Electronic Supplementary Material (ESI) for Journal of Materials Chemistry B.

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Cationic Nioplexes-*in*-Polysaccharide-Based Hydrogels as Versatile Biodegradable Hybrid Materials to Deliver Nucleic Acids

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SUMMARY

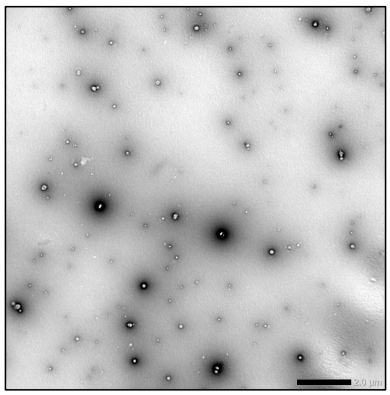


Figure S1 TEM images of nioplexes at N/P of 14. Original magnification 2500X.

Table S1 Encapsulation efficiencies of cationic nioplexes and rheological parameters for Hydrogel_**3** and Hydrogel_**4**. Native hydrogels (Hydrogel_**1** and _**2**) were used as controls for comparison purposes.

Entry	Polysaccharide[a]	Hydrogel	Entrapped nioplexes	EE[b] (%)	G'[c] (kPa)	G''[d] (kPa)	γ[e] (%)	*tan* δ
1	KC	3	yes	95.7	36742	8757	1.1	0.13
2	MC:KC	4	yes	98.4	2413	535.6	41	0.16
3	KC	1	-	-	71877	11615	0.68	0.21
4	MC:KC	2	-	-	1026	192	3.9	0.23

[a]κ-Carrageenan (KC) (4 %; *w/v*); 1:1 mixture of methylcellulose:κ-carrageenan (MC:KC) (2 %, *w/v*) (in total 4 % *wt* of polymers); [b]encapsulation efficiency; [c]storage modulus; [d]loss modulus; [e]γ at break.

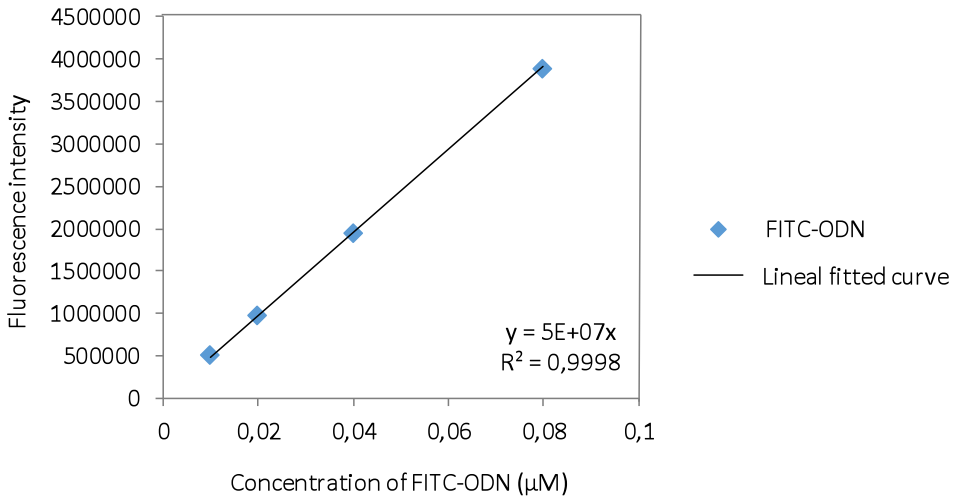


Figure S2 Standard calibration curve.

Table S2 Model release parameters for Hydrogel_**3** and _**4** according to Higuchi equation: $MtM\infty = K * t$

Entry	Hydrogel	*k*	r^2
1	3	3.57	0.9947
2	4	2.14	0.9690

Table S3 Model release parameters for Hydrogel_**3** and _**4** according to Korsmeyer-Peppas' equation. The model was fitted for the first 60 % of the niosomal FITC-ODN release: $MtM\infty = K * tn$

Entry	Hydrogel	*k*	*n*	r^2
1	3	2.58	0.55	0.9994
2	4	3.89	0.41	0.9928

Table S4 Model release parameters for Hydrogel_**3** and _**4** according to Weibull equation: $MtM\infty = \alpha * (1 - \exp(-kt)b)$

Entry	Hydrogel	*α*	*k*	*b*	r^2
1	3	561,8	0,0021	1,051	0.9567
2	4	104,2	0,0011	0,58	0.9837

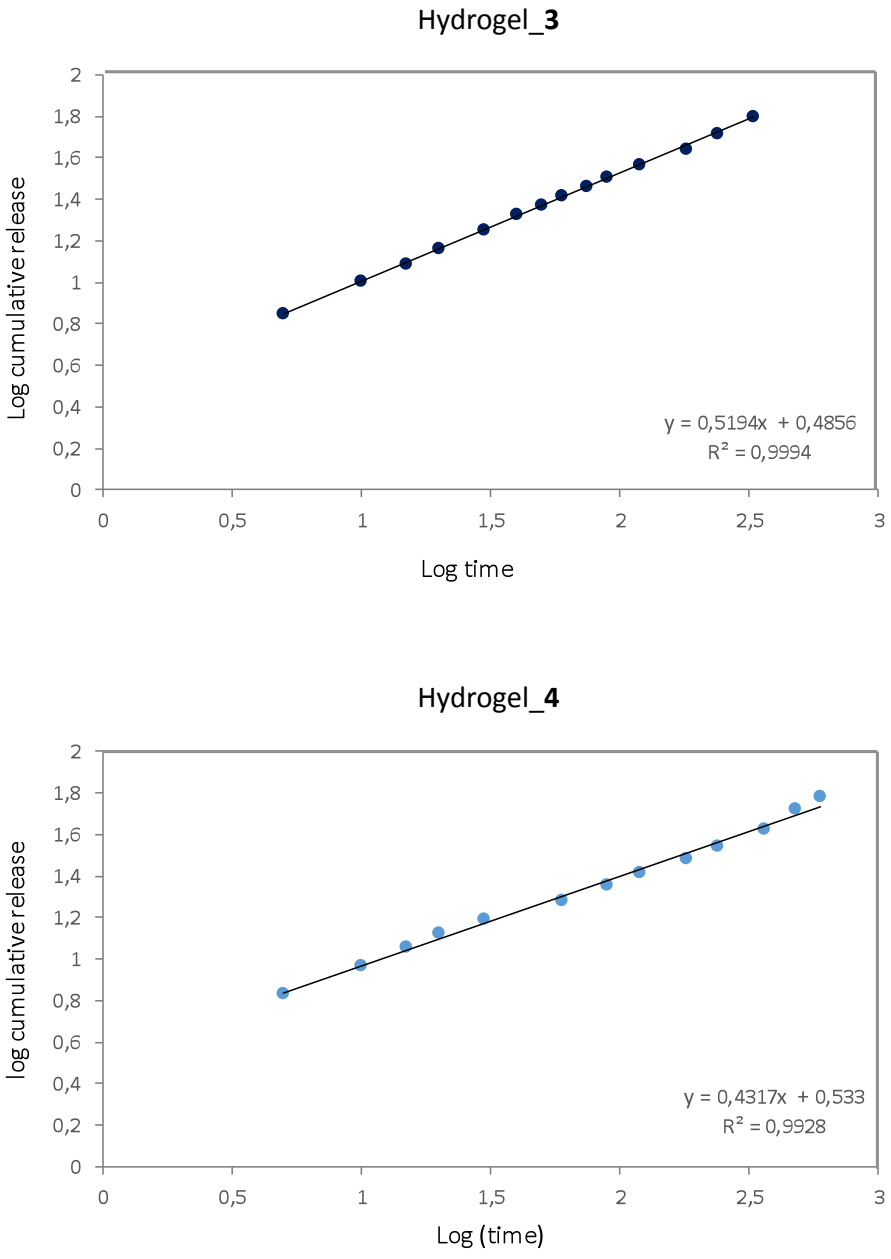
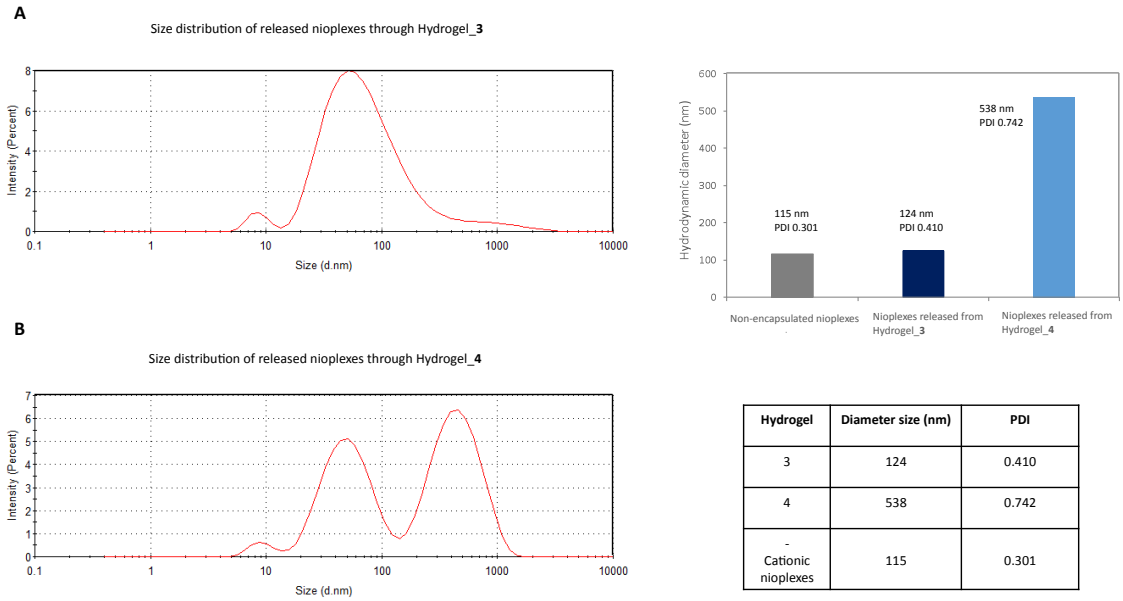


Figure S3 Niosomal release profiles of niosomal FITC-ODN from Hydrogels **_3** and **_4** according to Korsmeyer-Peppas' equation. The regression coefficient (r^2) for the Korsmeyer-Peppas equation was 0.9994 and 0.9928 for Hydrogel_**3** and **_4**, respectively (using the first 60 % of niosomal release). On the contrary, r^2 values were lower when Higuchi equation (0.9947 and 0.9690) and Weibull release model (0.9567 and 0.9837) were used for Hydrogel_**3** and **_4**, respectively.



Hydrogel	Diameter size (nm)	PDI
3	124	0.410
4	538	0.742
- Cationic nioplexes	115	0.301

Figure S4 Average hhydrodynamic diameter and polydispersity degree of cationic nioplexes after complete KC (Fig. S3A) and MC:KC (Fig. S3B) hydrogels degradation. Hydrodynamic diameter of nioplexes before being encapsulated within KC and MC:KC hydrogels were measured as a control.

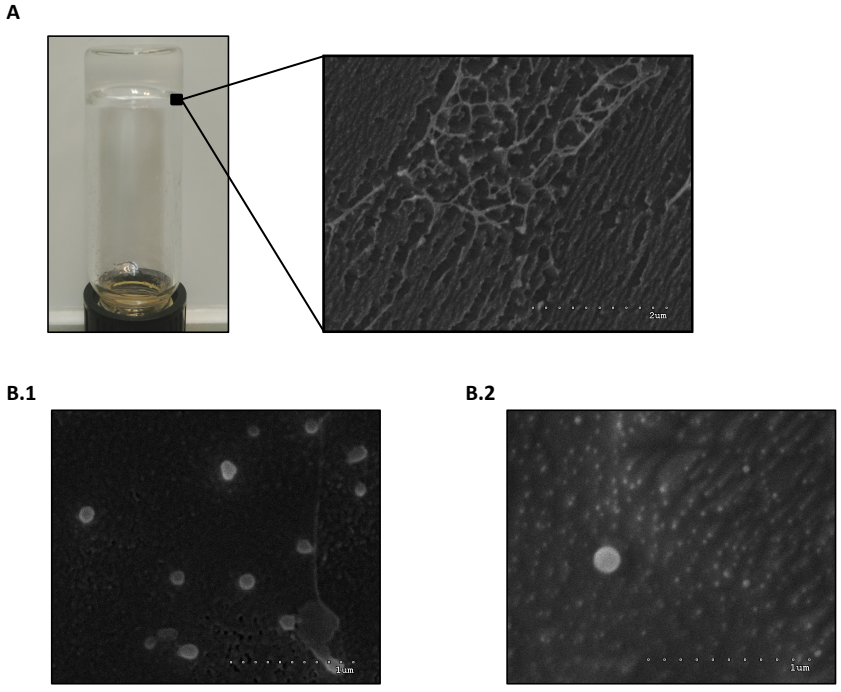


Figure S5 Cryo-SEM images of A) KC hydrogels (Hydrogel_**1**) and B) native cationic nioplexes loaded in KC hydrogels (Hydrogel_**3**). Cationic nioplexes were obtained using 300 nM of FITC-ODN with a N/P ratio of 14.

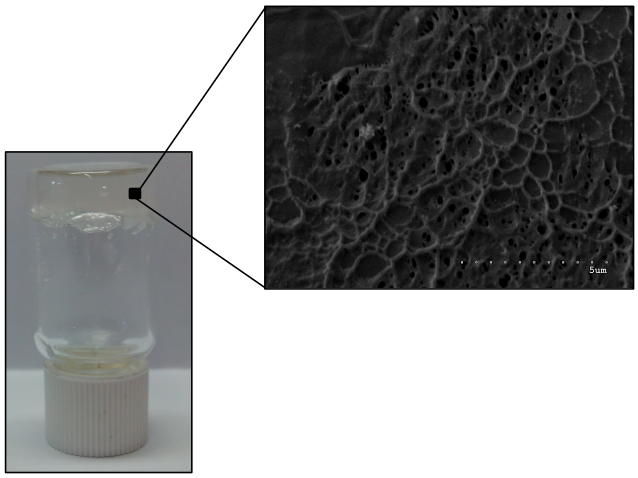


Figure S6 Cryo-SEM images of 1:1 mixture of MC:KC hydrogels (Hydrogel_**3**).

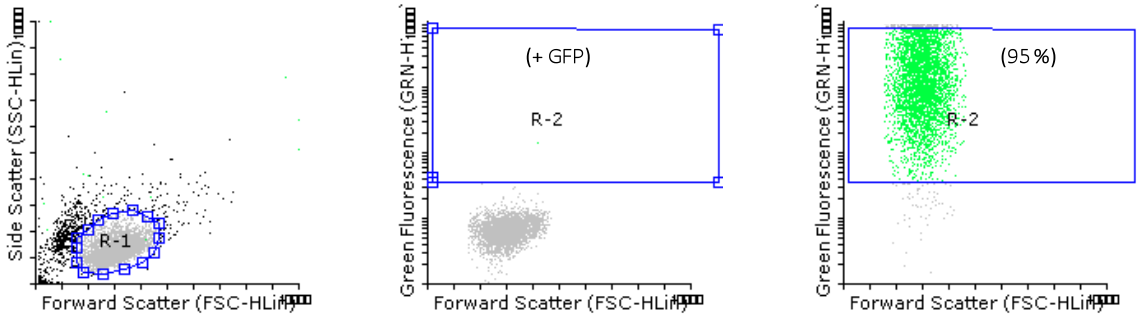


Figure S7 Flow cytometry analysis of HeLa cells treated with pGFP (formulated in liposomes with lipofectamine).

NOTE: *NANBIOSIS* is one of the 29 Singular Scientific Technological Infrastructures (ICTS) recently recognized by the Spanish Council for Science Policy, Technology and Innovation (MINECO).