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A new family of Cu(II) photoactive complexes: Enhanced DNA intercalation and fragmentation

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Statement of the Problem: Treatment of aggressive and not accessible tumors, such as glioblastoma multiforme, is based on the synergistic result of surgical operation, radiotherapy and chemotherapy. However, these techniques come not only with serious side effects, but also with marginal improvement of the patient's life expectancy.¹ Photodynamic Therapy (PDT) has emerged as an attractive alternative to conventional cancer treatment. It induces destruction of cancer cells upon irradiation of specific photoactive compounds called photosensitizers (PS), usually by generating the highly reactive single-state oxygen 1O_2 .²⁻⁴ Transition metal complexes have been utilized in PDT exactly because they can promote such photochemical transformations, exhibit strong absorption in the UV-Vis region of the electromagnetic spectrum, and relatively long emission lifetimes of their triplet metal-to-ligand charge transfer state (3MLCT).⁵⁻⁶ The present study reports the synthesis of three novel Cu(II)-based complexes, bearing bidentate bipyridine-type ligands able to intercalate to the DNA strand and cleave it upon irradiation, resulting in apoptosis of the treated cells. Methodology & Theoretical Orientation: Three novel Cu(II)-based complexes were synthesized and characterized using mass spectroscopy, FT-IR and UV-Vis. The binding constants of these complexes with DNA were determined (before and after irradiation) by calculating the concentration of the complex at 50% quenching of DNA-bound ethidium bromide emission intensity. Agarose gel electrophoresis helped visualize the ability of these complexes to bind and cleave DNA upon irradiation. Findings: These novel complexes show high affinity for DNA, (calculated binding constants were one order of magnitude lower than that of ethidium bromide). When incubated in the dark, complexation with DNA resulted in only a small amount of fragmentation, which was substantially enhanced after irradiation, especially when the concentration of the complexes was increased to 200 μ M or higher. As a result, these complexes could potentially be used as photosensitizers in PDT.

Biography

Theodoros Mikroulis is a chemist working at the interface of Organic and Medicinal Chemistry for the development of drugs and other biologically-related compounds against various diseases. He graduated from the Department of Chemistry of the National and Kapodistrian University of Athens and obtained a M.Sc. degree in Medicinal and Biological Chemistry at the University of Edinburgh. He is currently working towards his PhD on the synthesis of photoactive compounds that can potentially be used as anticancer agents, in the research group of Professor Georgios C. Vougioukalakis in the National and Kapodistrian University of Athens.

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