

# The Synergic Action of 5-fluorouracil and Caffeic Acid Loaded on Carbon Nanotubes as a Strategy for Breast Cancer Treatment <sup>†</sup>

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**Abstract:** Single-walled carbon nanotubes (SWCNT) are smart nanocarriers of different pharmacological compounds that can be used as future therapeutic strategies for breast cancer. In this context, the aim of this research was the investigation of the anticancer efficiency of SWCNT conjugated with caffeic acid (CA) and 5-fluorouracil (5-FU) on breast cancer cells. MCF7 cells were exposed to SWCNT-NH<sub>2</sub>\_CA, SWCNT-NH<sub>2</sub>\_5-FU, and SWCNT-NH<sub>2</sub>\_CA\_5-FU nanoconjugates. Various doses of CA (0.71 - 11.43 μg/mL) and 5-FU (0.5 - 8 μg/mL) were tested. Untreated cells and those exposed to free drugs were used as control. After 24 and 48 h of treatment, the cellular viability and morphology, membrane integrity, and oxidative stress were evaluated. The results revealed a decrease of cellular viability in a time-dependent manner in the presence of SWCNT-NH<sub>2</sub>\_CA\_5-FU, the highest decrease (by 72.25% relative to untreated cells) being registered after the treatment with 11.43 μg/mL CA and 8 μg/mL 5-FU for 48 h. In the same condition and after the treatment with SWCNT-NH<sub>2</sub>\_5-FU (8 μg/mL 5-FU), LDH activity reached the most elevated level. Also, a reduction of cellular density and an altered cellular morphology were observed. Induction of oxidative stress was highlighted by the high level of ROS produced in the presence of SWCNT-NH<sub>2</sub>\_5-FU and SWCNT-NH<sub>2</sub>\_CA\_5-FU after 48 h. In correlation, the GSH concentration decreased by 67.54% and 31.61% after the incubation with the highest doses of SWCNT-NH<sub>2</sub>\_5-FU, respectively SWCNT-NH<sub>2</sub>\_CA\_5-FU. In conclusion, the results revealed a synergic action of CA and 5-FU in MCF7 cells demonstrated by the high cytotoxicity of SWCNT-NH<sub>2</sub>\_CA\_5-FU.

**Keywords:** breast cancer; caffeic acid; 5-fluorouracil; single-walled carbon nanotubes.

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## **Conflicts of Interest**

The authors declare no conflict of interest.