

## DNA cleavage and anti-proliferative activity of COX-2 inhibitor derivatives on human breast adenocarcinoma and chronic myeloid leukemia cells

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**Background and Aims:** Celecoxib, a specific cyclooxygenase-2 (COX-2) inhibitor, has been shown to possess antitumor activity in a variety of cancer cells. However, the antitumor activity of celecoxib derivatives as specific COX-2 inhibitors in chronic myeloid leukemia (CML) and breast cancer has not been well established. This study was designed to investigate the effect of COX-2 inhibitor derivatives on growth and cell cycle arrest in human leukemia and breast cancer cell lines (K562 and MCF7 cells).

**Methods:** The DNA cleavage experiments were performed by agarose gel electrophoresis. pEGFP-N1 DNA was treated with two compounds at various concentrations. Then, bands visualized by UV light and photographed to determine the extent of cleavage of the supercoiled (SC) to Nicked (NC) DNA. Human breast adenocarcinoma (MCF7) and chronic myeloid leukemia cell lines (K562) routinely cultured. Cell cytotoxicity was determined by MTT assay and flow cytometry performed to analyze the cell cycle distribution.

**Results:** The results obtained from DNA cleavage assay demonstrated that with increasing concentration of compounds 1 and 2, SC DNA is gradually converted to NC DNA. Cells were exposed to various concentrations (0.1-100  $\mu$ M) of each compound for 24 h. All compounds demonstrated remarkable cytotoxic effect on MCF-7 and K562 cell lines in a concentration-dependent manner with IC<sub>50</sub> values ranging between 6.5–22.23  $\mu$ M. Treatment of these cells with these compounds significantly cause arrest of the cell cycle.

**Conclusions:** Collectively, our data indicate that these derivatives of celecoxib may present promising chemotherapeutic agents, possibly targeting DNA and inducing cell death in the selected cancer cell line which needs further research.

**Keywords:** Celecoxib; Cancer; Cytotoxicity; DNA cleavage