

Supplementary material

Simple elaboration of drug-SPION nanocapsules (hybridsomes®) by solvent shifting: effect of the drug molecular structure and concentration

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Table SI- 1 : Correspondance between mass and molar fractions for the sorafenib and the sorafenib tosylate samples. Incertitudes on mass fractions are estimated to be (± 0.1)

Mass fraction of sorafenib	Molar fraction of sorafenib	Mass fraction of sorafenib tosylate	Molar fraction of sorafenib tosylate
$1.0 \cdot 10^{-5}$	$4.7 \cdot 10^{-7}$	$3.3 \cdot 10^{-5}$	$1.1 \cdot 10^{-6}$
$2.0 \cdot 10^{-5}$	$9.4 \cdot 10^{-7}$	$5.0 \cdot 10^{-5}$	$1.7 \cdot 10^{-6}$
$2.3 \cdot 10^{-5}$	$1.1 \cdot 10^{-6}$	$6.5 \cdot 10^{-5}$	$2.2 \cdot 10^{-6}$
$6.0 \cdot 10^{-5}$	$2.8 \cdot 10^{-6}$	$8.0 \cdot 10^{-5}$	$2.7 \cdot 10^{-6}$
$8.0 \cdot 10^{-5}$	$3.7 \cdot 10^{-6}$	$1.0 \cdot 10^{-4}$	$3.4 \cdot 10^{-6}$
$1.0 \cdot 10^{-4}$	$4.7 \cdot 10^{-6}$	$1.4 \cdot 10^{-4}$	$4.8 \cdot 10^{-6}$
$1.5 \cdot 10^{-4}$	$7.0 \cdot 10^{-6}$	$2.0 \cdot 10^{-4}$	$6.8 \cdot 10^{-6}$
$2.0 \cdot 10^{-4}$	$9.4 \cdot 10^{-6}$	$3.0 \cdot 10^{-4}$	$1.0 \cdot 10^{-5}$
		$4.0 \cdot 10^{-4}$	$1.4 \cdot 10^{-5}$

$\Phi_{\text{soraf,initial}}$	Encapsulation rate (%)
$5 \cdot 10^{-5}$	84
10^{-4}	88
$1.2 \cdot 10^{-4}$	84
$1.6 \cdot 10^{-4}$	88

Table SI-2: Encapsulation efficiency for various initial mass fractions of sorafenib: ($\varphi_{\text{soraf,initial}} = 5 \cdot 10^{-5}$; 10^{-4} ; $1.2 \cdot 10^{-4}$; $1.6 \cdot 10^{-4}$) after capsule preparation and (b) kinetics of release of sorafenib ($\varphi_{\text{soraf,initial}} = 1.2 \cdot 10^{-4}$)

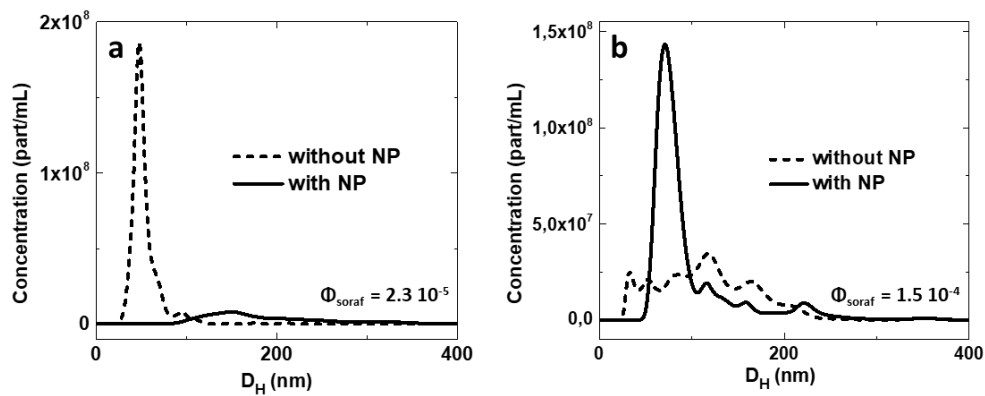


Figure SI-1: Comparison of size distributions measured by NTA for sorafenib nanoprecipitate and sorafenib-SPION Hybridosomes®, for two sorafenib mass fractions: (a) $2.3 \cdot 10^{-5}$ (SFME); (b) $1.5 \cdot 10^{-4}$ (Ouzo).

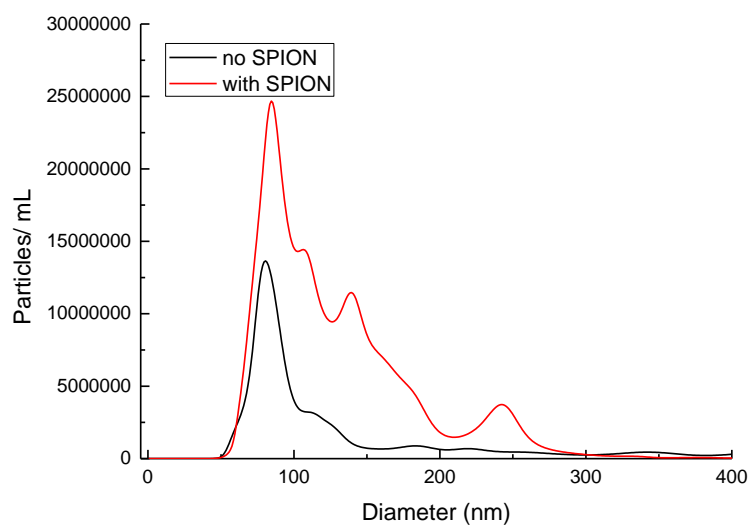


Figure SI-2: Comparison of size distributions measured by NTA for sorafenib nanoprecipitate and sorafenib-SPION co-nanoprecipitate (prior to polymer addition and solvent evaporation). Sorafenib mass fraction: $2.3 \cdot 10^{-5}$

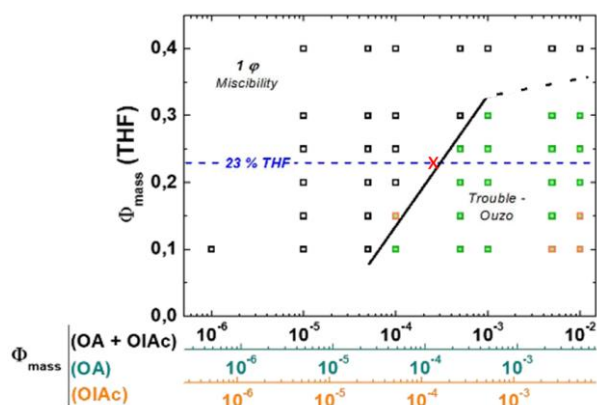


Figure SI-3: phase diagram of the system “water/THF/(Octyl amine + Oleic Acid)” prepared using equimolar amounts of octylamine (OA) and oleic acid (OIAc). Samples are observed visually. \blacksquare transparent samples; \blacksquare : turbid samples; \blacksquare : transparent or slightly turbid (undetermined). The red cross (x) shows the composition corresponding to a mass fraction of THF of 23% (as used to elaborate the capsules) and assuming that all octylamine and oleic acid molecules used in the synthesis of the SPION are present in the sample.

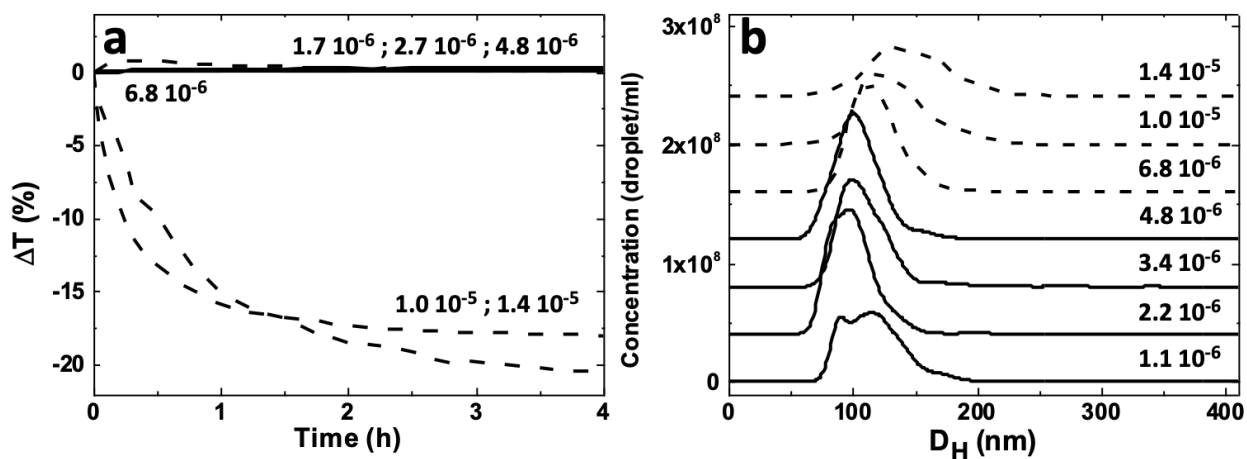


Figure SI-4: Characterization of compositions in the system water/THF/sorafenib tosylate. (a) Stability analysis using SMLS. (b) Size distribution measured using Nanoparticle Tracking Analysis.

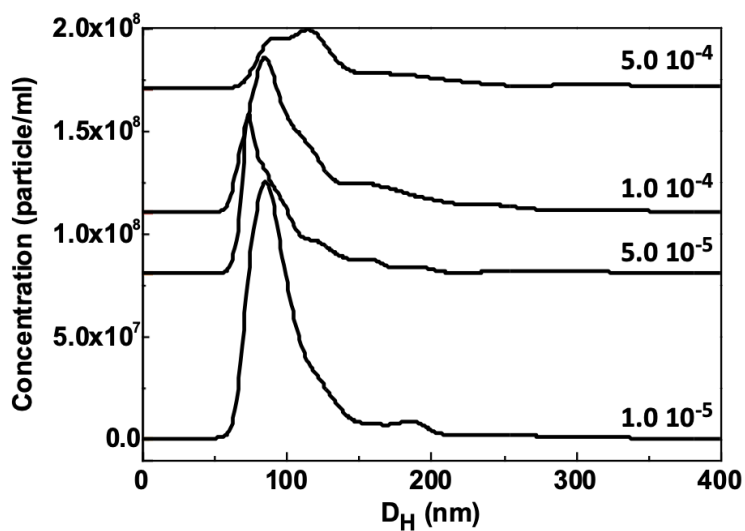


Figure SI-5: Size distribution of the dispersions of hybridosomes made from α -tocopherol in the Ouzo domain by NTA. Mass fractions as indicated on graph.

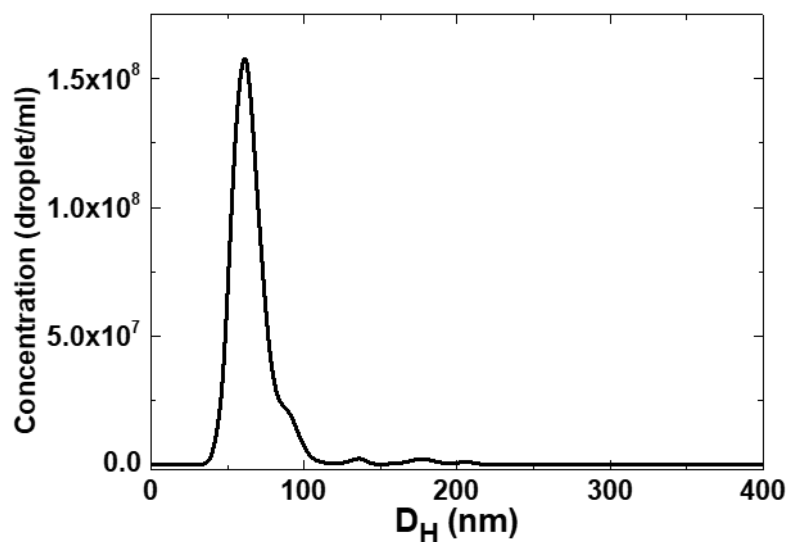


Figure SI-6: Nanoparticle tracking analysis of the paclitaxel composition with mass fractions: $\Phi_{THF} = 0.23$ and $\Phi_{Pacli} = 1 \cdot 10^{-6}$ showing the presence of a SFME.

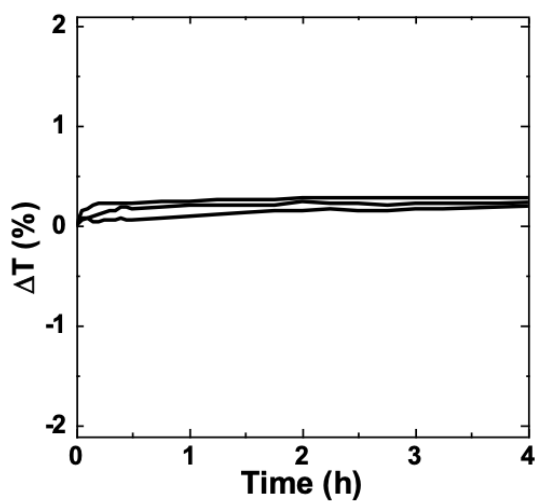


Figure SI-7: Investigation of the stability of water/THF/paclitaxel compositions using SMLS for the mass fractions (paclitaxel): 10^{-6} ; 10^{-5} and 10^{-4}

As shown in Figure SI-8 below, the cytotoxicity of the different products used to synthesize hybridosomes was evaluated. Even at the highest concentration tested (25 mM), which was itself much higher than the synthesis conditions, no cytotoxicity was observed.

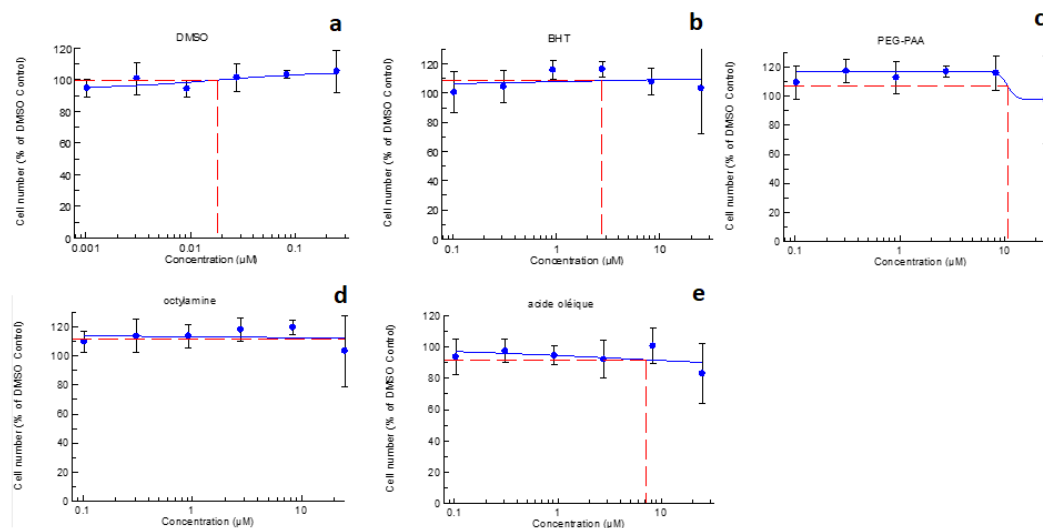


Figure SI-8: Cell viability of HuH7-LUC cells after 48 h of incubation in the presence of different products (b-e) used during the synthesis of hybridosomes[®]: (b) BHT (c) PEG-PAA, (d) octylamine, (e) oleic acid. (a) DMSO is used as negative control.