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Poster 56

Chalcone Derivatives with Potential Antimitotic Activity

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Abstract

Background: Cancer remains one of the leading causes of mortality worldwide, with incidence rates rising in recent years [1]. Among various therapeutic strategies, microtubule-targeting agents have demonstrated significant efficacy in cancer treatment. However, their clinical application is often limited by high toxicity and tumor resistance [2]. Therefore, the discovery of novel small molecules with antitumor activity and improved efficacy is crucial. Several studies have shown that the presence of a 3,4,5-trimethoxyphenyl fragment is a key structural feature for interacting with tubulin, a microtubule subunit protein essential for mitotic spindle formation, and consequently for cell division and proliferation [3]. In this study, 16 chalcone derivatives (compounds 1–16) were synthesized, and their *in vitro* cytotoxic activity was evaluated in different cancer cell lines. **Objectives:** This study aimed to assess the antitumor and antimitotic activity of 16 chalcone derivatives and investigate the cellular mechanism of action of the most promising compounds. **Methods:** The chalcone derivatives were synthesized through Claisen-Schmidt condensation. Their cytotoxic activity was evaluated using the sulforhodamine B (SRB) assay to determine the GI_{50} in cancer cell lines, including melanoma (A375-C5), breast adenocarcinoma (MCF-7), and non-small cell lung cancer (NCI-H460). Antimitotic activity was assessed by indirect immunofluorescence, analyzing DNA (stained with DAPI) and spindle morphology (through microtubule labeling with an anti-α-tubulin antibody). Additionally, Annexin V/PI double staining followed by flow cytometry was performed to assess apoptotic cell death induction. **Results:** Among the 16 studied compounds, 4 exhibited promising antitumor activity (GI_{50} < 10 µM) and were selected for further mechanistic characterization. These 4 compounds displayed potent growth-inhibitory activity and disrupted microtubule dynamics during mitosis, leading to spindle assembly defects. This instability resulted in prolonged mitotic arrest, ultimately triggering apoptosis. **Conclusions:** The studied chalcone derivatives demonstrated promising potential as antitumor and antimitotic agents, impairing cell division and promoting cancer cell death. These findings support their potential for further development in cancer therapy.

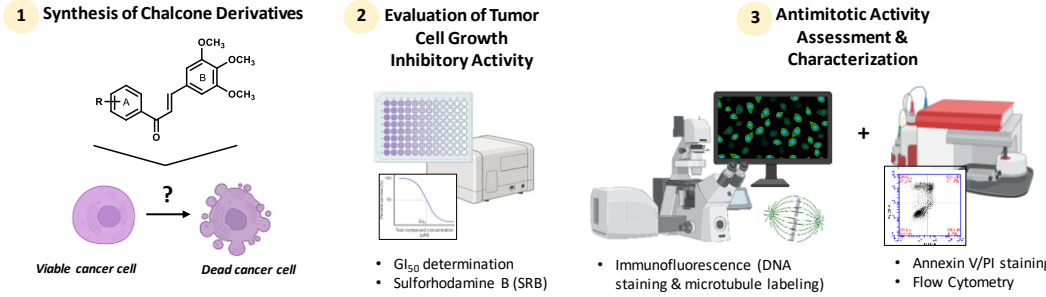

Figure 1. Graphical representation of the approach used to evaluate the potential of chalcone derivatives as antitumor and antimitotic agents.

Keywords: chalcone derivatives; anticancer; antimitotics

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