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Silver Complexes Derived from Isatin-Thiosemicarbazones: Synthesis, cytotoxicity and initial DNA binding studies

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In recent years, studies using silver complexes have gained visibility due to their significant potential uses as antitumor drugs and nontoxic effects of silver ion in lower doses[2]. The present work aims to evaluate the antiproliferative activity against a panel of normal and tumor cells mediated by complexes of the formula $[AgCl(ITSCHH)(PPh_3)_2]$ (**C1**) and $[AgCl(ITSCEt)(PPh_3)_2]$ (**C2**) (ITSCHH = isatin-thiosemicarbazone, ITSCEt = isatin-3-ethyl-thiosemicarbazone). All the complexes were synthetized based on adaptations of the procedure described by Silva *et al*.[1]. The characterization of silver (I) complexes was performed using elemental analysis, IR and NMR spectroscopy techniques. The results indicate that coordination of isatin-thiosemicarbazones to the metal center occurred through the sulfur atom in a neutral form. Studies of the behavior of complexes in DMSO-d_6 solution using ^{1}H NMR demonstrated that **C1** and **C2** remained intact during 0, 24, and 48 h. The cytotoxic effects of stable compounds in solution were evaluated against breast (MCF-7, SKBr3 and MDA-MB-231), lung (A549) cell lines and against non-tumor cell lines MCR-5 (lung) and MCF-10A (breast) by MTT assay. The complexes exhibited IC_{50} values ranging of 2.99 – 13.69 µM. Particularly, **C1** exhibited appreciable cytotoxic activity against SKBr3 cells (2.992 ± 0.284) while **C2** was more active against A549 (lung) cell line with a value of 7.985 ± 0.987 µM. DNA binding studies by spectroscopic titration and competitive assays with Hoechst 33258 and Thiazole Orange (TO) suggested that the Ag(I) metal complexes interact weakly with ct-DNA possibly through minor groove or by electrostatic forces.

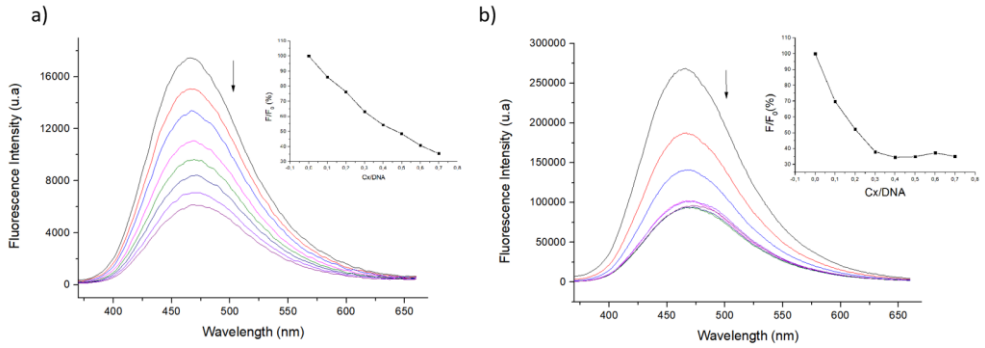

Figure 1. Emission spectra of DNA-Hoechst 33258 adduct in the presence of **C1** (a) and **C2** (b).

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References

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