Valproic Acid Zn(II) Complexes modified with 1,10-Phenanthroline or 2,2'-Bipyridine are capable to select and cleave specific nucleic acid sites

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Introduction: Once metal ions participate in cell metabolism in various pathways, the research on metal complexes coordinated to new ligands is increasing, and new drugs or biotechnology tools are becoming available. Three new Zn(II) complexes with valproic acid, an anticonvulsant drug, and 1,10-phenanthroline or 2,2'-bipyridine were synthesized. **Objective:** The aim of this work is to characterize the interference with DNA of the Zn_2Valp_4 (1), $ZnValp_2$1,10-phenanthroline (2) and $ZnValp_2$2,2'-bipyridine (3) complexes. **Material and Methods:** Complexes were synthetized and the procedures were realized as described in the literature with small modifications. The plasmid cleavage assay was performed at 0, 10, 100 and 1000 µM concentrations in the absence of light (AL), or presence of ultraviolet-B light (UV) at pH 7.0, 7.5 and 8.0. Kinetic studies were performed AL or UV at pH 7.5. Circular Dichroism (CD) was performed using CT-DNA at 50µM and different complex concentrations. Oligonucleotide cleavage assay was realized with a 49 mer oligonucleotide. **Results and Discussion:** All complexes cleaved supercoiled plasmid DNA to circular open and linear forms. The UV-B light exposure increased the cleavage ability in 1, 2 and 3 but was stronger in 2 and 3 as demonstrated by kinetic studies. CD demonstrated that complexes are DNA groove binders, but 2 can also act as an intercalation agent. Oligonucleotide cleavage assay showed that the three complexes cleave specifically at thymine containing nucleotide sequences probably due to the metal complex exchange of a coordinate bond and formation of a new one with a thymine nitrogen. **Conclusion:** The three complexes cleave plasmids and reacts with DNA specifically at thymine sites. They can be photoactivated by UV-B but 2 and 3 are far more active than 1 and probably more suitable for modelling drugs or biotechnology tools.

Key-words: Zn(II) complexes, circular dichroism, thymine nucleotide recognition.

Financial support: CNPq Bolsa PDJ projeto 503066/2014-1.