X CONGRESSO NAZIONALE DI CHIMICA SUPRAMOLECOLARE

Perugia 25-28 settembre 2011

PROCEEDINGS

Università degli Studi di Perugia

Dipartimento di Chimica

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Proceedings

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DNA binding and biological activity of Cu(II) and Zn(II) complexes of a 2,5-diphenyl[1,3,4]oxadiazole macrocycle ligand.

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The interaction of native DNA with [Cu**L**(ClO_4)]$ClO_4 \cdot H_2O$ and [Zn**L**Br]$Br \cdot H_2O$ complexes[1] in aqueous solution at neutral pH, was investigated by variable-temperature UV-vis absorption, circular dichroism and fluorescence spectroscopy. The values of the DNA-binding constants of these complexes, determined by competitive binding spectrofluorimetric titrations of ethidium bromide (EB)-DNA solutions, are $(6.7 \pm 0.5) \times 10^6$ M^{-1} for $[Cu\mathbf{L}]^{2+}$ and $(4.7 \pm 0.5) \times 10^5$ M^{-1} for $[Zn\mathbf{L}]^{2+}$. These data together with a throughout analysis of the spectroscopic behaviour consistently suggest that both compounds are strong DNA binders, being DNA-intercalation the main interaction mechanism.

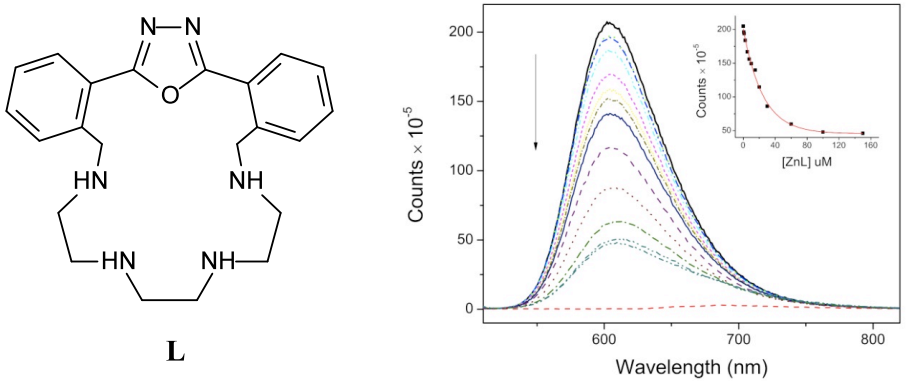

Figure 1. (a) Representation of the ligand **L**; (b) Effect of addition of [Zn**L**Br]Br to EB–DNA complex fluorescence. (λ_{ex} = 500 nm, $[DNA_{phosphate}]$=30 μM; [EB]=10 μM, $[Zn\mathbf{L}]/[DNA_{phosphate}]$=0.00-5.00. The intensity at 600 nm as a function of $[Zn\mathbf{L}]^{2+}$ is reported in the inset.

The DNA-binding strength of both complexes has been found to be correlated to their *in vitro* cytotoxic activity toward mammalian carcinoma cells. In fact, flow cytometric assays showed that, when the compounds are delivered through the cell membrane within their intracellular environment by a lipidic carrier, cell survival is sensibly reduced, of 40% with [Cu**L**(ClO_4)]$ClO_4 \cdot H_2O$ and of 24% with [Zn**L**Br]$Br \cdot H_2O$.

1. (a) G. Ambrosi, M. Formica, V. Fusi, L. Giorgi, E. Macedi, M. Micheloni, G. Piersanti, R. Pontellini, *Org. Biomol. Chem* **2010**, 8, 1471-1478; (b) G. Ambrosi, M. Formica, V. Fusi, L. Giorgi, E. Macedi, M. Micheloni, P. Paoli, R. Pontellini, P. Rossi, *Inorganic Chemistry* **2010**, 49, 9940-9948.