Production and Characterization of Radioactive Antitumor Platinum complexes-derived thiosemicarbazone

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INTRODUCTION. The use of platinum based drugs for cancer therapy has been limited due to development of resistance. An alternative for better therapeutic effect with reduction of the toxic effects is the targeted radionuclide therapy (TR). We have already demonstrated that a radioplatinum analog of cisplatin is more potent against glioblastoma cells than natural cisplatin. In the search for new metallodrugs, platinum complexes of thiosemicarbazones have showed promising results, but their potential for TR has not been evaluated so far. **OBJECTIVES.** The objective was to produce radioactive platinum analogs of platinum complex of N (4)tolyl 2-acetylpyridine thiosemicarbazone and platinum complex of chalcone derived thiosemicarbazone and evaluate their cytotoxic effect against glioblastoma cells. **MATERIAL AND METHODS.** Radioactive analogs of the platinum complexes were produced by irradiation on the Central position of the TRIGA MARK-I IPR-R1 nuclear reactor at the CDTN-CNEN, with a thermal neutronic flux of $4.1x10^{12}$ $n.cm^{-2}.s^{-1}$. Specific activity was determined by gamma spectrometry. Glioblastoma cells (GBM) p53-wild type (U87) and p53-mutant (T98) were cultured in Dulbecco's Modified Eagle Medium supplemented with 10% Fetal Bovine Serum and 1% penicillin. Metabolic viability was measured after treating the cells with the platinum complexes. **RESULTS.** Radioactive platinum complexes derived from thiosemicarbazones were successfully produced with low specific activity. All platinum complexes induced morphological alterations indicative of programmed cell death, as well as cisplatin. Radioplatinum complexes of thiosemicarbazones kept their cytotoxic activities. The observed cytotoxic effects were dose response with fifth inhibitory concentration (IC_{50}) around micromolar range. Radio-Cisplatin and radioplatinum complex of N (4)tolyl 2-acetylpyridine thiosemicarbazone were slightly (~two-fold) more potent than their non-radioactive analogs indicating the potential as a tool for the development of target radionuclide therapy for GBM. **CONCLUSION.** Production of radioactive platinum complexes derived from thiosemicarbazones may constitute a good strategy for the preparation of innovative therapy for malignant GBM.

Key words: Platinum complex of thiosemicarbazone, radionuclide therapy, glioblastoma, neutron activation.
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