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# Binding interactions between nickel schiff base complexes and quadruplex DNA

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**Abstract**
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**ABSTRACT BODY:**

**Abstract Body:** Quadruplex DNA (qDNA) is a less common nucleic acid secondary structure present in non-coding regions at the ends of chromosomes known as telomeres. Since many base pairs are lost from the ends of DNA strands during replication, telomeres function to protect chromosomes during this process. However, when DNA becomes so short that it can no longer function as the template for protein synthesis, the cell enters apoptosis, or programmed cell death. In contrast, approximately 85% of tumour cells possess elevated levels of the enzyme telomerase, which is responsible for maintaining the length of telomeres and contributes to tumour cell immortality. The normal substrate for telomerase is the single stranded overhang regions present at the end of telomeres. These regions are rich in guanines, and consequently prone to forming qDNA structures. Drugs that can bind selectively to existing qDNA structures or induce formation of such structures may be able to inhibit telomerase and act as novel anti-cancer agents. One group of compounds that has shown promise in this area are substituted Schiff base complexes of various metals. The work presented here further explores the potential of nickel(II) Schiff base complexes as selective qDNA binders, and inhibitors of telomerase, by varying the number and position of aromatic ring systems in the Schiff base structure, as well as the identity of side chains designed to interact with the qDNA grooves. One complex of interest is **(1)**, which includes the meso-1,2-diphenylethylenediamine unit as part of its structure. This complex binds poorly to duplex DNA, but is able to bind to a tetramolecular qDNA structure, indicating that it is possible to engender selectivity for qDNA structures through the usage of the above non-planar moiety. We are currently using a variety of methods, including electrospray ionisation mass spectrometry (ESI-MS) and CD spectroscopy, to explore the interactions between different types of qDNA and the nickel complexes.

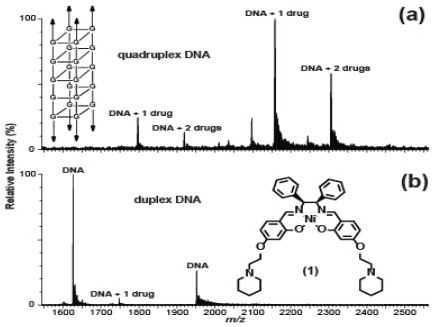


Figure 1. (a) ESI mass spectrum of a solution containing a 3:1 ratio of (1) and a tetramolecular qDNA molecule. (b) ESI mass spectrum of a solution containing a 3:1 ratio of (1) and a duplex 16mer DNA molecule.