Supporting Information

$CaCO_3$ as an environmentally friendly renewable material for drug delivery systems: uptake of HSA-$CaCO_3$ nanocrystals conjugates in cancer cell lines

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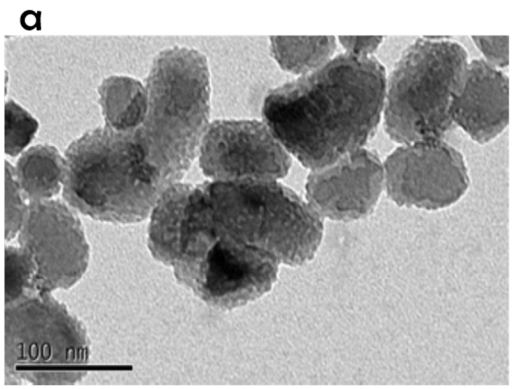
Figure S1. $CaCO_3$ physico-chemical characterization

Figure S2. Cytofluorimetric analysis: uptake kinetics

Figure S3. Cytofluorimetric analysis: Propidium Iodide assay

Figure S4. MTT assay

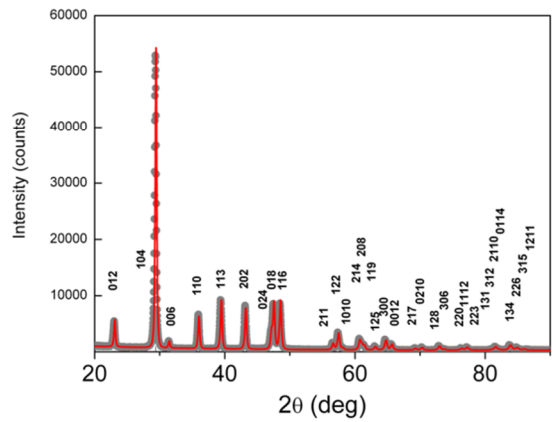


Size

Sample	Ultra-pure water	PBS	DMEM
	Mean size ± S.D(nm)/PDI	Mean Size ± S.D(nm)/PDI	Mean size ± S.D. (nm) /PDI
$CaCO_3$NCs	222.7±9.2/0.235	188.8±4.4/0.310	344.0±32.8/0.691

ζ-potential

pH	Ultra-pure water	PBS	DMEM
7.4	6.8±0.1	-25.1±0.3	-11.2±0.2
5.5	8.9±0.2	-28.4±0.1	-7.1±0.3



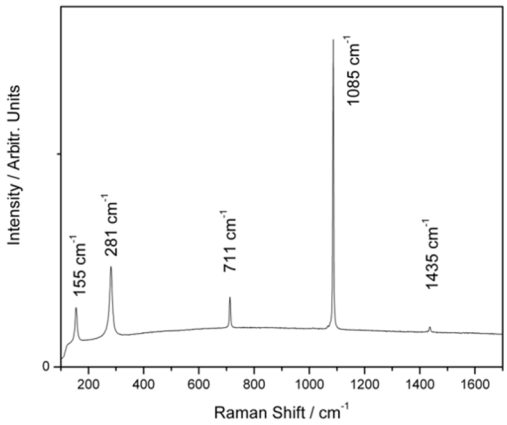


Figure S1. $CaCO_3$ chemical characterization: a) TEM image, scale bar 100 nm; b) Dynamic Light Scattering measurements (size and zeta-potential); c) XRD pattern; d) Raman spectrum.

The XRD pattern (Figure S1 c) was indexed as rhombohedral calcite phase (ICSD collection code 040544). The Raman spectrum (Figure S1 d) showed five bands which matched perfectly the literature one for calcium carbonate in calcite phase.

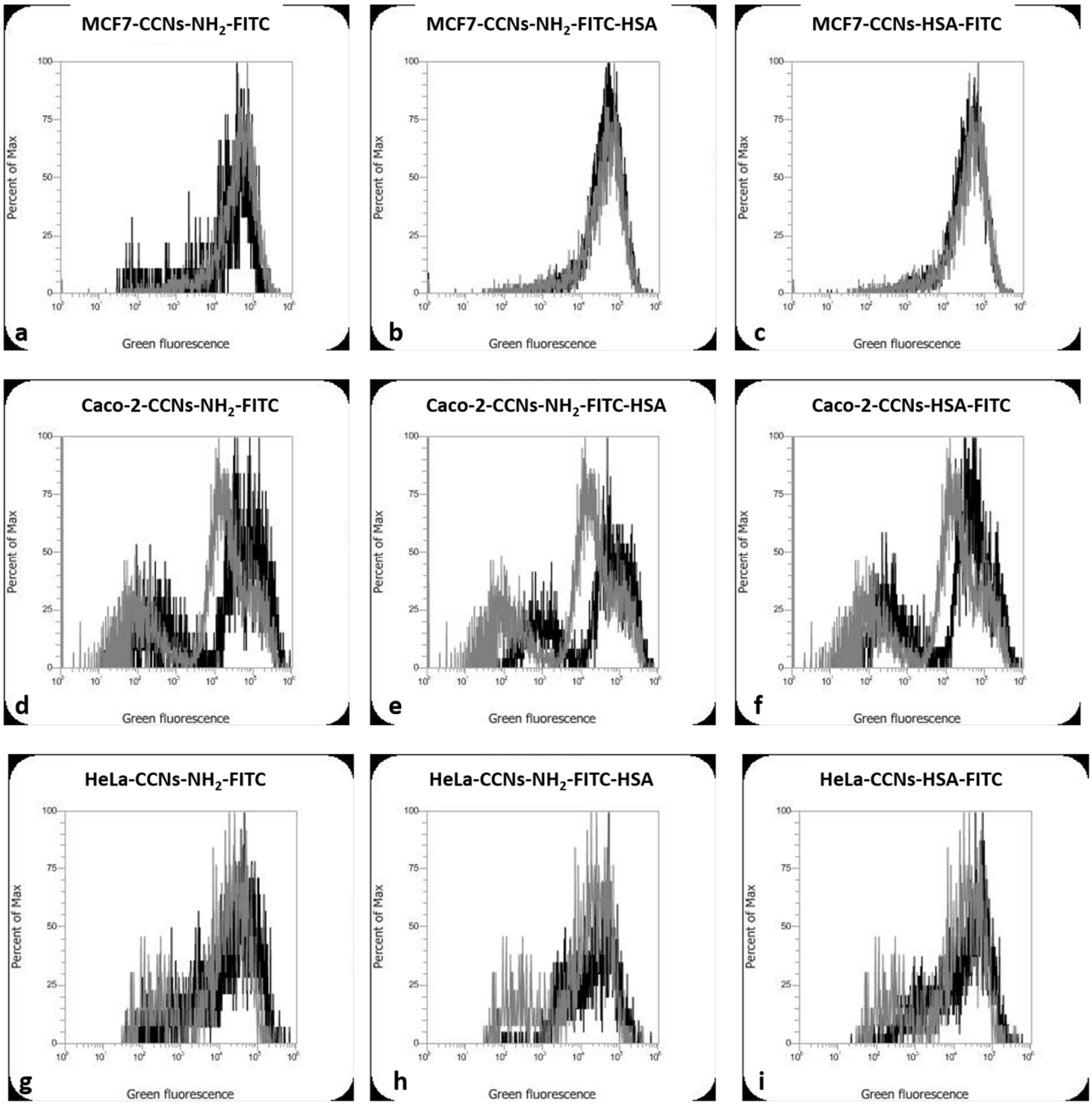


Figure S2. One representative flow cytometry measurements assessing the uptake kinetics of CCNs-NH_2-FITC (a, d, g), CCNs-NH_2-FITC HSA (b, e, h) and CCNs-HSA-FITC (c, f, i) performed in MCF7 (a-c), Caco-2 (d-f) and HeLa (g-i) cells.

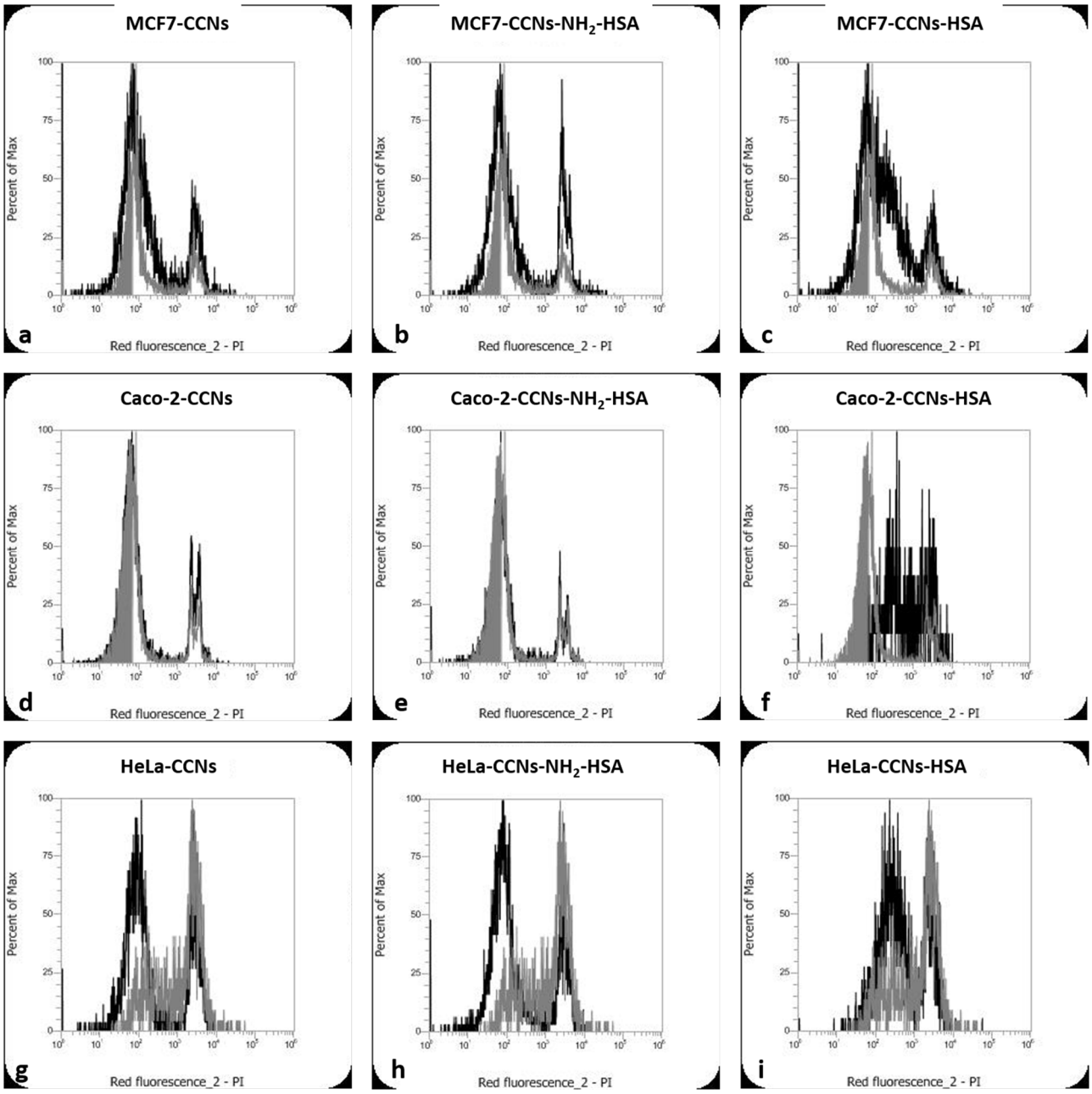


Figure S3. One representative flow cytometry measurements assessing the biocompatibility through Propidium Iodide assay of naked CCNs (a, d, g), CCNs-NH_2-HSA (b, e, h) and CCNs-HSA (c, f, i) performed in MCF7 (a-c), Caco-2 (d-f) and HeLa (g-i) cells.

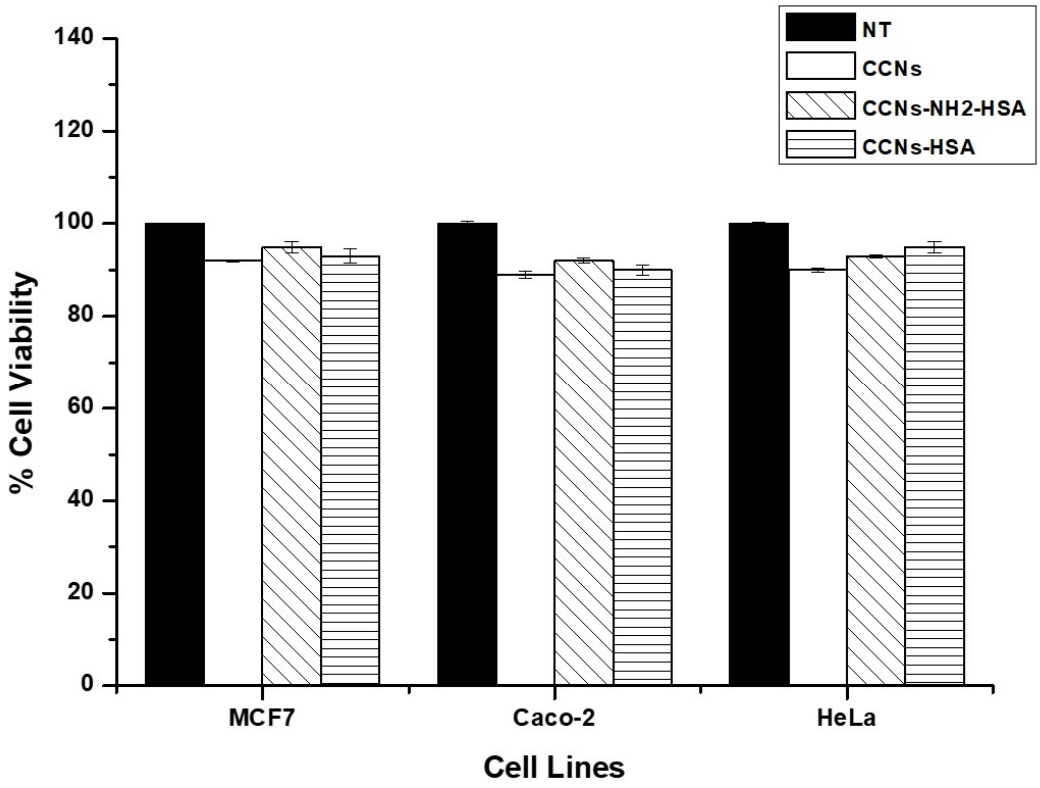


Figure S4. MTT assay to assess the biocompatibility of naked CCNs (white), CCNs-NH_2-HSA (diagonal lines) and CCNs-HSA (horizontal lines) performed on MCF7, Caco-2 and HeLa cells; the controls (NT = Non-treated cells) are labelled in black. Data were obtained from replicate experiments (n = 3).