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Exploring the Anti-Cancer Efficacy of a Cu(II) Complex Containing a Imine - Phenolato Ligand

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Cancer is a global health challenge and the second leading cause of death, with projections indicating a 63.4% increase in cases by 2040 [1]. Although chemotherapy with platinum compounds is common, its effectiveness is often compromised due to the nonspecific binding of these agents, resulting in severe systemic toxicities. Copper (Cu) complexes offer a promising alternative, as endogenous metals like Cu may be less toxic to normal cells, reducing side effects [2]. This study evaluates the cytotoxic and genotoxic effects of an imine-phenolate pro-ligand and its Cu (II) complex [3]. Using genotoxicity assays (alkaline comet), cell proliferation (clonogenic), and cell viability (MTT) in normal and tumor human cell lines over 72 hours of treatment. We found that both the phenolate-imine pro-ligand (**1**) and its Cu(II) complex (**2**) exhibit promising cytotoxic effects in human tumor cell lines, as shown in **Fig. 1**. The IC_{50} was calculated for MCF-7 (HER2- breast cancer), MDA-MB-321 (triple-negative breast cancer), SKBR-3 (HER2+ breast cancer), SW620 (colorectal adenocarcinoma), and HCT116 (colorectal carcinoma) cell lines. The IC_{50} values ranged from 24.05 - 81.70 µM for the ligand (**1**) and 4.1 - 7.3 µM for the Cu(II) complex (**2**). In the clonogenic assay, the ligand (**1**) showed greater inhibition of cell proliferation in the SW620 cell line. The Complex (**2**), on the other hand, inhibited MCF-7 more than the MRC-5 (normal lung fibroblast) cell line. Regarding the genotoxicity of the compounds, we observed that both compounds induced DNA damage starting at 10 µM, with the ligand (**1**) causing more damage in colorectal tumor cells and the complex (**2**) in breast tumor lines. The study shows that the phenolate-imine pro-ligand and Cu(II) complex have promising cytotoxic effects, with the Cu(II) complex being more effective. More experiments are underway to investigate their biological effects and molecular mechanisms further.

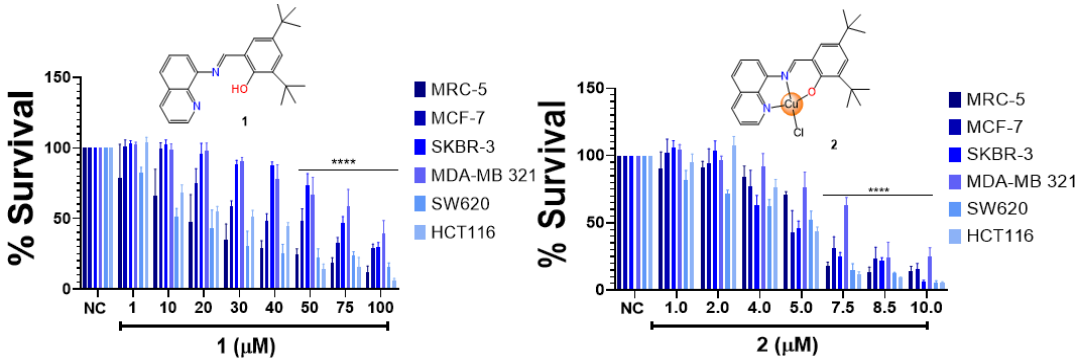

Figure 1. Comparison of the dose-response survival diagrams of cell lines exposed to compounds **1** and **2** for 72 h (10-100 µM). The asterisk denotes significance levels when compared to the control group: (****) $p < 0.0001$ (two-way ANOVA by Dunnett's test).

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References: [1] J.Wang et al.,New.J.Chem, **43**, 2529 (2019). [2] T.W.Hambley et al., Science, **318**, 1392 (2007). [3] A.C.Pinheiro et al., Pharmaceutics, 15, **376** (2023).