DELOS-SUSP for the Preparation of Multifunctional Nanovesicles with Application in Nanomedicine

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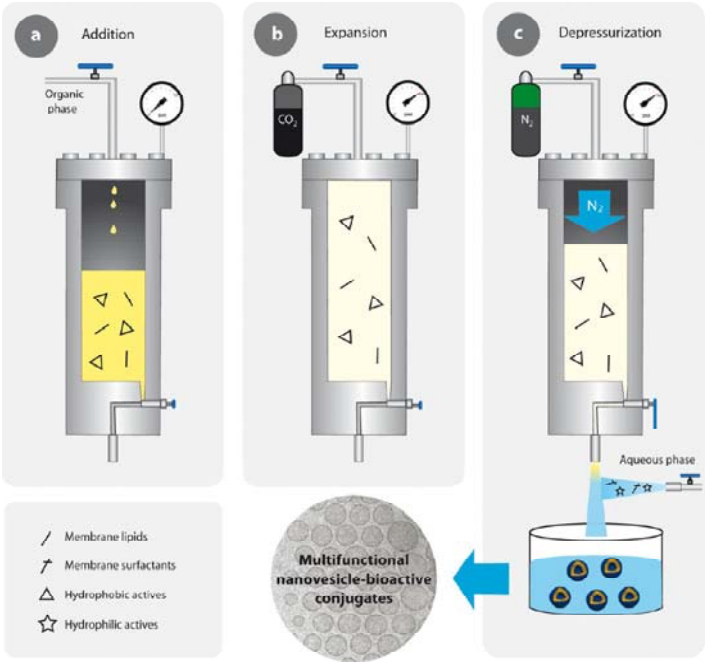
INTRODUCTION

Nanovesicles are one of the most promising supramolecular assemblies for nanomedicine due to their great versatility respect to composition, surface characteristics and capacity for integrating bioactive molecules. Besides, they are well recognized as pharmaceutical carriers because of their biocompatibility, biodegradability and low toxicity [1]. They constitute one of the most successfully translated delivery systems that are currently in clinical use for a variety of indications against cancer, inflammatory, dermatological diseases and in various types of vaccines. Despite their versatility, a high degree of structural homogeneity is crucial for an optimal performance of vesicles as delivery carriers. Thus, the formation stage of these supramolecular entities must be tightly controlled in order to achieve a homogeneous assembling of the lipids and other components constituting the vesicular membrane. In this communication will be shown the potential of DELOS-SUSP methodology for the one-step preparation of nanovesicle-bioactive conjugates containing peptides, proteins, enzymes and biocompatible polymers, with outstanding vesicle-to-vesicle homogeneity [2].

MATERIALS AND METHODS

Nanovesicle production by DELOS-SUSP. The whole procedure includes the loading (a) of an organic solution of the lipidic membrane components and the desired hydrophobic active compounds/molecules into an autoclave at a working temperature (T_w) and atmospheric pressure; the addition of CO_2 (b) to produce a CO_2-expanded solution, at a given X_{CO2}, working pressure (P_w), and T_w, where the hydrophobic active and membrane components remain dissolved; and finally, the depressurization (c) of the expanded solution over an aqueous solution, which migh contain membrane surfactants and hydrophilic biomolecules, to produce an aqueous dispersion of the nanovesicle-bioactive(s) conjugates with vesicle-to-vesicle homogeneity regarding size and morphology.



RESULTS

DELOS-SUSP technology platform has already yield two new nanomedicine candidates, which are now under pre-clinical development. Indeed, a new nanomedicine candidate for the treatment of Fabry's rare disease, based on nanoliposomes functionalized with targeting RGD-peptides and loaded with enzyme alpha-galactosidase(GLA) [3]. Positive results according to in vitro efficacy studies and in vivo pharmacokinetics have been obtained, compared to current treatments. In more detail, in vitro efficacy studies performed with MAEC cells from Fabry Knock-Out (KO) mice have shown that the new GLA@nanoliposomes conjugates have a higher capacity to reduce intracellular fat deposits GB3 characteristics of Fabry disease, than the free enzyme GLA. Pharmacokinetic studies carried out using KO Fabry mice model has shown that, once encapsulated in the peptide functionalized nanoliposomes, the GLA enzyme does not undergoes a first-pass effect as sharp as when is administered freely. These are very promising and motivating results, since this could mean a higher efficacy and a reduction on the doses required of the new nanoconjugate in relation to the free enzyme already in commercialization.

The second nanomedicine candidate, composed by an Epithelial Growth Factor (EGF) conjugated to a new highly stable nanovesicular structures, branded Quatsomes [4] is showing very promising results for the topical treatment of diabetic foot ulcer and other complex wounds. In compassionate treatments with this nanopharmaceutical candidate, complete epithelisation of the lesion was achieved in few weeks for a significative number of patients, improving remarkably the healing capacity of free EFG administered by infiltration [5].

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