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Synthesis, characterization, BSA and HSA binding studies and anticancer activity of a new copper complex with phenolate-imine ligand

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In recent years, the global increase in cancer cases has driven research into new anticancer drugs to mitigate the side effects of chemotherapy. Compounds containing copper, a bioessential metal, have garnered interest in Bioinorganic Chemistry due to their biological activities and low cost. Schiff bases (CH=N-) are being investigated for their structural flexibility and pharmacological applications. [1] To develop new candidates for metallopharmaceuticals, complex **1**, containing ligand **L1**, was recently synthesized under mild reaction conditions with a 90% yield, as shown in **Figure 1**. The complex was characterized by FT-IR, UV-visible, and ESI-MS spectroscopy. UV-vis spectrum revealing electronic bands at 230-280 nm (π-π*), 312 nm (n-π*), 393 nm (L-M), and 610 nm (d-d). The vibrational spectrum showed bands at 3503 cm^{-1} (H_2O), 1642 cm^{-1} (C=N), and 1075 cm^{-1} (ClO_4). The stability tests conducted in DMSO for 168 h showed a hyperchromic effect in the UV-Vis spectra. Additional methods of characterization are currently in progress. The stability and reactivity of the compounds were investigated by examining their spectroscopic properties, specifically considering the impact of the counter anion (ClO_4^- in **1**) and co-ligand (H_2O in **1**, Cl^- in **2**). To investigate the biology, we conducted interaction tests by titrating the compound with fixed concentrations of BSA and HSA using spectrophotometry. *In vitro,* cytotoxicity studies were performed with **L1** and **1** after 72 h of treatment using the MTT assay against two human tumor cell lines: MCF-7 (breast adenocarcinoma) and SW620 (colorectal carcinoma). Selectivity was assessed using MRC-5 (normal lung fibroblast). **L1** exhibited high cytotoxic potential against human tumor cells with IC_{50} = 10.5 ± 5.3 µM, but the effect was non-selective, showing similar cytotoxicity against normal cells (MRC-5). Complex **1** was selective against SW620 and MRC-7 cells with IC_{50} values of 64.19 ± 1.8 µM and 51.01 ± 1.7 µM, respectively. These results were compared with complex **2**, previously published by the group [1], which showed IC_{50} = 16.4 ± 2.4 (72 h) against the SW620 cell line. Nevertheless, compound **2** indicates a lack of selectivity towards tumor cells. Complex **2** demonstrates moderate cytotoxicity and selectivity against the SW620 cell line. It is important to note that the coordination of the ligand with the metallic center, as well as the presence of different co-ligands, affects cytotoxicity and has a significant impact on the selectivity and stability of these complexes.

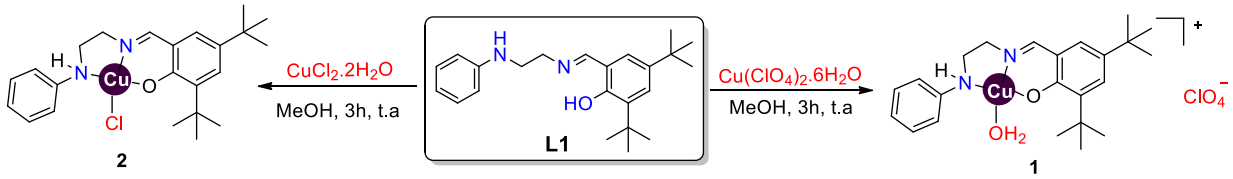

Figure 1. Schematic of the synthesis of complexes **1** and **2**.

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References

[1] Pinheiro, A.C. et al, Pharmaceutics, **15**, 376 (2023).