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Synthesis, DNA binding and anticancer properties of new Cu(II) and Zn(II) complexes of a Schiff base ligand containing a triphenylphosphonium as a lipophilic cation

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ABSTRACT

A new quinoline-Schiff base ligand (L_{TPP}) containing the lipophilic triphenylphosphonium cation and its complexes [Cu(L_{TPP})Cl]Cl and [Zn(L_{TPP})Cl]Cl were synthesized and characterized. The structures of the ligand and metal complexes were characterized by FTIR, elemental analysis, NMR (for ligand), UV–Vis absorption and fluorescence spectroscopies. DNA binding interactions of the ligand and its metal complexes were investigated by UV–vis absorption and fluorescence spectroscopies as well as viscosity measurements. The DNA binding affinity (K_b) for the ligand and complexes [Cu(L_{TPP})Cl]Cl and [Zn(L_{TPP})Cl]Cl) obtained from absorption spectra were found as 4.33, 4.66 and 6.01 ($\times 10^5$ M^{-1}), respectively. The ligand and its Cu(II) complex showed similar propensities to interact with DNA, yet the DNA binding affinity of the Zn(II) complex was relatively higher than free ligand and its Cu(II) complex. Docking studies were conducted in order to further investigate the DNA binding interactions. The ligand and its complexes were screened for their cytotoxic properties towards malignant mesothelioma (H2452) and healthy human umbilical vein endothelial (HUVEC) cells. The Cu(II) and Zn(II) complexes that were loaded into the cells (H2452) confirm their intracellular uptake by fluorescence-based cell imaging. Complex [Zn(L_{TPP})Cl]Cl emitted fluorescent light even after entering the cell suggesting that the compound can be used for cell tracking purposes. In order to find out whether the compounds we synthesized had the potency to enter human cells, we measured the florescent light emission of H2452 cells treated with the products at their IC_{50} concentration for 24 h. In vitro antioxidant properties of the ligand and its metal complexes were also studied.

1. Introduction

Metal complexes make up a significant proportion of the compounds that are biologically important. Metal complexes are widely used as contrast agents in medicine as anticancer, anti-inflammatory, antibacterial, antirheumatic, antimalarial, and contrast agents [1]. Many chemists have been intrigued by the success of cisplatin and carbo-platin as anticancer agent [2]. Although platin based compounds are effective anticancer agents, they suffer from selectivity and severe side effects. To overcome the disadvantages of these drugs, scientists have focused [3] on developing new metal-based drugs. In addition to being necessary for numerous biological processes, copper is also important for the growth and spread of malignancies [4]. Its versatile activities encompass pivotal roles in DNA synthesis and repair. Serving as an indispensable component in DNA-binding proteins featuring Zn-fingers, it plays a crucial role in shaping transcription factor functionality and facilitating the translation of genetic messages. Furthermore, it assumes a central position in overseeing cell metabolism and providing vital protection against oxidative damage [5]. The presence of zinc is essential for the survival of cells and the maintenance of tissues, in particular for cell proliferation, differentiation, apoptosis, immunity and reproduction. Moreover, zinc complexes, along with numerous other metal (II) complexes, are being explored as promising candidates for novel anti-cancer drugs, offering a metal-based alternative to traditional platinum derivatives [6]. This is mainly due to the fact that zinc(II) is not significantly toxic at higher doses compared to other metals (e.g. Fe, Cu, Hg), and then zinc

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