

Osmium (II) Octahedral Complexes Featuring Orotic Acid: Anticancer Activity and DNA/protein Interaction Studies [†]

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Abstract: The pyrimidine-like ligand orotic acid (6-carboxyuracil) has been bound to two rigid octahedral Os(N,N)₂ scaffolds, where (N,N) stands for 2,2'-bipyridine and 1,10-phenanthroline, respectively. Orotic acid is involved in the de Novo biosynthesis of pyrimidine bases – key components of nucleic acids - in living organisms and has displayed bacteriostatic and cytostatic properties. This study represents a continuation of our previous work and is based on the recently clinically proven efficacy of metal- polypyridyl scaffolds by TLD-1433, which has entered pivotal phase II clinical studies against bladder cancer. The physicochemical properties and structural features of these two Os(II) complexes have been investigated by spectroscopic techniques (FT-IR, UV–Vis, mass spectrometry, ¹H, and ¹³C NMR) and X-ray crystallography. Their cytotoxicity was tested against various cancer (breast, colon) cell lines and healthy cells. As a means to study the mechanism underlying the cytotoxic effects of the complexes, interactions with calf thymus DNA and serum proteins were also carried out. While the complexes display low affinity towards DNA, they bind to proteins, with a higher affinity towards human serum albumin than apo-transferrin.

Keywords: orotic acid; osmium; anticancer; DNA binding; serum proteins.

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Conflicts of Interest

The authors declare no conflict of interest.