



# Toxicity of Carbon Nanomaterials and Their Potential Application as Drug Delivery Systems: In Vitro Studies in Caco-2 and MCF-7 Cell Lines

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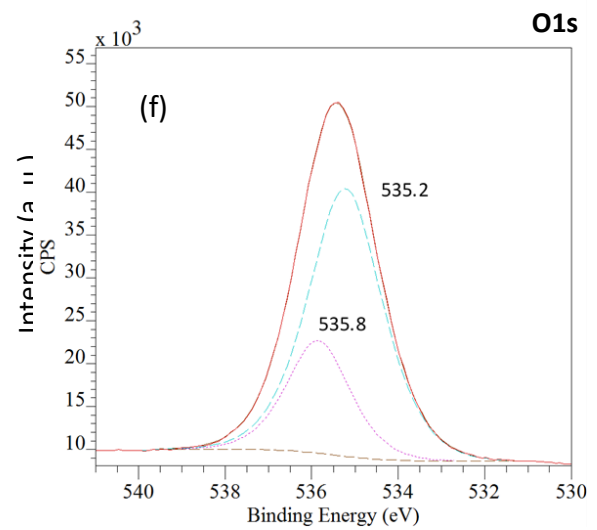
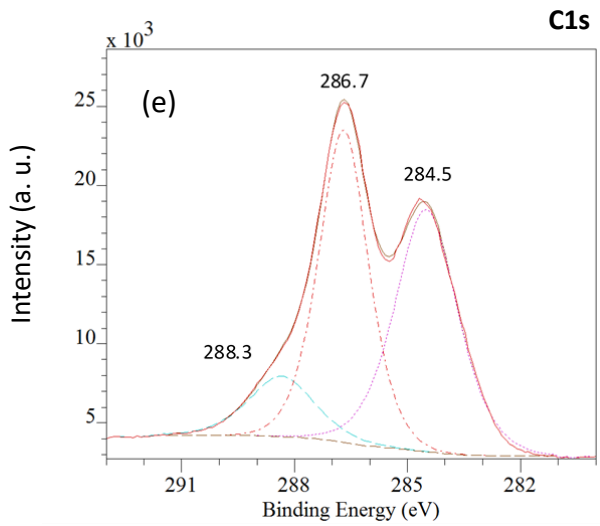
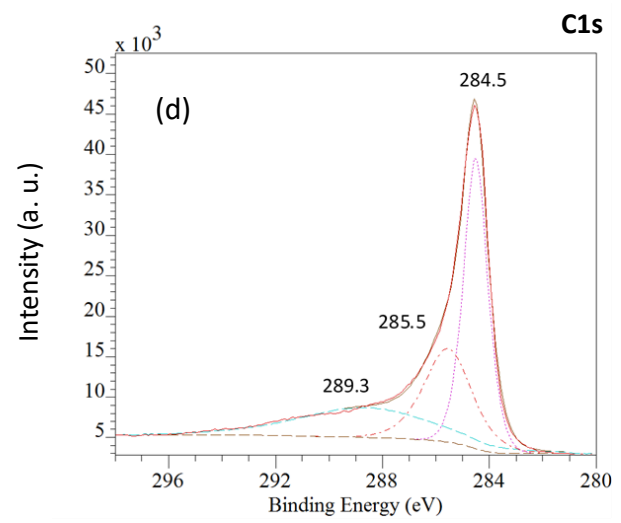
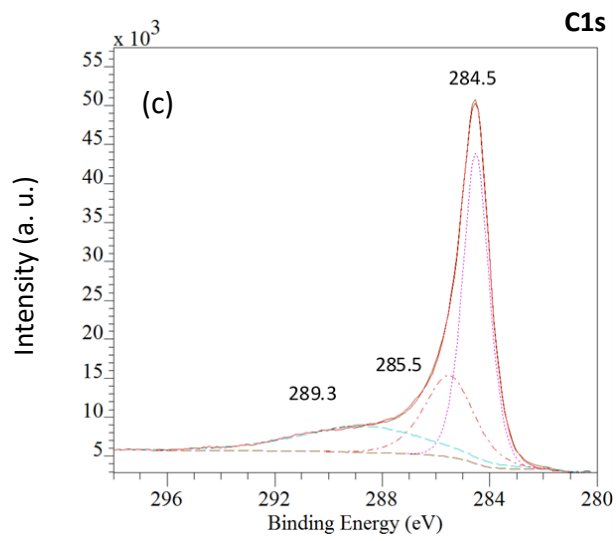
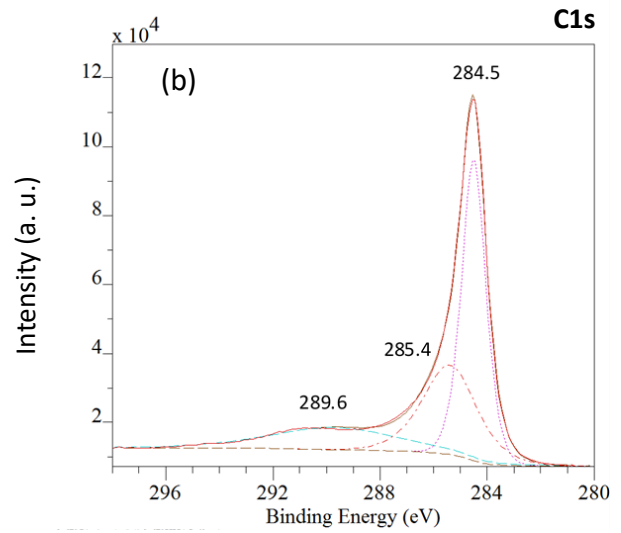
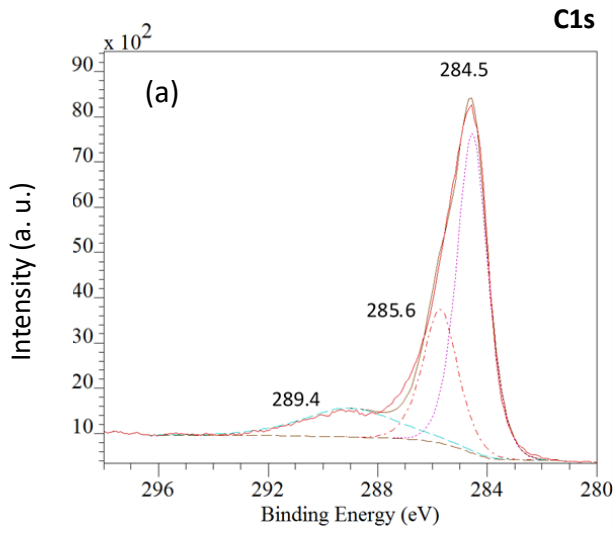
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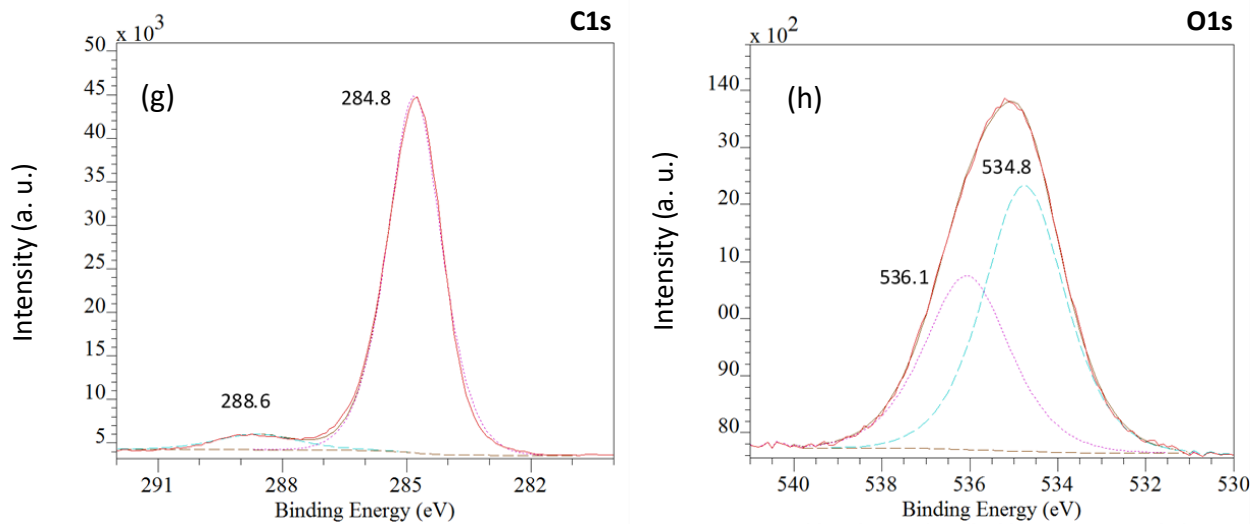
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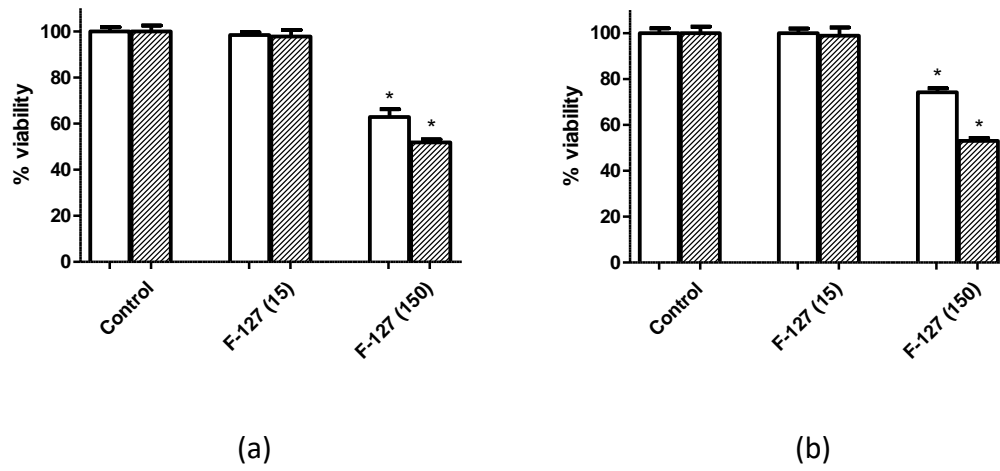
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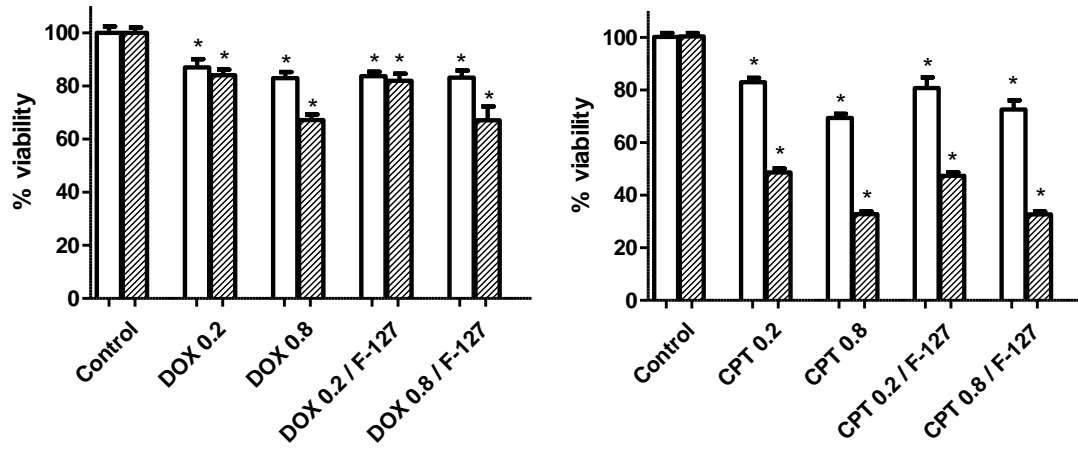


**Figure S1.** C1s and O1s regions in high resolution XPS spectra of carbon nanomaterials: (a) CNH, (b) CNT, (c) CNP, (d) RGO, (e, f) GO and (g, h) ND. In (a-d), C1s features at 284.5, ~285.4, and ~289.5 eV are assigned to  $sp^2$  C=C,  $sp^3$  C-C, and  $\pi$ - $\pi^*$  transitions, respectively. In (e), C1s XPS spectra show a wide peak at 284.5 ( $sp^2$  C=C,  $sp^3$  C-C), at 286.7 (C-O-C, C-OH) and at 288.3 eV (C=O, COOH). In (g), C1s peaks at 284.8 and 288.6 eV correspond to  $sp^3$  C-C diamond bonds and (C=O, COOH), respectively. Oxygen content (% at.) of these carbon nanomaterials, obtained from XPS spectra, are collected in Table 1.

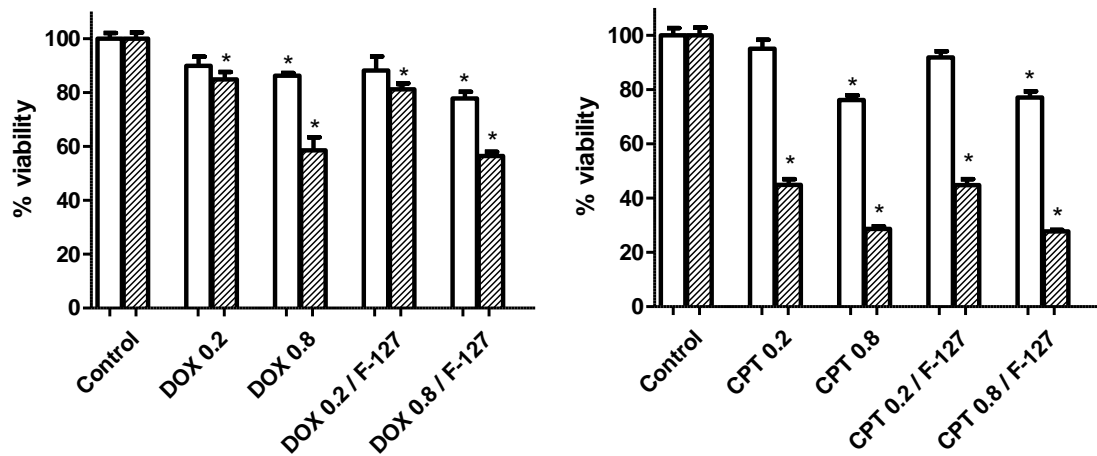


**Figure S2.** Cell viability assays after treatment with F-127 at 15 µg-mL<sup>-1</sup> and 150 µg-mL<sup>-1</sup> for 24 h (white) and 72 h (striped), on (a) Caco-2 and (b) MCF-7 cells. (\*represents significance at  $p < 0.05$  when compared to untreated control cells).

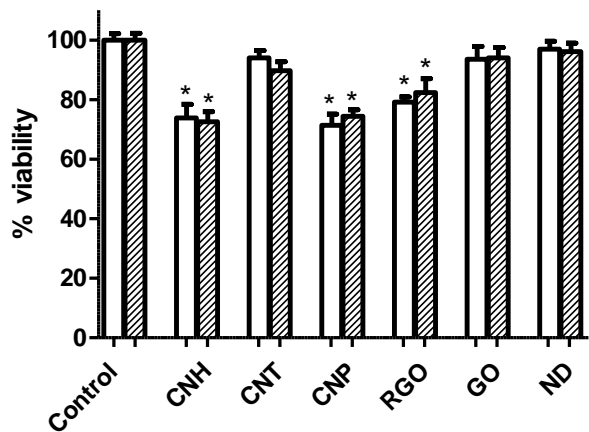
(a)



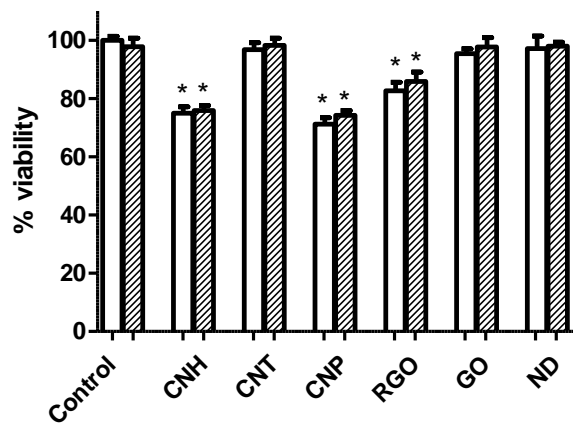
(b)



**Figure S3.** Cell viability assays after treatment with DOX and CPT at 0.2  $\mu\text{g}\cdot\text{mL}^{-1}$  and 0.8  $\mu\text{g}\cdot\text{mL}^{-1}$  for 24 h (white) and 72 h (striped), on (a) Caco-2 and (b) MCF-7 cells, showing no significant differences in the absence or in the presence of F-127 at 15  $\mu\text{g}\cdot\text{mL}^{-1}$ . (\*represents significance at  $p < 0.05$  when compared to untreated control cells).

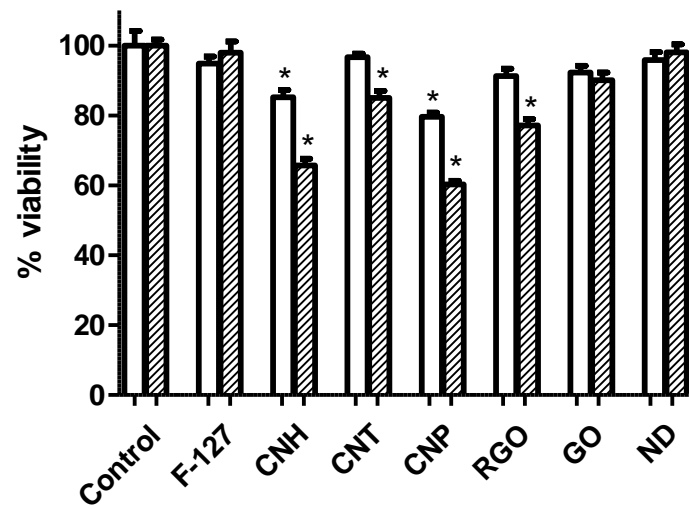


(a)

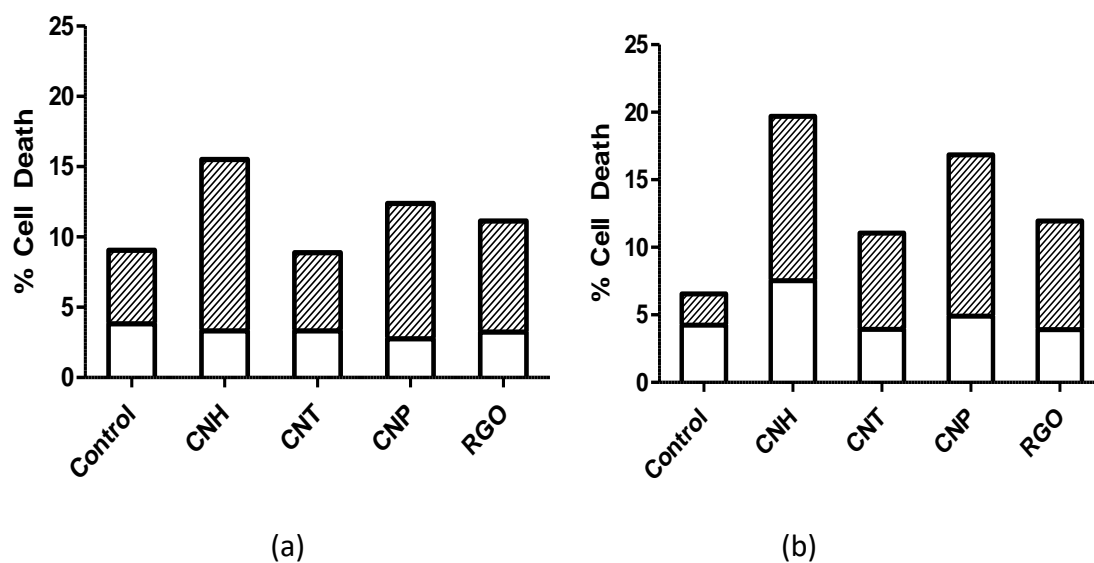


(b)

**Figure S4.** Cell viability assays after 24 h (white) and 72 h (striped) of incubation with various carbon nanomaterials at  $0.6 \mu\text{g}\cdot\text{mL}^{-1}$  showing differential effects on (a) Caco-2 and (b) MCF-7 cells. Values that are significantly different from the control ( $p < 0.05$ ) are denoted with asterisk (\*). Untreated cells were used as control.

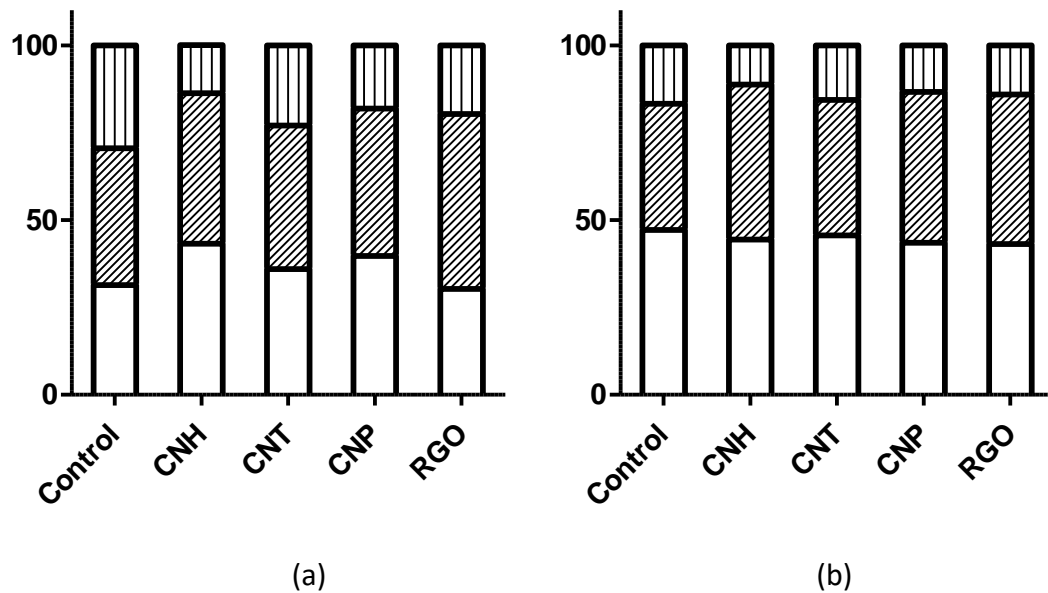


**Figure S5.** Cell viability assays after 24 h (white) and 72 h (striped) of incubation with various carbon nanomaterials at  $3.0 \mu\text{g}\cdot\text{mL}^{-1}$ , and also F-127 at  $15 \mu\text{g}\cdot\text{mL}^{-1}$ , showing differential effects on human dermal fibroblasts. Values that are significantly different from the control ( $p < 0.05$ ) are denoted with asterisk (\*). Untreated cells were used as control.



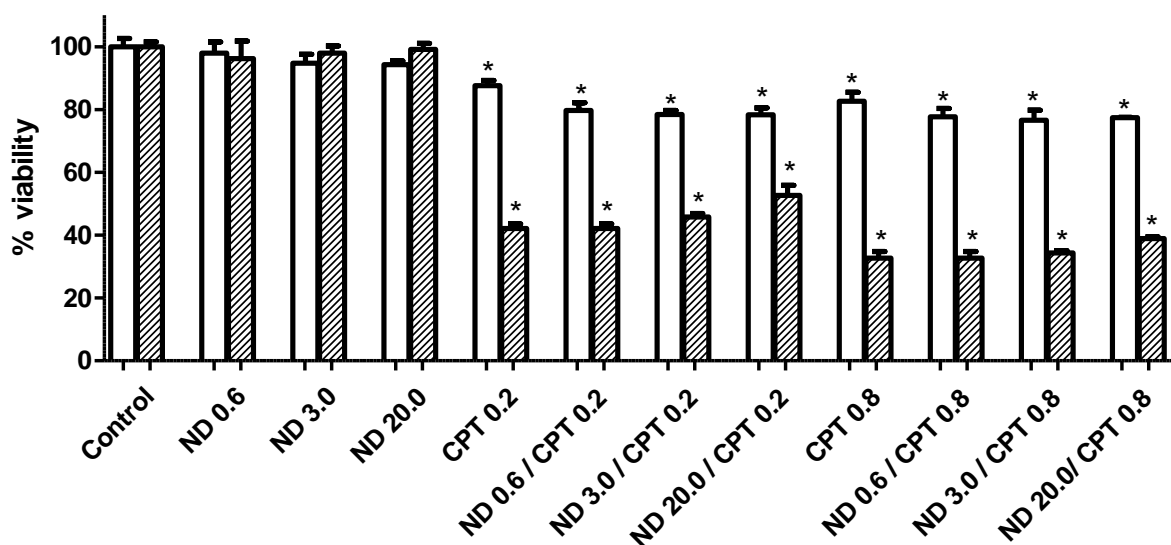
**Figure S6.** Bar graphs corresponding to flow cytometry analysis, quantifying the percentage of early-stage apoptotic (white), and late-stage apoptotic/necrotic (striped) cells in response to exposure for 72 h to different carbon nanomaterials at  $3 \mu\text{g}\cdot\text{mL}^{-1}$  for (a) Caco-2 and (b) MCF-7 cells. Control represents untreated cells.



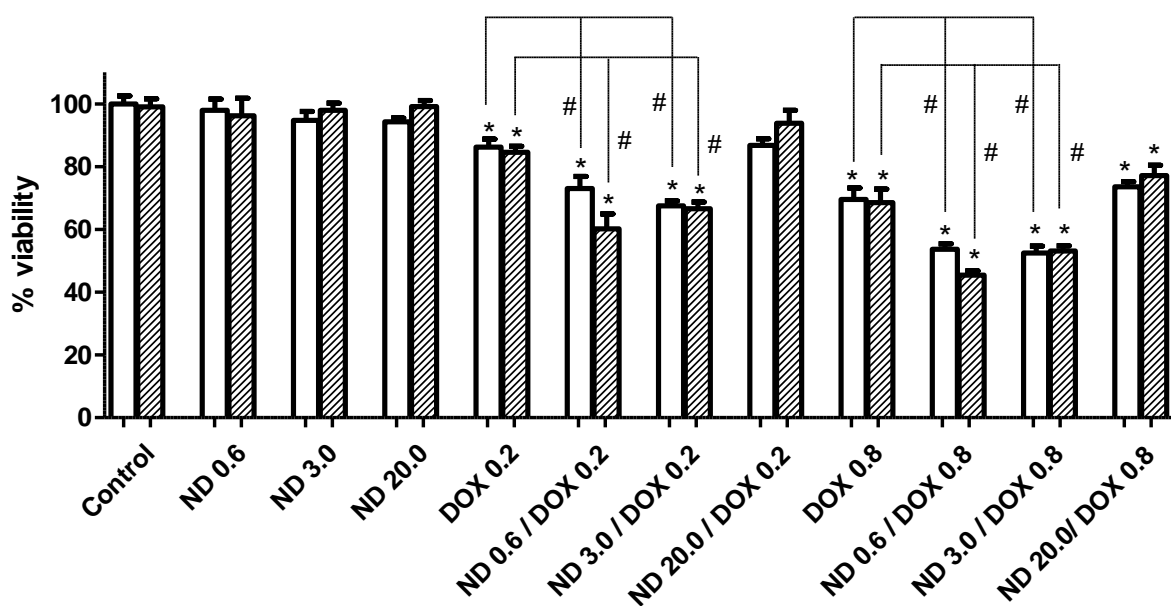


**Figure S7.** Quantitative distribution percentages of cell cycle phases for (a) Caco-2 and (b) MCF-7, after treatment with carbon nanomaterials at 3 µg·mL<sup>-1</sup> for 72 h. Control represents untreated cells. ( □ G1, ▨ S, ▤ G2).

(a)



(b)



**Figure S8.** Cell viability assays for Caco-2 cells after 24 h (white) and 72 h (striped) of incubation with ND at 0.6, 3.0 and 20.0  $\mu\text{g}\cdot\text{mL}^{-1}$ , free drugs (a) CPT and (b) DOX, at 0.2 and 0.8  $\mu\text{g}\cdot\text{mL}^{-1}$ , and (a) CPT- and (b) DOX- loaded carbon nanomaterials. (\* and # represent significance at  $p < 0.05$  when compared to untreated control cells and free drug-treated cells, respectively).