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Antitumor potential of GSK343 in breast cancer cells: an in vitro study

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Introduction: Breast cancer is a heterogeneous and multifactorial disease, requiring specific therapeutic approaches for each subtype. Among promising molecular targets is EZH2, a methyltransferase associated with tumor progression and poor prognosis. **Objective:** This study aimed to investigate the cytotoxic and antiproliferative potential of the selective enhancer of zeste homolog 2 (EZH2) inhibitor, GSK343, in breast cancer cell lines MDA-MB-231 (triple-negative) and BT-474 (luminal B/ human epidermal growth factor receptor-type 2-positive [HER2+]), treated with different concentrations of GSK343. **Methods:** Cells were cultured in appropriate medium (37°C, 5% CO_2) and treated with GSK343 at established concentrations (1, 5, 15, 30, and 60 µM). Assays were performed after 24, 48, and 72 hours of exposure. Cell viability was assessed using the MTT assay, while apoptosis was quantified using a deoxyribonucleic acid (DNA) fragmentation assay kit. Statistical methods included the use of analysis of variance (ANOVA), followed by Tukey's post hoc test, with significance set at $p<0.05$. **Results:** Cytotoxicity assays showed a dose- and time-dependent effect of GSK343 in both cell lines. In MDA-MB-231, a significant reduction in cell viability was observed from 15 µM at 48 hours ($p<0.01$), which intensified at 72 hours, with a marked increase in apoptotic cells at 30 and 60 µM ($p<0.001$). In BT-474, the effect was more modest at lower doses but still showed a significant reduction in proliferation and induction of apoptosis at concentrations above 30 µM after 72 hours ($p<0.05$). **Conclusion:** The GSK343 inhibitor can exert significant cytotoxic and antiproliferative effects, particularly on MDA-MB-231 cells, suggesting greater sensitivity of the triple-negative subtype to EZH2 inhibition. These findings indicate the therapeutic potential of GSK343 as an epigenetic agent in aggressive breast cancers and reinforce the need for further studies for clinical validation.

Keywords: breast neoplasms; genomic instability; apoptosis.