

## INDUCTION OF APOPTOSIS IN HUMAN GLIOBLASTOMA CELLS BY THE FLAVONOID RUTIN

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In our previous study, rutin demonstrated antiproliferative effect on GL-15 glioblastoma cells. In this study we investigated whether rutin exerted its inhibitory effect on GL-15 cells by inducing apoptosis or necrosis. Cells (100,000 cells/plate) were grown in supplemented DMEM medium and treated with rutin (100 $\mu$ M) for 24-72h. Negative controls were treated with 0.5% DMSO. Annexin V-FITC/Propidium Iodine staining and flow cytometry, revealed that after 24h treatment, 87.4% of GL-15 cells exposed to rutin were annexin V-positive. On the other hand rutin did not modify the proportion of Propidium Iodine stained necrotic cells compared with control. Moreover, nuclear condensation and fragmentation were observed by Hoechst staining in about 30% of cells after 72h exposure to rutin. DNA integrity and single-strand breaks, monitored using single cell gel electrophoresis (comet assay), revealed that the frequency of comets in the negative control was 5.4 $\pm$ 0.9% after 24h, and 28.0 $\pm$ 5.7% after 72h treatment. Exposure to rutin induced DNA breaks in GL-15 cells since 24h exposure and the frequency of comets ranged from 22.0 $\pm$ 8.5% to 52.0 $\pm$ 11.3% after 24-72h treatment, respectively. Taken together, these results demonstrated that the growth inhibitory effect on GL-15 glioblastoma cells of rutin is related to apoptosis. Supported by FAPESB and CNPq.