Palladacycles Induce Apoptosis in Hepatoma Cells

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A recent study showed that palladacycles compounds (PdC) obtained from the reaction of *N,N*-dimethyl-1-phenethylamine (dmpa) with the 1 or 2-ethanebis(diphenylphosphine) (dppe) were able to induce mitochondrial permeabilization in isolated rat liver mitochondria due to cross-linkage of vicinal thiols present in the mitochondrial membrane proteins with formation of disulfide bonds (SANTANA et al., 2009). Since PdC-induced MPT was followed by cytochrome *c* release in isolated rat liver mitochondria, in this work, we studied the cell death induced by PdC in HTC cells. Our results showed that PdC induced a decrease of cell viability assessed by MTT reduction test after 24 h incubation in a a concentration-dependent manner, with the IC_{50} value of approximately 7.5 µM. Flow cytometry analysis using the annexin V-FITC/propidium iodide double-staining revealed that PdC induces predominantly apoptotic cell death in HTC cells at extremely low concentration (2.5 µM). In addition, PdC induced the dissipation of the mitochondrial transmembrane potential and decreased significantly the content of reduced thiol groups and the pre-incubation of the cells with DTT inhibited partially this effect. These results suggested that mitochondrial permeabilization due to thiol oxidation was involved with the pro-apoptotic activity exhibited by PdC in HTC cells. Keywords: Hepatoma cells, palladacycles, apoptosis, mitochondrial permeabilization, thiol oxidation. Supported by CAPES, FAPESP, CNPQ and FAEP-UMC.