DPPC, PHYT) and polymers (e.g. Poloxamer P407 (PEO98-PPO67-PEO98), poly (ethylene oxide)–b–poly(ε-caprolactone) were studied (FIG. 1).

Materials and Methods

Hexosomes and cubosomes were prepared by Bottom Up Method and Top Down Method, For chimeric liposomes the thin film hydration method was used.
The morphology of prepared systems was studied by cryogenic transmission electron microscopy (cryo-TEM) using a Tecnai F20 X TWIN microscope (FEI Company) equipped with field emission gun, operating at an acceleration voltage of 200 kV. The hydrodynamic radius (Rh) and the size dispersity (PDI) of the prepared nanosystems were measured by dynamic light scattering (DLS).

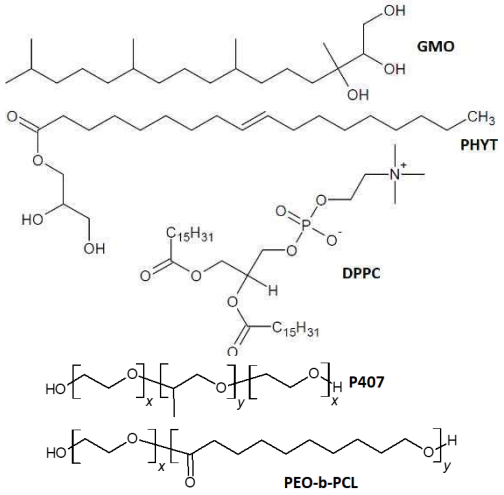

FIG. 1. Chemical structures of some used lipids and polymers.

Results and Discussion

The method of preparation, nature and amount of lipid and block copolymer used to form lipid-polymer structures, dictates the morphology of the resulting objects. There is a gamut of complementary techniques for characterization of the particles [3] (DLS, XRD, SAXS, m-DSC). Cryo-TEM can be distinguished because it allows for morphological visualization at near native state. Cubosomes of GMO:P407 9:1 had a hierarchically ordered internal structure, as shown in FIG. 2. Bicontinuous cubic (Q_{II}) phase was confirmed by FFT patterns.
For all studied lipid-copolymes systems cryo-TEM revealed the coexistence of different categories of structures with different grades of organization, including vesicles with no internal structure and more intricate, liquid crystalline confined nanoparticles. The comprehensive characterization is possible by a combination of cryo-TEM with Dynamic Light Scaterring as is demonstrated for chimeric liposomes in FIG. 3.

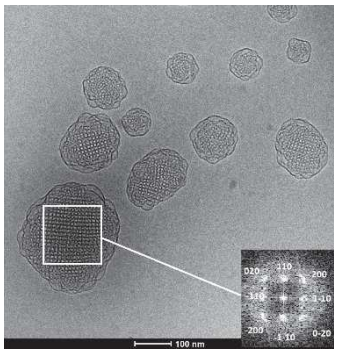

FIG. 2. Cryo-TEM image of GMO:P407 9:1.

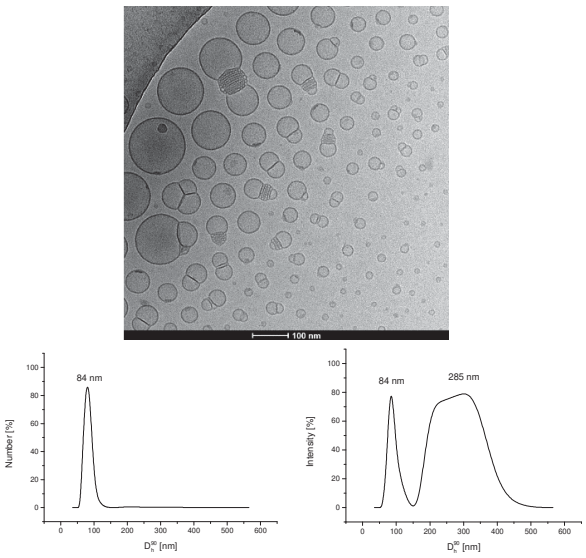

FIG. 3. Cryo-TEM image and size distributions from DLS of GMO-PDMAEMA-b-PLMA 9:1.

Conclusions

The aim of this study was to combine different techniques in order to characterize more comprehensively lipid-copolymer structures with a different architectures and compositions. We used cryo-TEM and DLS to examine the impact of block copolymers for lipid based particles. These techniques resulted to be effective in studying the case of lipid-copolymer systems.

References

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