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SYNTHESIS AND EVALUATION OF THE BIOLOGICAL ACTIVITY OF GOLD(I) COMPOUNDS WITH DITHIOCARBAMATE LIGANDS

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Cancer is one of the most urgent public health challenges in the world, being one of the leading causes of death and consequently a significant obstacle to increasing life expectancy.[1] Gold(I)-based drugs have been widely studied and tested in cancer chemotherapy since the discovery of the antitumor properties of auranofin. However, the toxic side effects and intrinsic or acquired cellular resistance of these gold compounds compromise their efficacy and stimulate the search for analogs with a more favorable side effect profile.[2] This work presents the synthesis and structural characterization of three novel gold(I) complexes, with the general formula [Au(DTC)PPh_3], DTC are ligands derived from dithiocarbamate, aiming to obtain potential antitumor agents. The characterizations were performed through elemental analysis, thermogravimetric analysis, infrared spectroscopy, ^{1}H, ^{13}C, and ^{31}P NMR, mass spectrometry, and single-crystal X-ray diffraction (figure 1).

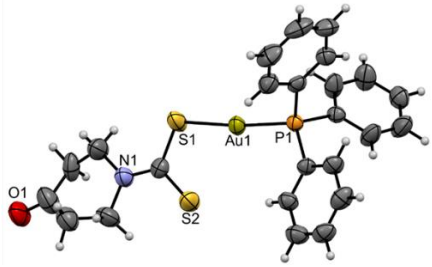

Figure 1 - Figure 1 Crystal structure of the CL3 complex.

The interaction of the synthesized complexes with DNA and BSA was also evaluated through spectrophotometric and fluorimetric assays and agarose gel electrophoresis. The *in vitro* antiproliferative activity of the compounds was evaluated against breast cancer cell lines (MDA-MB-231 and 4T1) and the non-tumoral breast cell line (MCF-10a), demonstrating the potentiation of cytotoxic action after complexation with gold.

All the complexes and their respective ligands showed promising activity. Complexes CL2 and CL3 performed better than CL1, with CL2 standing out by exhibiting excellent activity against the triple-negative MDA-MB-231 cell line with an IC_{50} = 0.69 ± 0.1 µM, and CL3 showing excellent activity against the 4T1 cell line with an IC50 = 0.99 ± 0.01 µM and a significant selectivity index (SI) of 2.7. Therefore, the presented results provide significant contributions to the literature and may aid in the development of gold compounds as prototypes of metallodrugs.

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References

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