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CATIONIC PORPHYRIN-DNA INTERACTIONS : IMPORTANCE OF THE NUMBER AND POSITION OF THE CHARGES.

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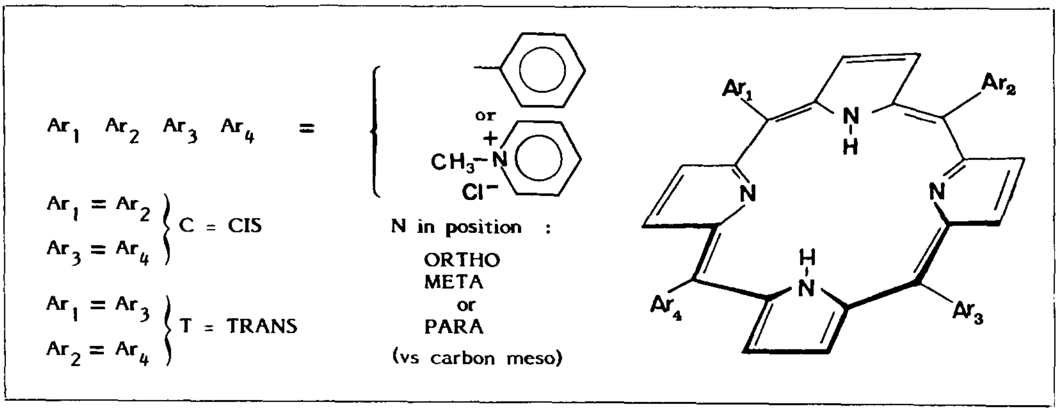
Water soluble cationic porphyrins as meso-(para- or meta-NMePy)$_4$PH$_2$ exhibit a high affinity for DNA (1). Moreover these porphyrins which can attain even temporarily a planar configuration are able to intercalate into DNA or polynucleotides (1,2).

Recently (3), we have determined the apparent binding constants of some meso-tetra-aryl-porphyrins, bearing between 2 to 4 charges, using competitive experiments with ethidium bromide. Furthermore, fluorescence energy transfer measurements, UV visible and viscosimetric titration have been used as evidence for interaction.

Using these methods, we have now examined a large variety of cationic porphyrins, (o- or m- or p-NMePy)$_n$Ph$_{4-n}$PH$_2$ which differ not only by the number but also by the relative position of the cationic charges. Some of them have free rotating meta- or para-NMePyridyl substituents in position meso whereas others have ortho-NMePyridyl substituents which cannot rotate for steric reasons.



RESULTS :

High values of apparent binding constants (K_A) are obtained for all the porphyrins. The apparent binding constants decrease with the decrease of the number of charges (Figure 1) but remain high even with only 2 cationic charges (from 6 10^4 to $10^7 M^{-1}$) :

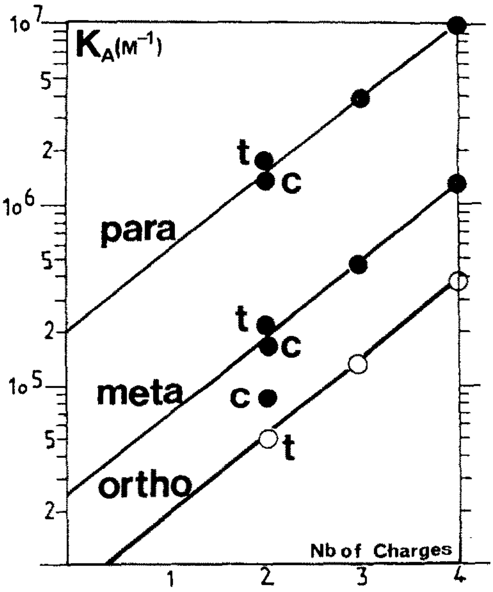


Figure 1: Apparent binding constants of various cationic porphyrins K_A (● intercalated, ○ not intercalated) toward Calf Thymus DNA (Tris HCl buffer 0.1M, NaCl 0.1M, pH 7.4).

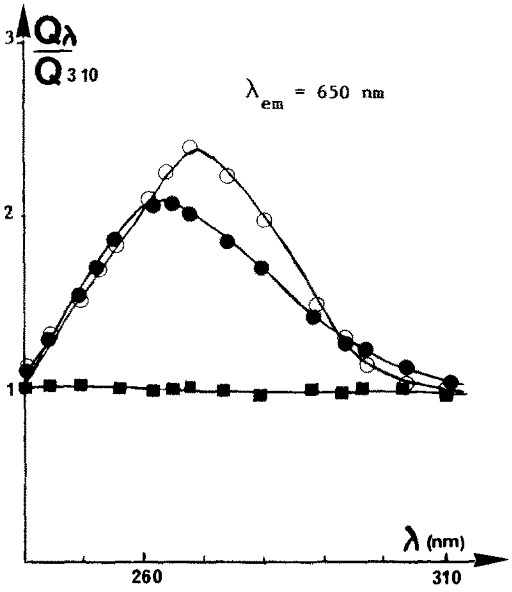


Figure 2 : Variation of the fluorescence quantum yield of different porphyrins in the presence of Calf Thymus DNA as a function of the excitation wavelength ($(para-NCH_3Py)_4PH_2$: ● $(ortho-NCH_3Py)_4PH_2$: ■ ; $cis(ortho-NCH_3Py)_2PH_2$: ○

Inside each class of porphyrins, having the $N-CH_3$ group in ortho, meta or para positions, a decrease of one charge results in a decrease of the apparent binding constant by a factor of about 3.

When going from para- to meta- meso-substituted porphyrins, an almost identical decrease (by a factor of 6) of K_A was observed whatever the charge number. This is also the case when going from meta- to ortho-substituted porphyrins by a factor of 3.

Fluorescence energy transfer experiments and UV visible spectra confirm the intercalation of the (para- or meta-$NMePy)_nPh_{4-n}PH_2$ (Figure 2). Interestingly, the cis-(ortho-$NMePy)_2Ph_2PH_2$ porphyrin bearing two cationic charges, but not the corresponding trans isomer, appeared to be able to intercalate into DNA. The last result shows for the first time that **only one part of the polyaromatic tetrapyrrole ring is required for the intercalation to take place.**

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