pharmaceutics

Supplementary Materials: Rational Development of Liposomal Hydrogels: A Strategy for Topical Vaginal Antiretroviral Drug Delivery in the Context of HIV Prevention

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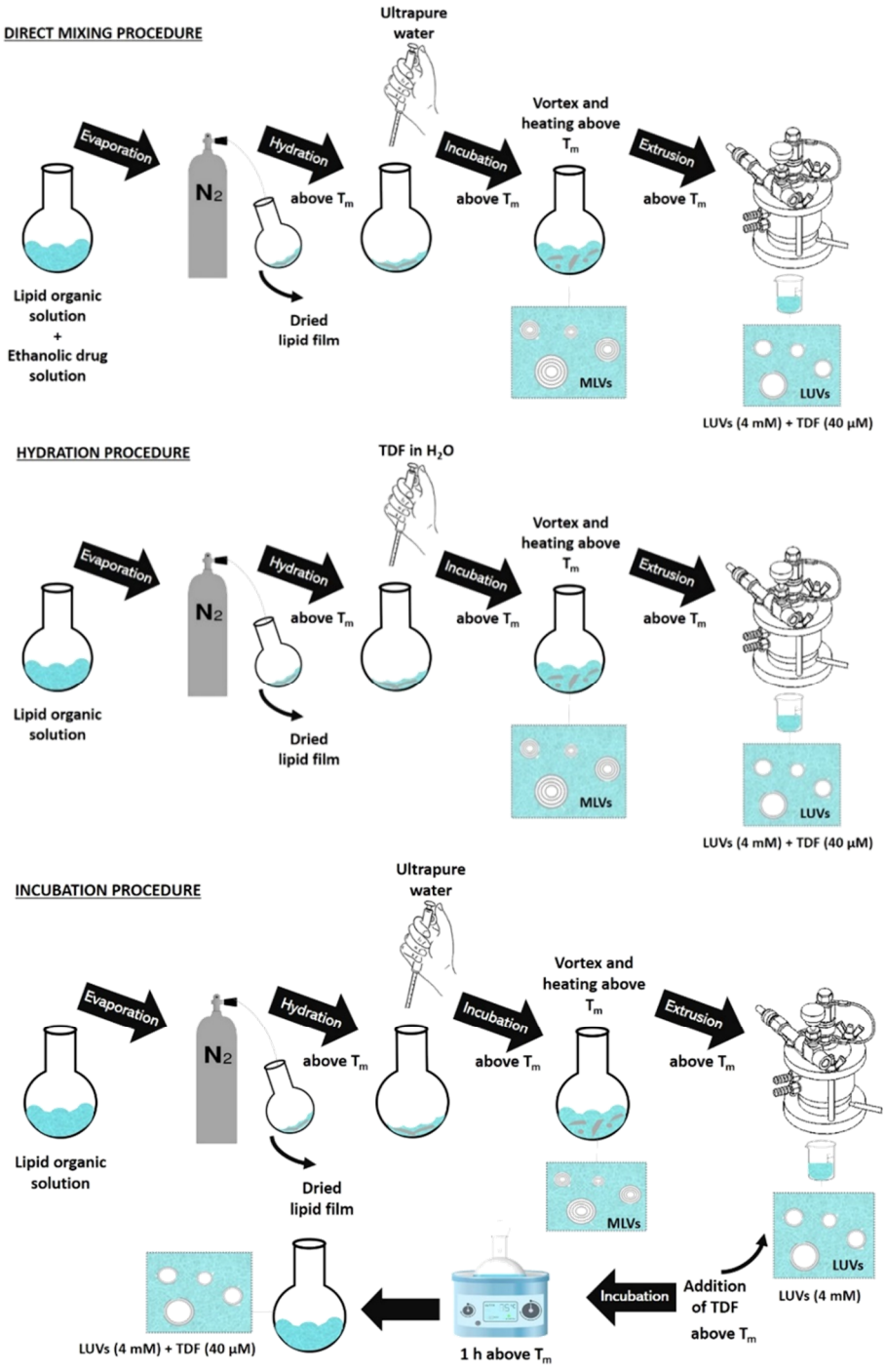

Figure S1. Schematic representation of encapsulation methods of TDF (final concentration 40 µM) in zwitterionic liposomes (4 mM) with different degrees of membrane rigidity.

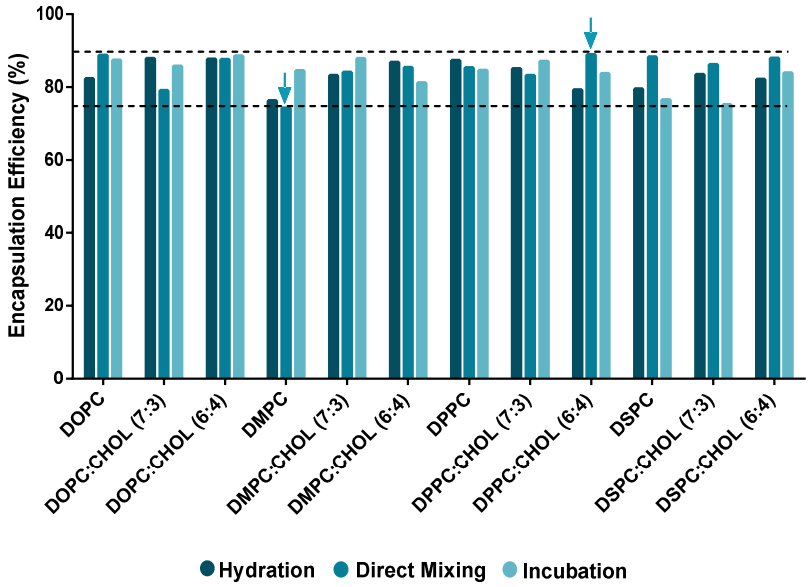

Figure S2. Encapsulation efficiency (EE %) of TDF (40 μM) in liposomes with different degrees of membrane rigidity (4 mM) by three encapsulation methods: hydration, direct mixing and incubation. The dashed lines define the interval between the highest and lowest encapsulation efficiencies obtained.

Table S1. Main phase transition temperature (T_m) and cooperativity of the phase transition (B) of the lipid formulations DMPC, DPPC and DSPC (4 mM) before and after TDF (40 μM) encapsulation by three different methodologies (incubation, hydration and direct mixing).

	DMPC	DMPC+TDF		
		Incubation	**Hydration**	**Direct Mixing**
T_m	23.76 ± 0.023	23.96 ± 0.02	23.79 ± 0.15	22.28 ± 0.41
B	857.70 ± 37.56	695.12 ± 34.29	514.99 ± 146.57	237.35 ± 41.24
R^2	0.999	0.999	0.848	0.991
	DPPC	**DPPC+TDF**		
		Incubation	**Hydration**	**Direct Mixing**
T_m	41.05 ± 0.03	41.19 ± 0.05	41.27 ± 0.02	41.49 ± 0.03
B	2780.89 ± 234.32	4116.88 ± 724.16	3921.77 ± 237.81	3135.08 ± 297.54
R^2	0.999	0.999	0.999	0.999
	DSPC	**DSPC+TDF**		
		Incubation	**Hydration**	**Direct Mixing**
T_m	54.08 ± 0.02	54.198 ± 0.07	54.45 ± 0.02	54.07 ± 0.02
B	4400.78 ± 391.19	3302.02 ± 556.45	6237.21 ± 668.93	4912.77 ± 290.35
R^2	0.999	0.975	0.997	0.989

Table S2 to S5. Fitting of FTC release from hydrogel (HG) and TDF release from liposomes included in hydrogel (LH) in aqueous medium (37 °C).

Table S2. 1st Order kinetics.

Mathematical Equation	pH	Adjusted Parameters	R^2	R^2 Adjusted
$F_{max}(1-e^{-kt})$	HG with FTC	F_{max} = 52.97 ± 1.628 k = 1.597 ±0.1882	0.9620	0.9585
	LH with TDF	F_{max} = 57.14 ± 1.461 k = 0.5026 ± 0.035	0.9934	0.9928

F_{max} is the total amount of drug released and k is the first order release constant.

Table S3. Korsmeyer–Peppas Model.

Mathematical Equation	pH	Adjusted Parameters	R^2	R^2 Adjusted
at^n	HG with FTC	a = 35.17 ± 1.322 n = 0.2728 ± 0.02555	0.9598	0.9561
	LH with TDF	a = 22.72 ± 0.9262 n = 0.5049 ± 0.02603	0.9875	0.9875

a is a constant of geometric and structural incorporation that takes into account the pharmaceutical form; n is a release representing the mechanism of diffusion of the drug, being based on Fick's law, (a value of n equal to or less than 0.5 indicates a Fickian diffusion, for values between 0.5 and 1 indicates a non- Fickian diffusion).

Table S4. Weibull Model.

Mathematical Equation	pH	Adjusted Parameters	R^2	R^2 Adjusted
$(1 - e^{(-at^b)})$	HG with FTC	a = 1.159 ± 0.08798 F_{max} = 56.49 ± 1.451 b = 0.6314 ± 0.04353	0.9945	0.9934
	LH with TDF	a = 0.7885 ± 0.02721 F_{max} = 66.11 ± 2.494 b = 0.4343 ± 0.02335	0.9990	0.9988

F_{max} is the total amount of drug released and a is a parameter a that defines the time scale. The parameter b characterizes the shape of the curve. For (b = 1) (Case 1), sigmoid, for (b > 1) (Case 2) S-shaped, curvature upwards followed by a turning point, for parabolic (b < 1) (Case 3) with greater initial slope and then exponential.

Table S5. - Higuchi Model.

Mathematical Equation	pH	Adjusted Parameters	R^2	R^2 Adjusted
$kt^{0,5}$	HG with FTC	k = 26.02 ± 1.735	0.7402	0.7402
	LH with TDF	k = 22.87 ± 0.4112	0.9885	0.9885

K is the Higuchi dissolution constant.

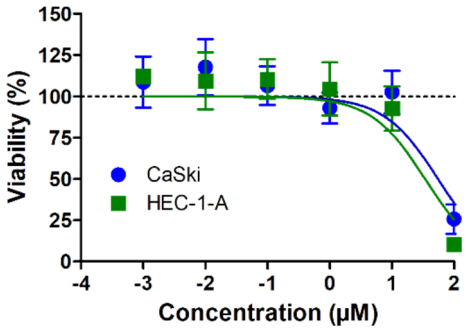

Figure S3. Viability of HEC-1-A and CaSki cells with increasing concentrations of TDF. Results are presented as mean ± standard deviation values (n = 3). Lines represent log-logistic regression fits.