Activation of caspases by novel thiazolidinone derivatives in MDA-MB-231 breast cancer cells

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Cancer is still a major healthcare issue in the world. Traditional chemotherapy still struggles with a limited therapeutic index or insufficient selectivity. One of the novel pathways in the search for new anticancer drugs is the synthesis of thiazolidinone derivatives. It is important to point out that thiazolidinone derivatives, form a class of chemicals that can serve as the foundation for the development of novel lead compounds because they exhibit a wide range of biological activities and offer significant potential for further chemical modifications.

Previous experiments revealed promising cytotoxic activity of two novel thiazolidinone derivatives (compound 3.4 and compound 3.10) in breast cancer cells. Therefore, additional tests were conducted to confirm the involvement of caspases in the mechanism of cell death induced by these compounds.

It was observed that the tested compounds increased the amount of caspase 8 active form in MDA-MB-231 cells. There were 26.5% (3.4) and 19.5% of (3.10) (both 5 μM) cells with active caspase 8, respectively. At the higher concentration (10μM) of the tested compounds: 68.5% (3.4) and 62.7% (3.10), respectively. The 24h incubation with 3.4 and 3.10 induced a number of cells with active caspase 9 compared to the control cells. In the presence of the compound 3.4, there were 20.2% (5μM) and 33.8% (10 μM) cells with active caspase 9. In the presence of the compound 3.10, there were 15.0% (5μM) and 32.6% (10μM) cells with active caspase 9. Additionally, changes in caspase 3/7 activity were observed when the compounds were added to MDA-MB-231cells. Following the compound 3.4 treatment, caspase 3/7 activation was observed in 11.6% (5μM) and 30.3% (10μM) of MDA-MB-231 cell populations, respectively, while the compound 3.10 treatment resulted in an increase in the active form of caspase 3/7 to 10.6% (5μM) and 20.6% (10 μM). Based on the obtained results, it can be concluded that the anticancer effect of the compounds 3.4 and 3.10 in MDA-MB-231 cells is related to the activation of apoptosis by both the intrinsic and extrinsic pathways through the activation of a number of caspases.

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