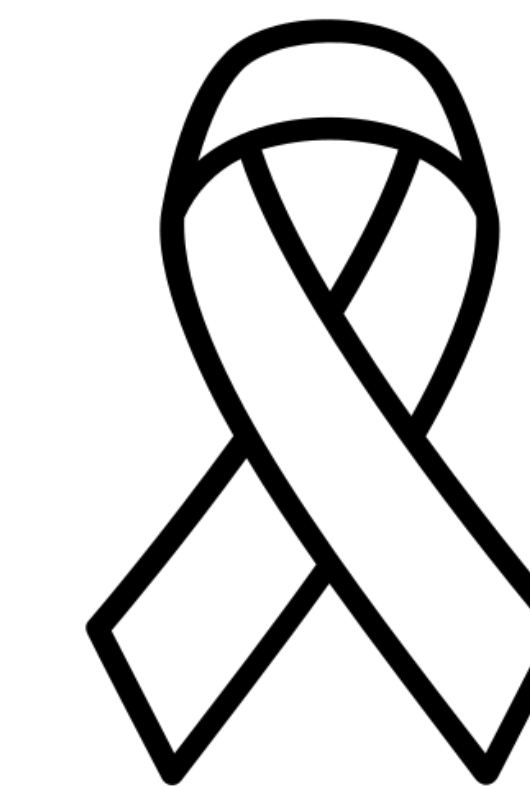


Recent Advances in Cancer Drug Discovery using Bidentate ligand complexes

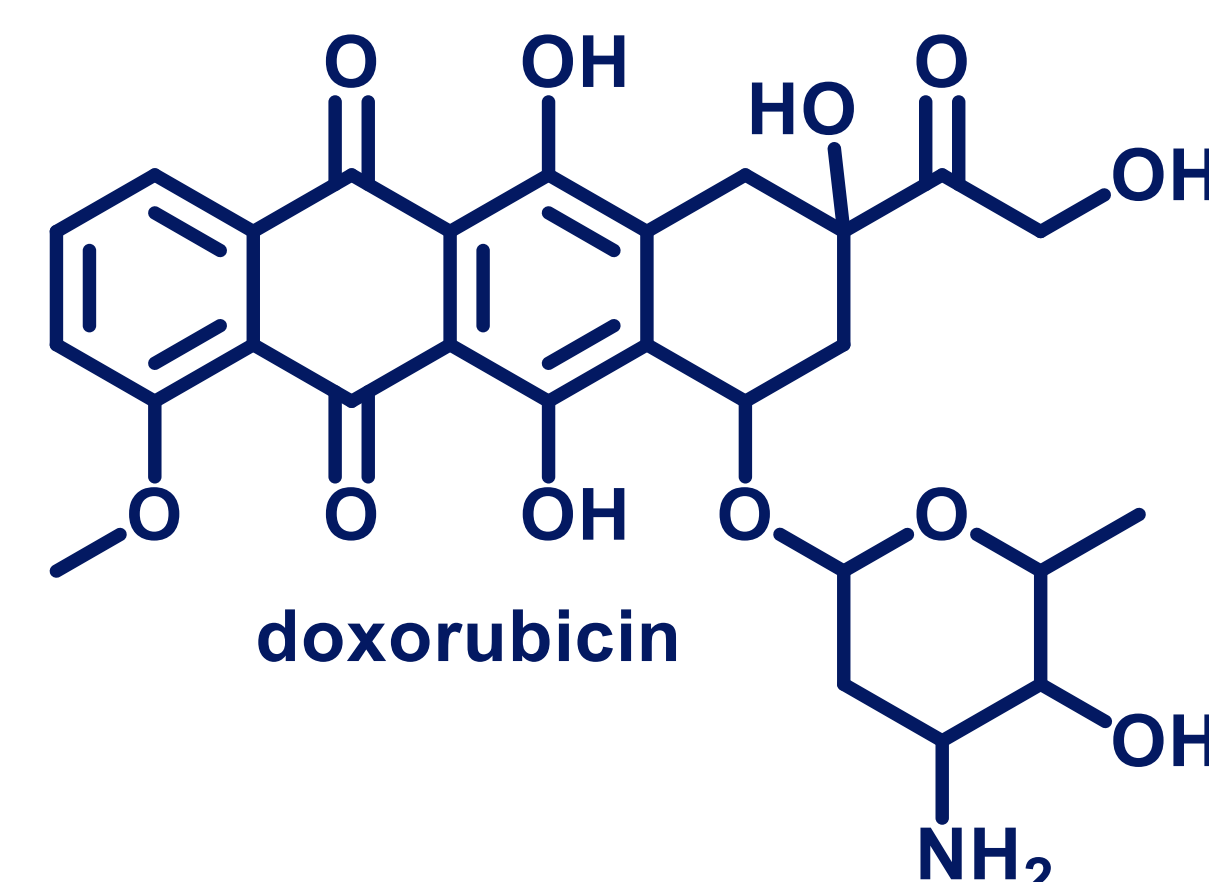
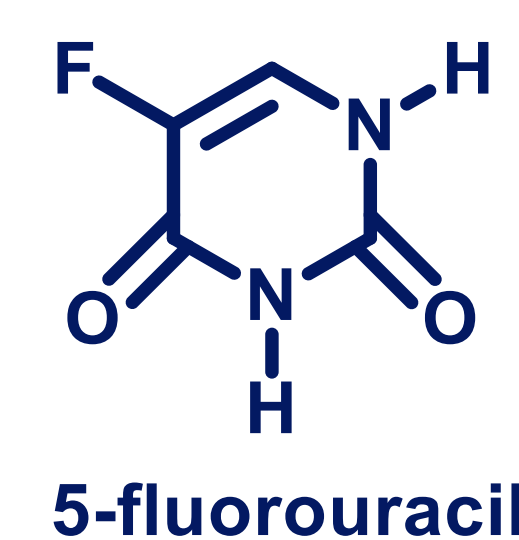
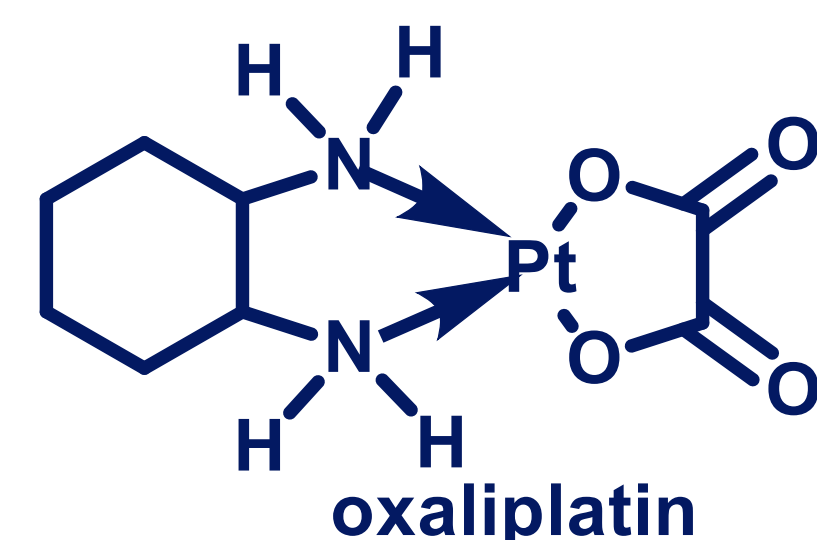
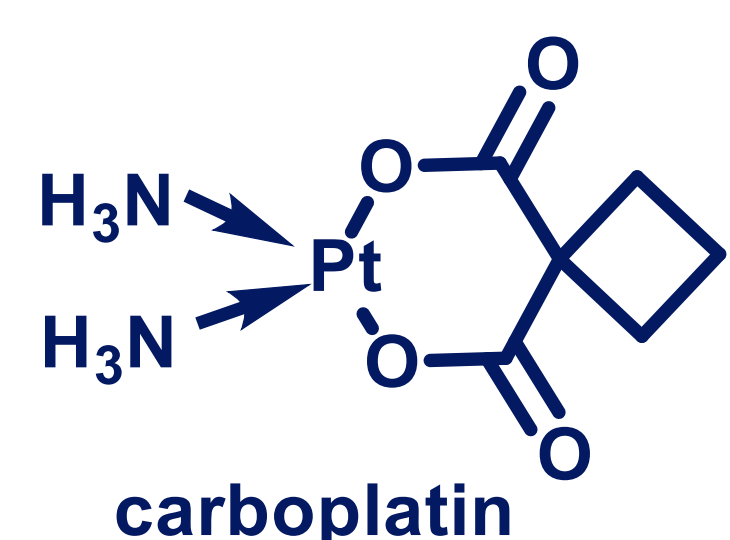
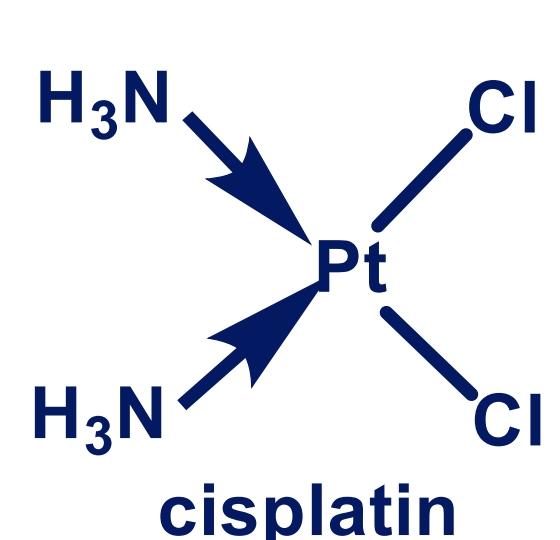


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Introduction

Cancer is a fatal illness that occurs when cells in an organ or tissue are divided and multiplied irregularly and indiscriminately. Globally, it is the second leading cause of death (after cardiovascular diseases) and was responsible for over 9.6 million death in 2018. A tumor could be benign when the abnormal mass formed does not spread or invade nearby tissues, cells, or organs while cancerous tumors are when the abnormal mass formed can spread to other cells, tissues, or organs. Bidentate ligands are neutral or negatively charged species with two donor atoms capable of forming a ring system usually called chelates with metal ions. The donor atoms can be O, N, S, P, C etc, that each donates a pair of electrons to the central metal atom.

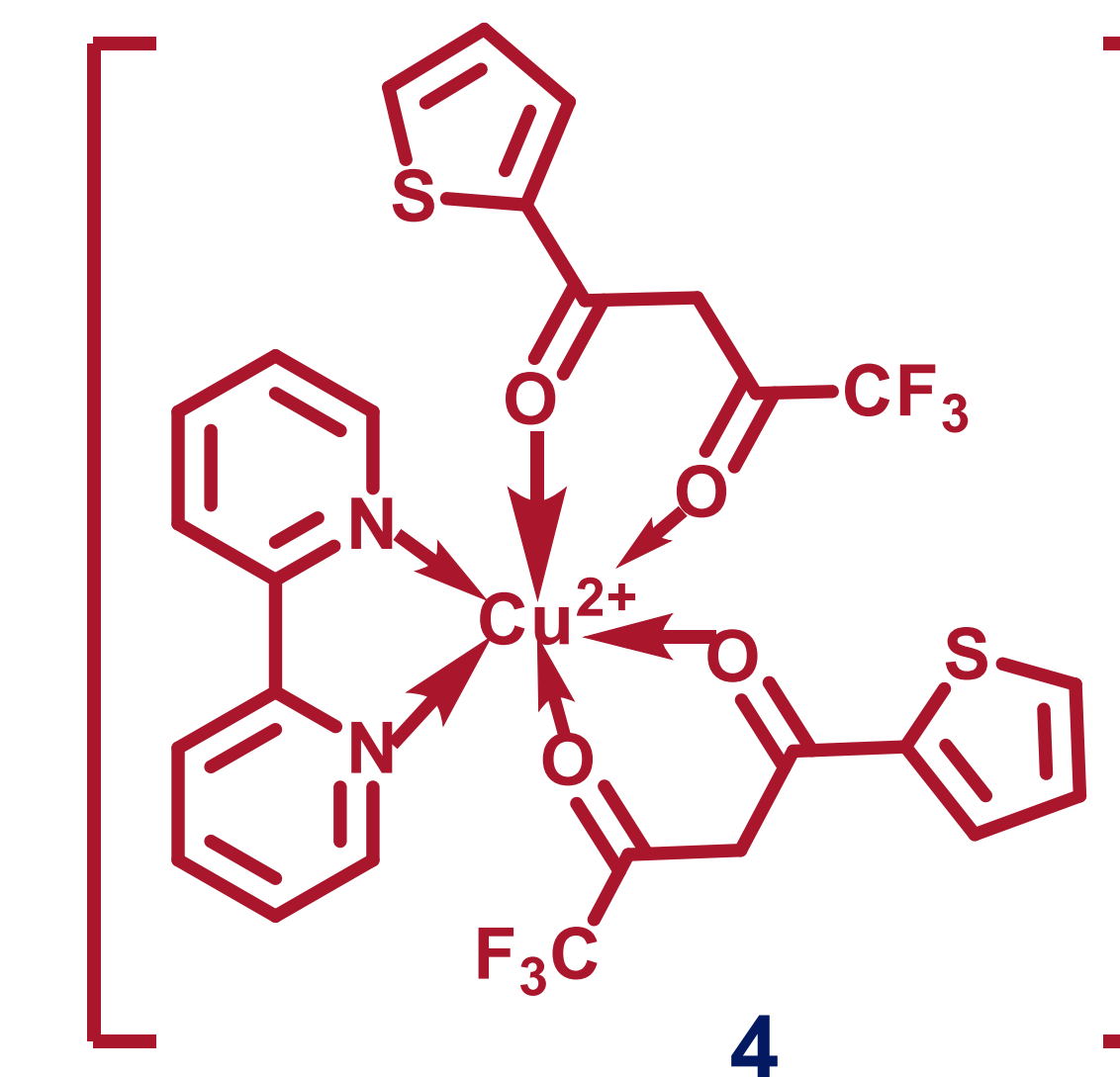
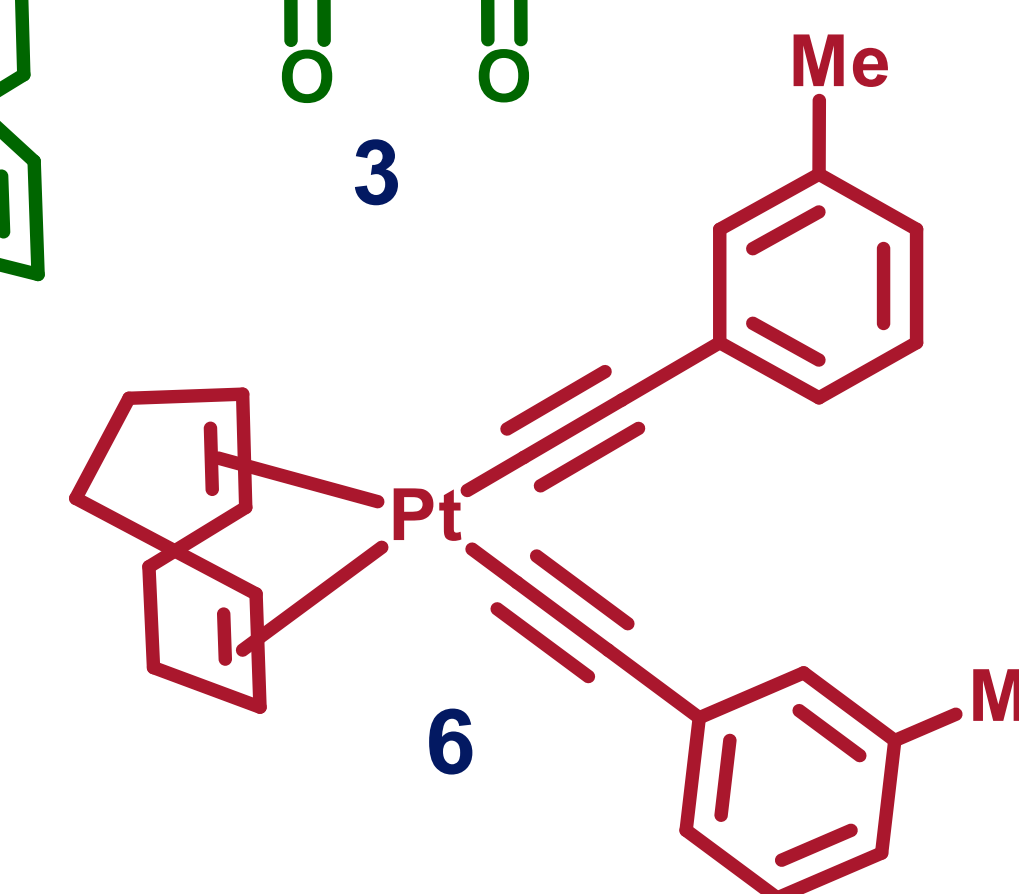
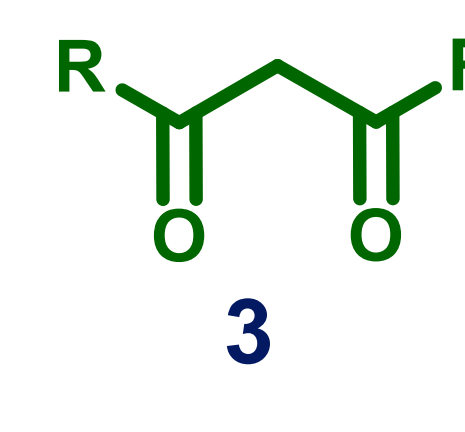
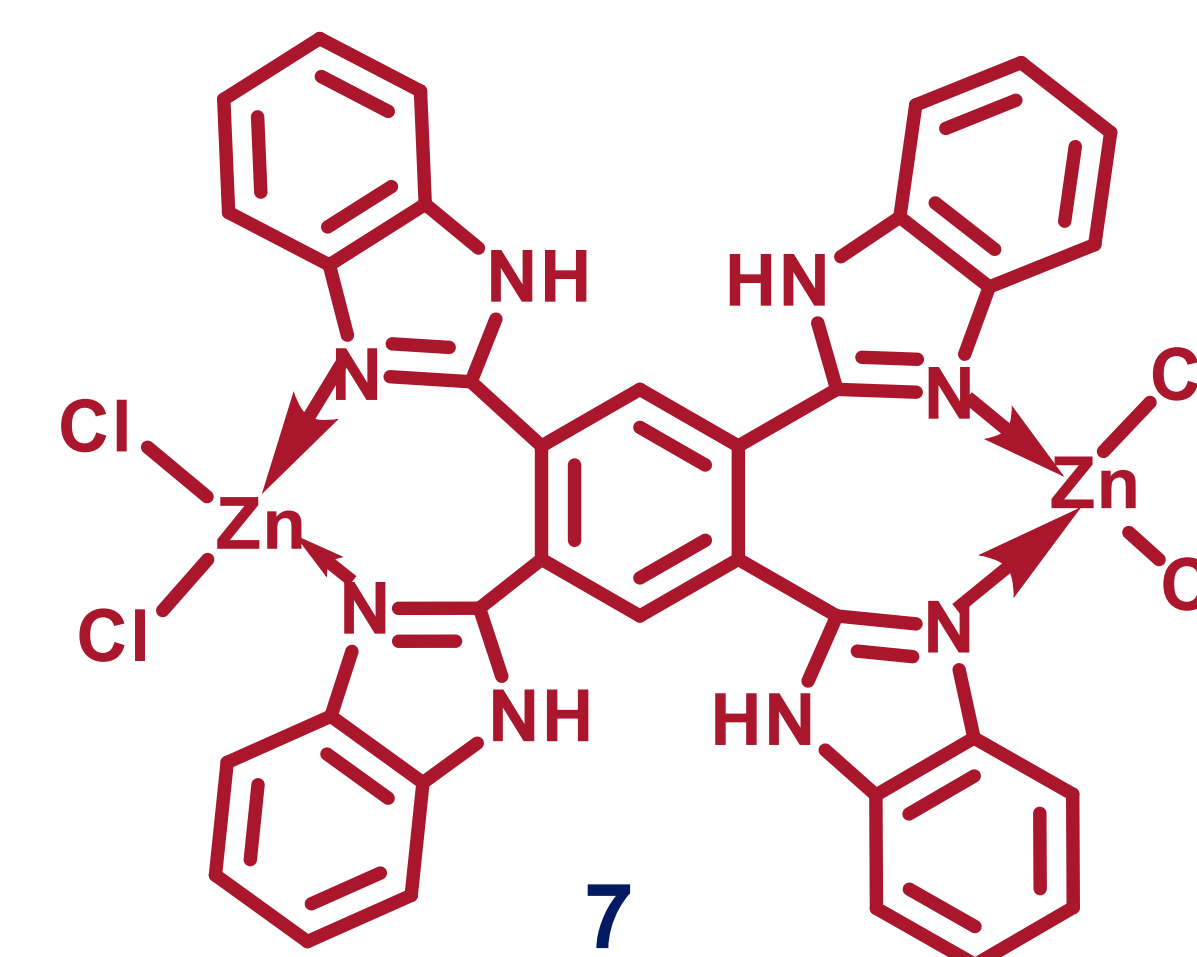
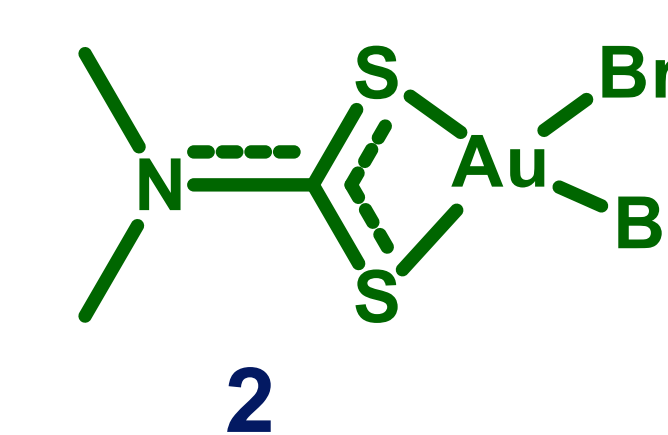
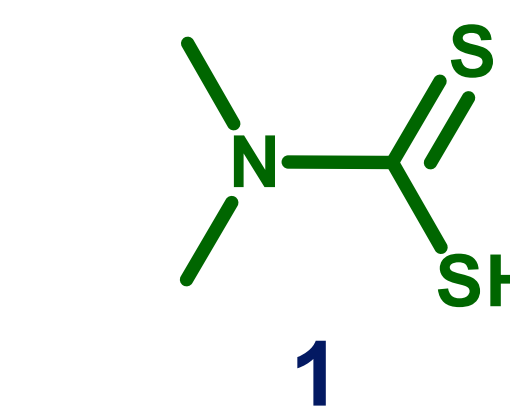


Examples of Cancer Drugs

There are numerous examples of compounds used for the treatment of cancer, examples of which are doxorubicin, cisplatin, carboplatin, oxaliplatin, 5-fluorouracil and many others. However, the toxicity of these drugs due to non-selectivity of cells limits their application. Among these drugs, carboplatin and oxaliplatin are bidentate ligand complexes modelled after cisplatin.

Anticancer properties of dithiocarbamate complexes

Dithiocarbamates (**1**) are distinctly structured molecules coordinating with the sulfur atoms and are very easy to functionalize due to the presence of a nitrogen atom. Ronconi and co-workers at the Padua reported gold dithiocarbamate complex (**2**) with 0.001 μM IC_{50} against human leukemic promyelocytes (HL60), human malignant melanoma (MeWo), human Burkitt's lymphoma (Daudi) while cisplatin had 25.6, 48, and 95 μM IC_{50} respectively.



Anticancer properties of β -diketone complexes

Arising from the numerous biological activities of β -diketone (**3**) and in the search for effective therapy for cancer, various metal complexes of β -diketone have been reported. Malekshah et al reported the anticancer properties of Cu(II)-complexes of mixed bidentate ligands containing a β -diketone (**4**) against the MKN-45 cell line. They observed that compound **4** (IC_{50} 0.1 μM) wherein β -diketone ligands participated as a bidentate ligand, was the most active anticancer agent with 50-fold activity better than 5-fluorouracil (IC_{50} 5.0 μM).

Anticancer Properties of Diolefin complexes

Diolefins (**5**) capable of forming complexes are systematically arranged such that the two olefins can participate as a bidentate ligand in forming metal complexes. Lüning et al reported platinum complex of dialkynyl (**6**) with 70-fold anticancer activity better than cisplatin against MCF-7 cell line.

Anticancer properties of other bidentate ligands

Xie and co-workers reported the anticancer properties of Zn(II)-complexes of benzimidazole (**7**) against resistant HepG2 cell lines. The complex was reported to have 20-fold better anticancer activity than doxorubicin and 5-fold better anticancer activity than cisplatin.

References: DI Ugwu, J Conradie, Anticancer properties of complexes derived from bidentate ligands, Journal of Inorganic Biochemistry 246 (2023) and references therein

Acknowledgements: NRF ZA; UFS