Cytotoxic activity of new 4-thiazolidinone derivatives in MDA-MB-231 breast cancer cells.

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Cancer remains a significant healthcare problem worldwide. World Health Organization estimates that it represents the first or second cause of death for people under 70 years of age in 2019. Conventional chemotherapy still faces insufficient selectivity or a narrow therapeutic index. Due to their broad biological activities, 4-thiazolidinones are promising compounds in modern cancer therapy.

The aim of this study was to synthesize and evaluate the biological activity of the new 4-thiazolidinone derivatives (compound 3.4 and compound 3.10) in MDA-MB-231 breast cancer cells. MTT assay was used to assess cell viability. Apoptosis induction assay was performed by Annexin V/Propidium iodide staining. Mitochondrial membrane potential ($\Delta\Psi m$) was tested by cytometric analysis using JC-1 dye. MDA-MB-231 breast cancer cells were incubated with the tested compounds and doxorubicin as a reference compound for 24 hours.

The new 4-thiazolidinone compounds exhibited a significant cytotoxic activity, with IC_{50} values of 7.45 μM for the compound 3.4, and 5.90 μM for the compound 3.10 in MDA-MB-231 breast cancer cells. Annexin V/Propidium iodide staining allowed for the differentiation of live cells, necrotic cells, early apoptotic cells, and late apoptotic cells in MDA-MB-231 breast cancer cells. In the case of the compound 3.4: 13.2% (5 μM) and 40.6% (10 μM) of apoptotic cells (the sum of early and late apoptosis) were detected, whereas in the case of the compound 3.10: 11.7% (5 μM) and 28.2% (10 μM). The number of apoptotic cells for the control was 8.9%. To investigate the effect of the tested compounds on mitochondrial membrane potential ($\Delta\Psi m$), MDA-MB-231 cells were treated with **3.4** and **3.10** at different concentrations (5 μM and 10 μM) for 24 h. In untreated cells (control group), the percentage of cells with depolarized mitochondria was 5.7%. A lower concentration (5 μM) of **3.4** and **3.10** has led to a decrease of $\Delta\Psi m$ in the tested breast cancer line – it was 18.4% (**3.4**) and 15.7% (**3.10**) of the cell population. Meanwhile, the concentration of 10 μM of the tested compounds increased this percentage over 3-fold (57.9%) in the case of **3.4** and over 2-fold (37.3%) in the case of **3.10** cells compared to the control group in MDA-MB-231 breast

cancer cells. The novel 4-thiazolidinone compounds represents promising multi-targeted potential in breast cancer, but further in vivo examinations are needed to confirm the claim.

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