A Promising Approach for Hard-to-Treat Breast Cancer: Photodynamic Therapy with ClAlPc Nanoemulsion Against Triple-Negative Cells

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Abstract

Triple-negative breast cancer is a highly aggressive subtype with the poorest prognosis among breast cancers. Around 20% of the annual breast cancer cases are triple-negative. Photodynamic therapy is a promising, minimally invasive technique already employed in Brazil's public health system (SUS) for the treatment of basal cell carcinoma. It relies on the activation of a photosensitizer (PS) by a specific light source, leading to the generation of reactive oxygen species (ROS) that trigger oxidative stress, cell death, and immune response activation. This *in vitro* study assessed the cytotoxicity of photodynamic therapy using a nanoemulsion containing chloroaluminum phthalocyanine (ClAlPc/Ne) in breast cancer cell lines exposed to varying PS concentrations and light doses.

Introduction

Triple-negative breast cancer is a highly aggressive subtype with the poorest prognosis among breast cancers. It is defined by the absence of estrogen (ER), progesterone (PR), and human epidermal growth factor receptor 2 (HER2), limiting the effectiveness of conventional hormone-based therapies. Around 20% of the 2.3 million annual breast cancer cases are triple-negative, and this subtype is linked to high metastasis and mortality rates. Its molecular heterogeneity and therapeutic resistance highlight the urgent need for alternative treatment strategies. Photodynamic therapy is a promising, minimally invasive technique already employed in Brazil's public health system (SUS) for the treatment of basal cell carcinoma. It relies on the activation of a photosensitizer (PS) by a specific light source, leading to the generation of reactive oxygen species (ROS) that trigger oxidative stress, cell death, and immune response activation. This in vitro study assessed the cytotoxicity of photodynamic therapy using a nanoemulsion containing chloroaluminum phthalocyanine (ClAlPc/Ne) in breast cancer MCF-7 and MDA-MB-231 cell lines, representing luminal A and triple-negative breast cancer, respectively, exposed to varying PS concentrations and light doses.

Methods and Materials

The cell lines, were incubated with ClAlPc/Ne for 24 hours before photoactivation, followed by a further 24-hour incubation before metabolic viability analysis using the MTT assay. Three experimental conditions were tested: (I) nanoemulsion without PS, (II) ClAlPc/Ne without irradiation, and (III) photoactivated ClAlPc/Ne. PS concentrations ranged from 0.01 µM to 2.0 µM, with light doses from 1 J/cm² to 16 J/cm². Absorbance was measured at 545nm.

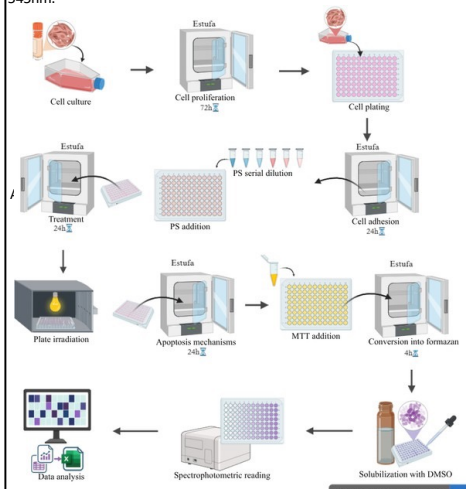


Figure 1. Description of phototoxicity analysis by PDT using the MTT assay. Source: Author (2025)

Results

The results showed selective phototoxicity of ClAlPc/Ne against the triple-negative breast cancer cell line MDA-MB-231, with IC_{50} (50% inhibitory concentration) values of 1.96 µM at 1 J/cm², 0.19 µM at 4 J/cm², and <0.01 µM at 16 J/cm². In contrast, MCF-7 cells demonstrated greater resistance, with IC_{50} values of >2.0 µM at 1 J/cm², 0.14 µM at 4 J/cm², and <0.06 µM at 16 J/cm².

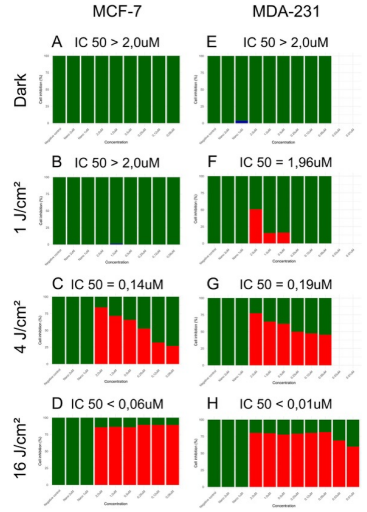


Figure 2. Dose-response curves of the compound (ClAlPc-NE) against the tested cells. Source: Author (2025).

Discussion

The results obtained in this study enabled the evaluation of the response to Photodynamic Therapy (PDT) mediated by Chloroaluminum Phthalocyanine Nanoemulsion (ClAlPc-NE) in breast cancer cell lines (MDA-MB-231 and MCF-7). These findings highlight the potential of this approach as a minimally invasive therapeutic alternative for breast cancer, particularly as this is the first study to demonstrate the efficacy of ClAlPc-NE on the triple-negative breast cancer cell line (MDA-MB-231).

The low IC_{50} value obtained for the MDA-MB-231 line (<0.01 µM) demonstrates the high phototoxicity of ClAlPc-NE. This value is significantly lower than that reported by Wang et al. (2020), who used the standard chemotherapeutic agent doxorubicin—a first-line drug for breast cancer—showing an IC_{50} against the same cell line in the range of 2.8 µM. Therefore, the value obtained for ClAlPc-NE is approximately *280 times lower*, indicating greater cytotoxic potency at much lower concentrations.

In summary, the results obtained in this study with MDA-MB-231 and MCF-7 cell lines align with a robust scientific framework that validates ClAlPc-NE as a potent phototoxic agent (Muehlmann et al., 2015), capable of inducing apoptosis via mitochondrial and endoplasmic reticulum (ER) pathways (Castilho-Fernandes et al., 2017), and demonstrating potential for combination with chemotherapeutic agents to achieve maximum efficacy (Candido et al., 2018; Cabral et al., 2021; Franchi et al., 2016).

Conclusions

These findings indicate that phototoxicity is dose-dependent and more pronounced in triple-negative breast cancer cells. The differential response between cell lines suggests that triple-negative breast cancer may be more sensitive to oxidative stress induced by photodynamic therapy. These findings reinforce the importance of molecular profiling in guiding treatment decisions and support the potential of photodynamic therapy as a targeted, less invasive approach for hard-to-treat breast cancer subtypes.

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