Empowering Naringin´s Anti-Inflammatory Effects through Nanoencapsulation

Andreia Marinho [1,2], Catarina Leal Seabra [1], Sofia A. C. Lima [3], Alexandre Lobo-da-Cunha [4], Salette Reis [1], Cláudia Nunes [1,3,*]

[1]LAQV, REQUIMTE, Faculdade de Farmácia, Universidade do Porto, R. Jorge de Viterbo Ferreira 228, 4050-313 Porto, Portugal

[2]LAQV, REQUIMTE, Faculdade de Ciências, Universidade do Porto, R. do Campo Alegre s/n, 4169-007 Porto, Portugal

[3]LAQV, REQUIMTE, Instituto de Ciências Biomédicas Abel Salazar, Universidade do Porto, R. Jorge de Viterbo Ferreira 228, 4050-313 Porto, Portugal

[4]Departamento de Microscopia, Instituto de Ciências Biomédicas Abel Salazar, Universidade do Porto, R. Jorge de Viterbo Ferreira 228, 4050-313 Porto, Portugal

*Correspondence: cdnunes@ff.up.pt

1. In vitro release studies

Table S1 lists the results obtained for the release kinetics studies with an indication of the correlation coefficient values and the constants obtained for each model under study.

Table S1: Correlation coefficient (R^2) for the release of NAR at different pH values, according to the models studied.

	Regime	Zero-order		First-order		Hixson-Crowell		Higuchi		Korsmeyer-Peppas	
		R^2	k_0	R^2	k_1	R^2	k_{HC}	R^2	k_H	R^2	k_{KP}
NAR@NPs	i	0.997	0.011	0.978	0.305	0.973	-9.449	0.9852	0.053	†**1.000**	1.279
	ii	0.991	0.029	†**0.998**	0.054	0.983	-4.914	0.9801	0.015	0.944	0.261
	iii	1.000	0.000	1.000	0.002	1.000	-0.492	1.000	0.002	1.000	0.041
NAR@NPs_CTAB	i	0.996	0.012	0.981	0.316	0.995	-10.555	0.981	0.032	†**1.000**	1.320
	ii	0.992	0.006	†**0.999**	0.060	0.975	-5.246	0.964	0.017	0.947	0.287
	iii	1.000	0.000	1.000	0.002	1.000	-0.419	1.000	0.002	1.000	0.040
NAR@NPs_HA	i	0.997	0.011	0.980	0.313	0.992	-11.064	0.983	0.028	†**1.000**	1.309
	ii	0.992	0.004	†**0.999**	0.055	0.963	-5.148	0.966	0.013	0.947	0.263
	iii	1.000	0.000	1.000	0.002	1.000	-0.421	1.000	0.001	1.000	0.037

† Represents models that best fit each release profile.

k_0: zero-order constant; k_1: first-order constant; k_{HC}: release constant of Hixcon-Crowell; k_H: release constant of Higuchi; k_{KP}: release constant of Korsmeyer-Peppas.

2. Cell uptake pathway inhibitors solutions

Table S2 lists the receptors used to study the internalization pathways of the development nanoparticles, as well as their respective functions.

Table S2: Selected inhibitors and respective functions applied to mechanistic studies of nanoparticles transport by THP-1 macrophages.

	Inhibitor	Concentration	Function
Endocytosis inhibitors	Chlorpromazine	10 μg·mL^{-1}	Clathrin-mediated endocytosis
	Cytochalasin-D	5 μg·mL^{-1}	Disrupt actin filaments and Macropinocytosis
	Filipin	1 μg·mL^{-1}	Caveolae-mediated endocytosis
Energy-dependence	Sodium azide	1 μg·mL^{-1}	Active transport inhibitor
	4ºC	-	Passive diffusion and active transport inhibitor