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Anticancer activity of a mononuclear Copper(II) complex with polypyridyl ligands, $[cu(tpy)(dppz)]^{2+}$: DNA binding and *in vitro* cytotoxicity

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Background and Aims: Metal-based pharmaceuticals emerging from interface of inorganic chemistry, pharmacology, toxicology and biochemistry have witnessed spectacular successes. In this study, a mononuclear copper(II) complex, $[Cu(tpy)(dppz)]^{2+}$, was prepared and its DNA binding was investigated by analytical techniques. An in-vitro cytotoxicity assay of the complex on human breast adenocarcinoma (MCF-7) cell line was also studied.
Methods: The interaction of the copper complex with double-stranded calf thymus DNA was studied by absorption spectroscopy, competitive fluorescence titration, linear dichroism, and voltammetric techniques. A gel electrophoresis mobility shift assay was also performed on a 1000 bp length segment for further evaluation of the interaction between DNA and the tested compound. The cytotoxicity of the complex on MCF-7 cells was evaluated by an MTT assay.
Results: In absorption spectroscopy, addition of DNA resulted in a hypochromism along with a small bathochromic shift in the absorption bands of the complex. The fluorescence intensity of the ''Δ-$[Ru(phen)_2(dppz)]^{2+}$–DNA system'' decreased upon the addition of the copper complex. Linear dichroism (LD) was used to probe the binding geometry of adduct between DNA and the complex. In voltammetric studies, it was found that the complex experienced a shift in its formal potential and a decrease of redox peak currents upon the addition of DNA. The gel retardation study showed that the migration of DNA bands was gradually hindered as the concentration of the complex was increased. Cytotoxicity assay revealed that the toxicity of the complex on MCF-7 cells was in a concentration-dependent manner with an IC_{50} value of 4.57 μM (3.62–5.77).
Conclusions: The obtained results confirm a moderate interaction of the complex with DNA presumably by an intercalative mode with the planar dppz ligand located between the base pairs of ds-DNA. The results also indicate that the title complex demonstrates a marked antiproliferative activity on MCF-7 cancer cells.

Keywords: Copper (II) complex; Polypyridyl ligand; DNA binding; Cell cytotoxicity