Tuning structure and morphology of lipidic cubosomes by encapsulation of novel porphyrin-derivatives

Luca Piccirillo [a,b], Valeria D'Annibale [a,b], Leonardo Ariodante [a], Claudia Marconi [a,b], Andrea D'Annibale [a], Donato Monti [a], Anita Scipioni [a], Karin Schillen [c], Luciano Galantini [a], Marco Fornasier [c,d]

[a] *Department of Chemistry, Sapienza University of Rome, P.le A. Moro, 5, Rome 00185, Italy*
[b] *Department of Basic and Applied Sciences for Engineering, Sapienza University of Rome, P.le A. Moro, 5, Rome 00185, Italy*
[c] *Division of Physical Chemistry, Department of Chemistry, Lund University, P.O. Box 124, Lund SE-221 00, Sweden*
[d] *Division of Nanobiotechnology, KTH Royal Institute of Technology and SciLifeLab, Tomtebodavagen 23B, Solna, Sweden*

luca.piccirillo@uniroma1.it

The encapsulation of biologically relevant molecules into non-lamellar lipid nanoparticles represents an effective strategy for drug delivery applications [1]. Cubosomes are suitable candidates as drug carriers, due to their intrinsic colloidal stability and higher loading capacity compared to vesicular systems [2]. However, the coexistence of different bicontinuous cubic phases induced by steric stabilizers, e.g., Pluronics, or the concurrent formation of vesicles during preparation can hinder a clear correlation between the physico-chemical properties of these nanostructures and their biological performance [1,2]. In this context, three novel porphyrin derivatives were synthesized and encapsulated into cubosomes composed of monoolein as the lipid building block and triblock copolymer Pluronic F108 as the steric stabilizer [3,4]: two target molecules were functionalized with bile acid moieties (cholic and deoxycholic) and one with a tetrapeptide, with the aim of developing advanced theranostic materials. Firstly, the effect of the cargo concentration was evaluated on the structure of the cubosomes, showing that the bile acid derivatives did not affect the lipid self-assembly, providing only the native cubic phase (Pn3m) of monoolein at the investigated concentrations. In contrast, increasing concentrations of the tetrapeptide derivative induced the formation of a mixed Pn3m + Im3m phase similarly to the behavior of the empty formulation, but also accompanied by a subsequent loss in crystallinity. The apparent hydrodynamic size or the polydispersity of the cubosomes after encapsulation was then studied at two different temperatures (25 and 37°C). Formulations containing 0.50 mg/mL of cargo exhibited higher colloidal stability over time, with no significant variations in size or ζ-potential for more than one month. Interestingly, formulations containing bile acid derivatives displayed the characteristic cubosome morphology and a reduced number of vesicles (approximately a 60:40 cubosomes-to-vesicles ratio), whereas the sample containing the tetrapeptide-linked porphyrin led to a cubosomes-to-vesicles ratio clot to 26:74, comparable to that of the empty formulation. Experiments conducted at physiological temperature (37°C) highlighted that the structural features of the formulations remained largely unchanged, with retention of the phases observed at room temperature. Overall, the promising physicochemical properties, particularly at body temperature, highlight the potential of these systems as effective nanoplatforms for drug delivery applications.

References:

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