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The Cancer Control Challenge:
Better Understanding It to Better Face It

EVALUATION OF THE CYTOTOXIC POTENTIAL OF AN AZACHALCONE DERIVATIVE COMPARED TO 5-FLUOROURACIL IN A GASTRIC CANCER CELL MODEL

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Introduction: Gastric Cancer is a malignant neoplasm that originates from epithelial cells of the gastrointestinal tract, being adenocarcinoma its most prevalent histological form. In the 2023-2025 triennium, approximately 21 thousand new cases per year are estimated to occur in Brazil, reflecting its major relevance in public health. Conventional treatments for this neoplasm include chemotherapy, such as 5-Fluorouracil (5-FU); however, this approach may be associated with significant adverse effects, namely nephrotoxicity, neurotoxicity, and acute mucositis. In light of this scenario, the development of new, safer, and more efficient therapeutic strategies is essential. In this context, natural products are emerging as prominent alternatives, especially those derived from azachalcones – a class of compounds that present high antioxidant, anti-inflammatory, and antiproliferative potential. Among them, (E)-3-(2-methoxyphenyl)-1-(pyridin-3-yl) prop-2-en-1-one (JA-03) is considered a promising candidate for antineoplastic therapy. **Objectives:** This study aimed to evaluate and compare the cytotoxicity and selectivity of 5-FU and JA-03 in a gastric cancer cell model. **Methods:** For this purpose, AGP01 cells (Metastatic Human Gastric Adenocarcinoma) and HEK-293 cells (Non-neoplastic Human Embryonic Kidney) were subjected to the MTT cell viability assay following 72-hour treatment with concentrations of 80 µM, 40µM, 20µM, 10 µM, 5 µM, 2.5 µM and 1.25 µM for 5-FU, and 150 µg/mL, 75 µg/mL, 37.5 µg/mL, 18.8 µg/mL, 9.4 µg/mL and 4.7 µg/mL for JA-03. For data analysis, a dose-response sigmoid equation using nonlinear regression was applied to determine the mean inhibitory concentration (IC50), using GraphPad Prism v9 software. Additionally, group comparisons were performed using one-way ANOVA followed by Bonferroni correction, with the significance level set at 95% ($p<0.05$). Finally, the selectivity indexes (IS) for each treatment were calculated. **Results:** Our results indicated that JA-03 exhibited an IC50 of 66.8 µg/mL for HEK-293 and 13.1 µg/mL for AGP01, while 5-FU showed an IC50 of 7.4 µM for HEK-293 and 5 µM for AGP01. From this perspective, the IS values were 5.09 and 2.17 for JA-03 and 5-FU, respectively, demonstrating that both treatments displayed high toxicity and selectivity when compared. **Conclusion:** In face of the obtained results, it is suggested that JA-03 shows promising pharmacological potential for the treatment of gastric cancer, as it

reduced cell viability in a selective manner, displaying greater toxicity toward tumor cells than non-tumor cells. Yet, further studies are needed to deepen the understanding about its mechanisms of action, safety and efficacy.

Keywords: Gastric Cancer; Azachalcone derivative; Treatment.