



## 21<sup>ST</sup> NATIONAL MEETING ON MEDICINAL CHEMISTRY



# BOOK OF ABSTRACTS

Palermo July 17 – 20, 2012



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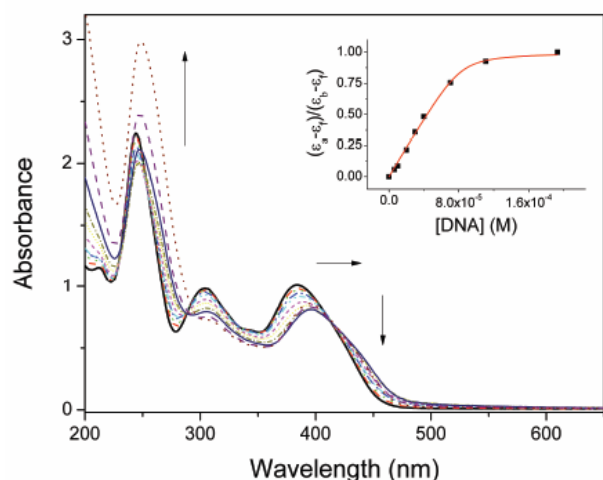
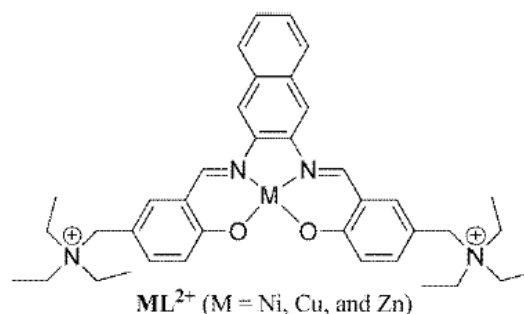
# Synthesis, characterization and DNA binding studies of potential G4 stabilizer metal complexes

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A series of square-planar and square pyramidal metal complexes,  $ML^{2+}$  (M= Ni, Cu, and Zn), characterized by an extended nearly planar area, have been synthesized as perchlorate salts and characterized. The selected ligand  $H_2L$  is a derivative of the  $N,N'$ -bridged tetradentate  $N,N'$ -Bis-salicylidene-2,3-naphthalendiamine, functionalized with triethylammonium methyl groups to improve its water solubility. Similar Schiff base transition metal complexes, where the metal is coordinated *via* a square planar  $N_2O_2$  system, have recently shown favorable features as DNA-intercalator compounds (1). Preliminary DNA interaction studies, performed by UV absorption spectroscopy, circular dichroism, fluorescence and viscosimetry, have shown that the complexes behave as typical intercalators, with values of the DNA-binding constant,  $K_b$ , within the range  $10^6$ - $10^7$   $M^{-1}$ , with the following decreasing order of interaction strength:  $NiL^{2+} > CuL^{2+} > ZnL^{2+}$ .



Interestingly, similar planar  $\pi$ -delocalized molecules are excellent DNA quadruplex binders (2, 3) due to their ability to stack on the face of the G-quartet. For such reason we have planned to investigate the interaction with G-quadruplex and the related *in vitro* cytotoxicity of the synthesized compounds.

Figure 1 - UV-vis absorption spectra of  $ZnL^{2+}$  in the presence of increasing amount of DNA in Tris-HCl 1 mM;

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- (2) Arola-Arnal, A.; Benet-Buchholz, J.; Neidle, S.; Vilar, R. *Inorg. Chem.* **2008**, *47*, 11910–11919.
- (3) Campbell, N. H.; Karim, N. H. A.; Parkinson, G. N.; Gunaratnam, M.; Petrucci, V.; Todd, A. K.; Vilar, R.; Neidle, S. *J. Med. Chem.* **2011**, *55*, 209–222.