MECHANISM OF VIOLACEIN-LOADED NANOPARTICLES TRIGGER APOPTOSIS ON LEUKEMIA CELLS

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Violacein, a pigment isolated from *Chromobacterium violaceum*, presents antileukemia activity. The aim of this study was to investigate the molecular mechanism mediating this activity concerning mainly the induction of cell death by apoptosis on HL60 leukemia cells. Thus, nanoparticles of poly (*D,L*-lactide-*co*-glycolide) (50:50 PLGA) containing violacein were prepared by the modified emulsification-solvent evaporation method. Violacein-loaded PLGA nanoparticles have a similar inhibitory effect evaluated by trypan blue assay when compared to free form. Flow cytometric analysis after treatment for 12 h showed that violacein-loaded PLGA induced apoptosis, with maximum cell death at a concentration of 2 µM. Violacein and violacein/PLGA induced opposite changes in the mitochondrial swelling indicating altered mitochondrial function. The mitochondrial activity evaluated by flow cytometry after JC1 labeling displayed a basal hypopolarised status of the mitochondrial in treated cells. Moreover it was obtained an increase of cytochrome c release around 4-fold after both treatments of the HL60 cells. Based on alterations in phospholipid asymmetry, in the $\Delta\psi$ mitochondrial and in the bcl-2 levels, violacein (free and in nanoparticles) was found to trigger cell death by apoptosis in HL60 cells through cytochrome c release and apoptosome formation.

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