

NON-COVALENT INTERACTIONS BETWEEN METALLOINTERCALATORS AND BOTH DUPLEX AND QUADRUPLEX DNA

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Over the past two decades there has been sustained interest in understanding the binding interactions of metallointercalators with B-form DNA, as well as developing novel metallointercalators for applications including selective DNA structure probes and anticancer drugs. Most such studies have focused on ruthenium(II) metallointercalators owing to their unique set of physical properties. Previous work from our laboratory showed that Electrospray Ionisation Mass Spectrometry (ESI-MS) provides considerable information about the binding of the ruthenium(II) metallointercalators $[\text{Ru}(\text{phen})_2(\text{L})]^{2+}$ ($\text{L} = \text{phen}, \text{dpq}, \text{dpqC}, \text{dppz}$) to B-form DNA, including the number, relative amounts and stoichiometry of individual metal/DNA complexes present in mixtures.¹

Currently we are exploring the binding of the corresponding nickel(II) metallointercalators $[\text{Ni}(\text{phen})_2(\text{L})]^{2+}$ ($\text{L} = \text{phen}, \text{dpq}, \text{dpqC}, \text{dppz}$) towards both quadruplex DNA and the same duplex DNA sequence used previously: d(CCTCATGGCCATGACC/GGTCATGGCCATGAGG). These systems are being examined using ESI-MS as well as other analytical techniques including isothermal titration calorimetry, absorption spectroscopy and circular dichroism spectrophotometry, in order to determine the validity of information obtained by the former method.

ESI-MS studies comparing the binding interactions of $[\text{Ru}(\text{phen})_2(\text{L})]^{2+}$ and $[\text{Ni}(\text{phen})_2(\text{L})]^{2+}$ towards quadruplex DNA, showed that $[\text{Ni}(\text{phen})_2(\text{L})]^{2+}$ complexes have a relatively weaker binding affinity towards quadruplex DNA compared to the $[\text{Ru}(\text{phen})_2(\text{L})]^{2+}$ complexes. MS/MS experiments of the metal-quadruplex complexes were carried out in order to investigate and compare the relative stability of these metal complexes with quadruplex DNA. Fragmentation of the $[\text{Ni}(\text{phen})_2(\text{L})]^{2+}$ complexes was observed upon binding to quadruplex DNA. This paper will present the results of these investigations.

- [1] Urathamakul, T.; Beck, J. L.; Sheil, M. M.; Aldrich-Wright, J. R. and Ralph, S. F. Mass spectrometric investigation of non-covalent interactions between ruthenium complexes and DNA, Dalton Trans. (2004) 2683-2690.

