Antitumoral Effect of Chalcone-derived Thiosemicarbazones Metal Complexes

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Introduction: Metallodrugs are commonly used in antitumor therapy and cisplatin is one of the most used drugs in clinics. However the toxicity of platinum drugs is a limiting factor and there is an urgent need for new metal complexes having lower toxicity and similar beneficial effects. We take the advantage of the antitumoral potential of chalcones and thiosemicarbazones in order to produce more potent antineoplastic compounds coordinated with different metals and in this work their cytotoxic activity was evaluated. **Objectives:** The aim of this work was to identify and characterize the antitumoral effect of chalcone-derived thiosemicarbazones metal complexes on malignant human tumors cells of glioblastoma, melanoma and breast adenocarcinoma. **Material and methods:** Lineages of human glioblastoma (T98,U87), human melanoma(UACC), and human breast adenocarcinoma (MCF7) Cells were grown in Dulbecco's Modified Eagle Medium (DMEM) at 37ºC in a humidified atmosphere of 5 % CO2 / 95% air and treated in different concentrations of palladium, platinum and copper metal complexes of chalcone-derived thiosemicarbazones (10^{-10} M - 10^{-4} M).The measure of metabolic viability were made by MTT assay, morphological changes were identified by phase contrast microscopy and acridine Orange/Ethidium Bromide (AO/EB) double staining was used to evaluate the cytotoxic mechanism. **Results and Discussion**: All compounds were highly cytotoxic inducing morphological changes, such as irregularities in the cell membrane, cell shrinkage and blebs formation indicative of cell death. Cytotoxic effects were dose dependent and treated cells presented acidic vacuoles indicative of autophagic vacuoles. Interestingly the copper complex was most potent with IC_{50} at submicromolar range. **Conclusions:** The metal complexes of chalcone-derived thiosemicarbazones proved to be potent cytotoxic agents against all cancer cells evaluated and indicate that the strategy to combine chalcones and thiosemicarbazones may constitute a good approach for the development of novel cancer therapeutic agents.

Key words: thiosemicarbazones, chalcones, cytotoxicity, metal complexes
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