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Abstract

Effect of the stereochemistry of gemini amphiphile on liposome physico-chemical and biological features †

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Abstract: Nanoparticles are widely studied in nanomedicine for their potential use as drug delivery systems due to their possibility of engineering them for multiple purposes. In the context of nanocarriers, liposomes can be a powerful tool for the transport of bioactive molecules, thanks to their unique characteristics, such as low toxicity and ability to encapsulate a wide range of drugs, and, above all, the ability to finely tune their features by modulating the formulation.

In this scenario, we studied how the presence of different lipid components can play a central role by influencing the physico-chemical characteristics of the final nanosystems. In particular, we mainly focused on how the inclusion of cationc diasteromeric amphiphiles within the formulation can define the characteristics of the liposomes as a whole, in terms of charge, size, fluidity, ability to encapsulate and retain different types of probes, and how these features can then dictate different biological outcome and final fate.

In this work, we design and investigated liposomes composed of natural phospholipids and cholesterol in mixture with synthetic diastereomeric cationic gemini amphiphiles. All formulations were characterized in terms of mean diameter, polydispersity index (PDI) and stability over time by dynamic laser light scattering measurements (DLS). The most promising nanosystems were then evaluated from a biological point of view, in particular uptake experiments were carried out on a monolayer of human iPSC derived brain microvascular endothelial cells (iBMECs) and transport experiment were performed across an *in vitro* human BBB model (iBMECs in coculture with human astrocyets), in order to evaluate the different biological response.

Keywords: Liposome; Gemini amphiphile; Stereochemistry, Drug delivery, Transport model, Brain monolayer endothelial cell

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