A NEW COPPER(II) COMPLEX-LOADED EUDRAGIT® NANOPARTICLES AGAINST TRIPLE-NEGATIVE BREAST CANCER CELLS

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Introduction

- Drug delivery systems offer significant benefits in cancer treatment by enhancing the delivery of therapeutics, reducing side effects and improving drug efficacy and bioavailability at tumor sites [1].
- Eudragit polymers are widely used in drug delivery systems due to their versatility in controlling the release profile of drugs, offering protection to active compounds, and enhancing targeted delivery to specific areas of the body [2].
- Previously, we have synthesized and reported a novel copper(II)-hydrazone complex ([Cu(N-N-Fur)(NO_3)H_2O], CuL1) that exhibited anticancer activity on MG-63 osteosarcoma cells [3].
- Our aim was to evaluate CuL1-loaded Eudragit® nanoparticles for the treatment of triple-negative breast cancer.

Methods

- The nanoparticles containing Eudragit® E100 and S100 loaded with CuL1 (ES-CuL1) were synthesized by nanoprecipitation technique followed by ultrasonication.
- Cell viability, apoptosis and clonogenic assays against MDA-MB-231, 4T1, and Hs 578T triple-negative breast cancer (TNBC) cells were carried out.

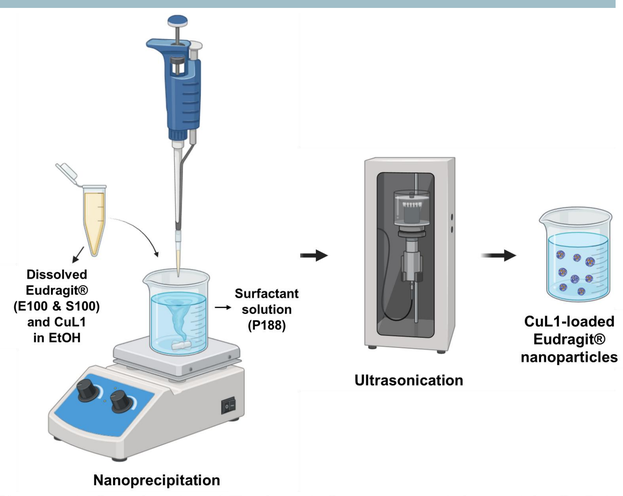

Figure 1. Synthesis of Eudragit® nanoparticles with CuL1.

Results

- The nanoformulation showed an encapsulation efficiency higher than 90%, with nanoparticles ranging from 253 nm (ES) to 342 nm (ES-CuL1).

- ES-CuL1 induced a significantly higher cytotoxicity in MDA-MB-231, 4T1, and Hs 578T TNBC cells compared to free CuL1 at 0.75 μM (**4T1**: 67 ± 10% ES-CuL1 vs. 94 ± 4% CuL1; **Hs 578T**: 84 ± 5% vs. 109 ± 6%, p<0.05) and at 2 μM in **MDA-MB-231**: 41 ± 6% vs. 60 ± 3%).

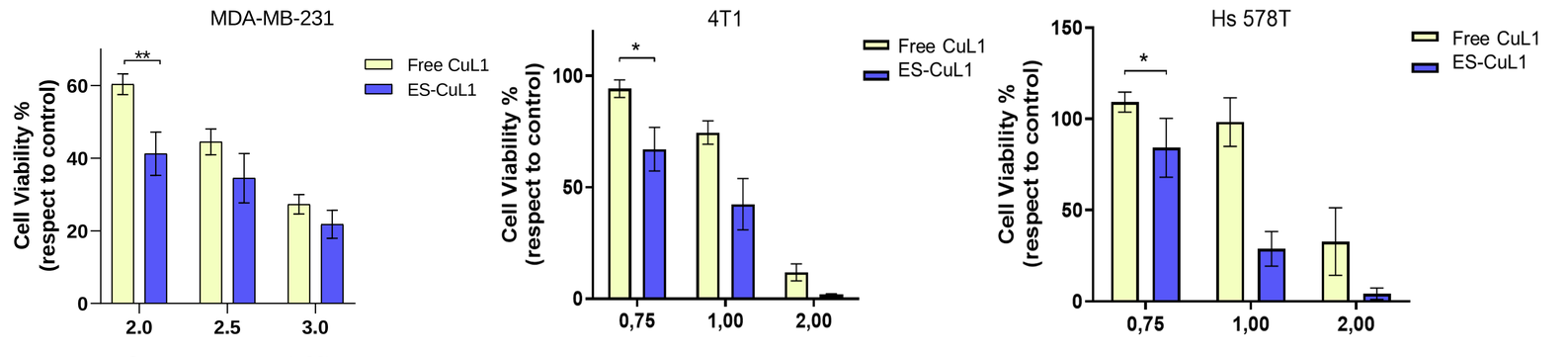

Figure 2. Cell cytotoxicity of the free CuL1 and ES-CuL1 against the MDA-MD-231, 4T1, and Hs 578T cell lines for 24 h. (*p<0.05; **p=0.0033).

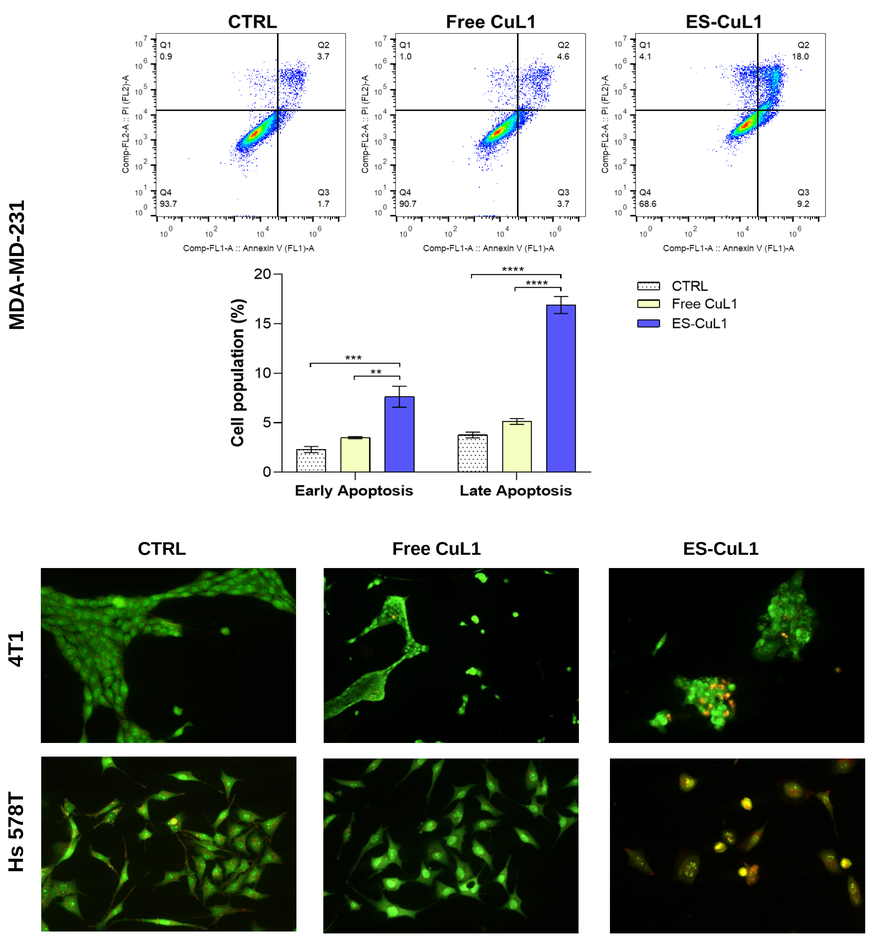

Figure 3. Apoptosis effect of the free CuL1 and ES-CuL1. (**p=0.001; ***p=0.0001; ****p<0.0001).

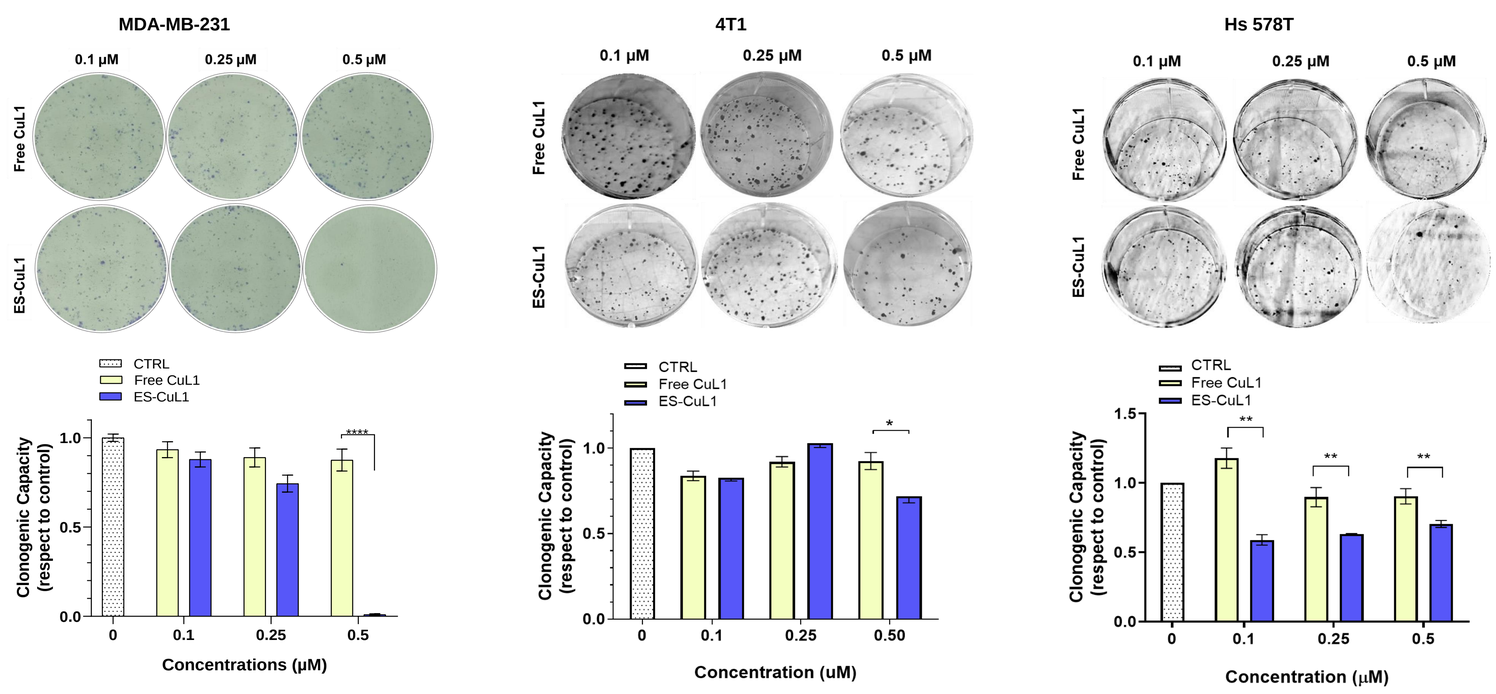

Figure 4. Clonogenic assay. (*p<0.05; **p<0.01; ****p<0.0001).

- ES-CuL1 increased the number of apoptotic cells compared to free compound, in every cell line.
- A significant decrease in cell clonogenic capacity with ES-CuL1 was observed compared to free CuL1, at 0.5 μM in MDA-MB-231, 4T1 and Hs 578T cells (**MDA-MB-231**: 0.01 ± 0 ES-CuL1 vs. 0.87 ± 0.06 CuL1; **4T1**: 0.72 ± 0.07 vs. 0.93 ± 0.08; **Hs 578T**: 0.90 ± 0.06 vs 70.4 ± 0.03, p<0.05).

Conclusions

- ES-CuL1 significantly increased the cytotoxicity against TNBC cells compared to the free CuL1 complex, suggesting that the nanoformulation improves the efficacy of the free complex.
- Treatment with ES-CuL1 induced a higher rate of apoptosis and substantially reduced the clonogenic capacity of TNBC cells, indicating that the nanoformulation may effectively suppress tumor cell proliferation and survival.

References

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