EXPLOITATION OF SYNTHETIC AND NATURAL LIPID-BASED SYSTEMS FOR THE DELIVERY OF ACTIVE AND BIOLOGICAL COMPOUNDS

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Synthetic and Natural lipid-based systems, such as Lipid Nanoparticles [1] or Extracellular vesicles [2, 3], are attracting particular interest [4, 5] due to their unique pharmacokinetic profiles and physico-chemical properties. Among them, it is worth mentioning the low toxicity, the ability of housing both hydrophilic and hydrophobic compounds and the reduced off-target effects [6] . Moreover, one key peculiarity lies in their biomimeticity, that combines with a low immunogenicity and improves both the transport and interaction in biological environments, also favoured by the high flexibility and permeability.

The lipid bilayer forming the surface of these structures dictates the achievement of the aforementioned characteristics, that are mostly related to the mechanical nature of the bilayer itself.

It is currently accepted the solid-fluid duality of lipidic molecules [7, 8], that behave fluid-like when laterally stressed, showing viscous effects, while they resist deformations when transversally stressed, by storing elastic energy [9] .

Spanning from natural to synthetic systems, the dynamic fluidity of lipid bilayers impacts on cellular activities as vesicle fusion and fission, signalling, membrane remodelling, as well as on the modulation of the biological identity [10] .

This PhD project aims to study the role, organization, thermodynamics and the transformation of lipid bilayer in different systems.

Specifically, it would be advisable to investigate the biological and thermodynamic mechanisms that are triggered by the stimulation of natural and synthetic systems, with the aim of identifying unique properties of the materials considered.

These properties could be related to the different penetration abilities and interaction in biological systems, giving insights also into the transition from the synthetic to the biological identity and the cellular uptake pathway activated.

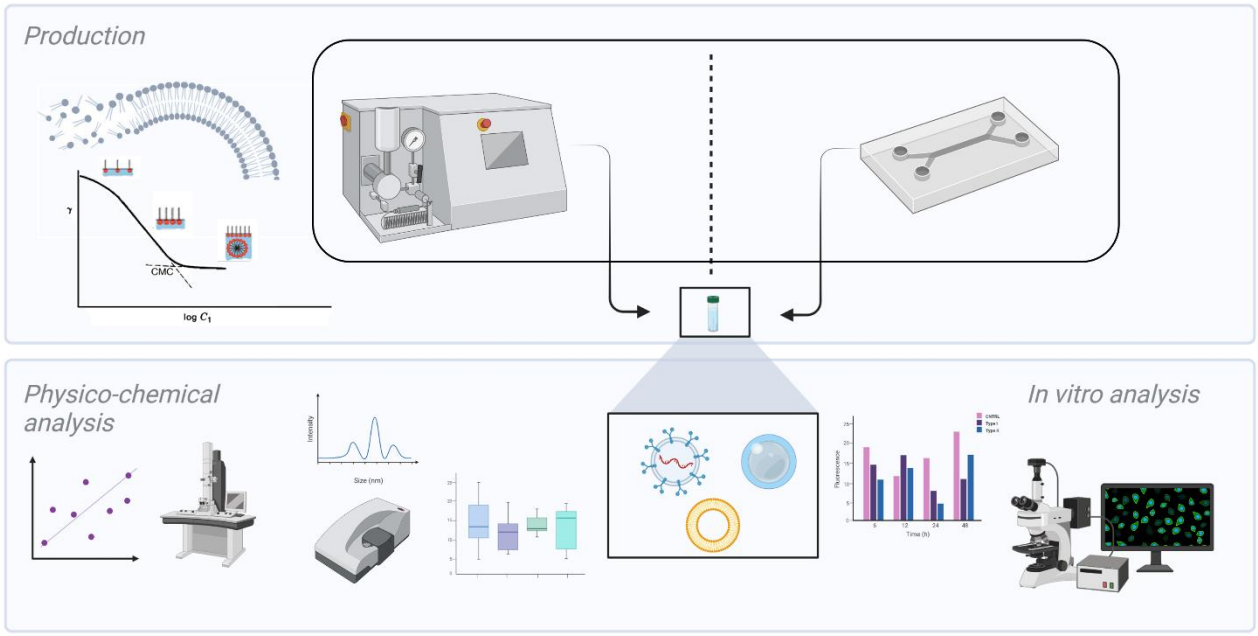
In this regard, different levels of investigation and analysis will be considered for the experimental plans.

Starting from the design of the systems, the microfluidic approach will be preferred to finely analyse, and control thermodynamics associated to both the production of synthetic vesicles, and the stimulation and loading of natural vesicles.

Then, physico-chemical analysis will be conducted to ascertain the robustness and reliability of the samples produced, as well as to identify possible biological mechanisms triggered or altered by external stimulation.

Once optimal properties and production setups will be identified, these systems will be prone to be tested for possible clinical translations. Active molecules and biological compounds will be loaded for this purpose, and their encapsulation efficiency will be measured and correlated with cytotoxicity and uptake tests on in vitro and in vivo models.

The key objective will be to achieve a broad thermodynamic understanding of the lipid bilayer properties by exploiting microfluidic technologies, with the aim of clarifying biological mechanisms and overcoming technical limitations that still hinder the clinical application of some lipid-based systems.



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