Scientific Letters

Poster Communication 34

Antitumor and antimitotic activity of aminochalcones in human cancer cells with differential P-glycoprotein expression

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Abstract

Background: Cancer remains a leading cause of mortality, with drug resistance, particularly mediated by P-glycoprotein (P-gp), limiting therapeutic efficacy [1]. Chalcones have emerged as promising anticancer agents due to their ability to inhibit tubulin polymerization and disrupt microtubule dynamics [2]. In this context, dual-targeting strategies combining antimitotic activity with P-gp inhibition, including chalcone-based derivatives, have recently been reported as a means to overcome multidrug resistance [3]. **Objective:** This study aimed to evaluate the antitumor and antimitotic activity of eight aminochalcone derivatives in human cancer cell lines of diverse origins: melanoma (A375-C5), breast adenocarcinoma (MCF-7), non-small cell lung carcinoma (NCI-H460), ovarian carcinoma with dual resistance to paclitaxel and carboplatin (OVCAR8 PTX/CBP-R), and colon adenocarcinoma (HCT-15), each exhibiting different levels of P-glycoprotein expression, with HCT-15 as a well-established model for multidrug resistance studies. **Methods:** The antitumor activity of all compounds was assessed in five cancer cell lines using the sulforhodamine B assay to determine the GI_{50} values at 48 h (defined as the concentration required to inhibit 50% of cell growth), with doxorubicin as a control. Selectivity indices were calculated using the non-cancerous breast MCF10A cell line. Antimitotic activity was evaluated by phase-contrast microscopy and DAPI staining. **Results:** Seven of the eight compounds demonstrated potent cytotoxic activity across all tested cancer cell lines. The strongest selectivity was observed in HCT-15 cells, which highly express P-gp. All compounds exhibited antimitotic activity, although the extent varied among derivatives. **Conclusions:** These findings support the potential of aminochalcone derivatives as antimitotic and anticancer agents, particularly for targeting P-gp-mediated drug-resistant cancer cells.

Keywords: antitumor activity; antimitotic potential; aminochalcones; human cancer cell lines; Pgp-resistant cells

Acknowledgments/Funding

This research was funded by national funds through FCT - Fundação para a Ciência e a Tecnologia, I.P., and by the European Commission's Recovery and Resilience Facility, within the scope of UID/04423/2025 (https://doi.org/10.54499/UID/04423/2025), UID/PRR/04423/2025 (https://doi.org/10.54499/UID/PRR/04423/2025), and LA/P/0101/2020 (https://doi.org/10.54499/LA/P/0101/2020). This research was also funded by the CESPU - Cooperativa de Ensino Superior Politécnico e Universitário Crl, under the grants "FlavScreen_GI2-CESPU-2023", "FlavCanAct-GI2-CESPU-2025", and "TargetMito-GI2-CESPU-2025".

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