Induction of cell cycle arrest and apoptosis by copper complex $Cu(SBCM)_2$ towards oestrogen-receptor positive MCF-7 breast cancer cells

ABSTRACT

Copper complexes have the potential to be developed as targeted therapy for cancer because cancer cells take up larger amounts of copper than normal cells. Copper complex Cu(SBCM)2 has been reported to induce cell cycle arrest and apoptosis towards triple-negative breast cancer cells. Nevertheless, its effect towards other breast cancer subtypes has not been explored. Therefore, the present study was conducted to investigate the effect of $Cu(SBCM)_2$ towards oestrogen-receptor positive MCF-7 breast cancer cells. Growth inhibition of $Cu(SBCM)_2$ towards MCF-7 and human non-cancerous MCF-10A breast cells was determined by MTT assay. Morphological changes of Cu(SBCM)2-treated-MCF-7 cells were observed under an inverted microscope. Annexin V/PI apoptosis assay and cell cycle analysis were evaluated by flow cytometry. The expression of wild-type p53 protein was evaluated by Western blot analysis. The intracellular ROS levels of MCF-7 treated with $Cu(SBCM)_2$ were detected using DCFH-DA under a fluorescence microscope. The cells were then co-treated with $Cu(SBCM)_2$ and antioxidants to evaluate the involvement of ROS in the cytotoxicity of Cu(SBCM)2. Docking studies of Cu(SBCM)2 with DNA, DNA topoisomerase I, and human ribonucleotide reductase were also performed. The growth of MCF-7 cells was inhibited by Cu(SBCM)2 in a dose-dependent manner with less toxicity towards MCF-10A cells. It was found that $Cu(SBCM)_2$ induced G2/M cell cycle arrest and apoptosis in MCF-7 cells, possibly via a p53 pathway. Induction of intracellular ROS was not detected in MCF-7 cells. Interestingly, antioxidants enhance the cytotoxicity of Cu(SBCM)2 towards MCF-7 cells. DNA topoisomerase I may be the most likely target that accounts for the cytotoxicity of $Cu(SBCM)_2$.