Structural characterization of [Cu(iminodiacetate)(diimine)] coordination complexes with *in vitro* antiproliferative activity

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Inorganic Medicinal Chemistry has made great advances in the search of new metal compounds presenting antitumor activity since the discovery of cisplatin, widely used in clinic for the treatment of cancer since it was approved in 1978. In this work we present ternary copper(II) complexes with iminodiacetate (ida) and diimine ligands, such as dimethyl-bipyridine (dmb), 4-methyl-1,10-phenanthroline (4met-phen) and 2,9-dimethyl-1,10-phenanthroline (neo). The obtained complexes were characterized by elemental analysis, infrared spectroscopy (FT-IR), electron paramagnetic resonance (EPR), single crystal X-ray diffraction and electronic spectroscopy (UV-vis). The pentacoordinated copper center is bonded to the diimine ligand through its N atoms and to the iminodiacetate anion through two carboxylate O atoms and one amine N atom (Fig. 1). Coordination geometries can be described as squared pyramidal with different degrees of distortion towards trigonal bipyramidal as measured by the tau parameter.

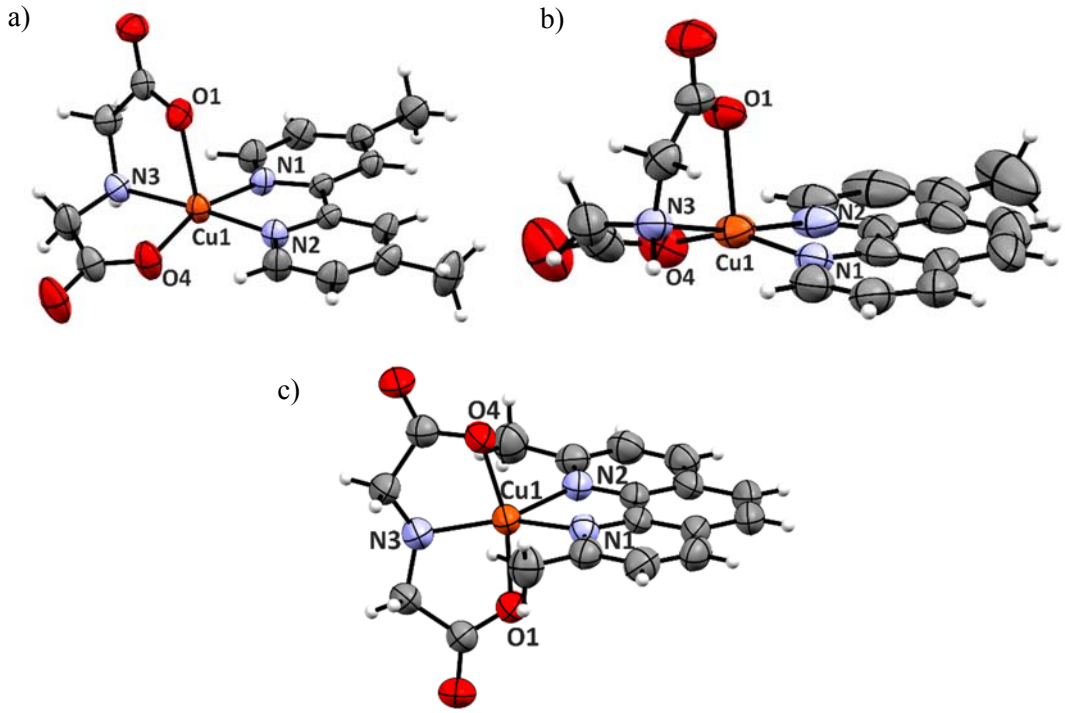

Figure 1. [Cu(ida)(diimine)] complexes, where diimine is a) dmb, b) 4met-phen and c) neo.

All complexes interact with DNA as determined by electronic spectroscopy ($K_{affinity}$ = 2 - 2.5x10^3 M^{-1}) and circular dichroism studies, with varied interaction modes depending on the diimine ligand (DNA condensation for dmb, B to A conformation change for 4met-phen and partial intercalation for neo). Antiproliferative activity in the MDA MB 231 (human metastatic breast adenocarcinoma) cell line was tested at a fixed dose (5 μM) showing that they are more active than *cisplatin*.

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