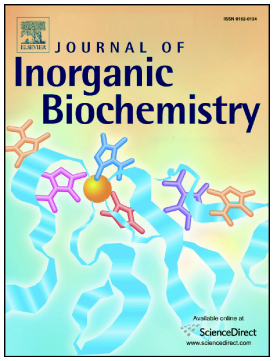

A novel porphyrin-based molecular probe ZnTCPPSpm4 with catalytic, stabilizing and chiroptical diagnostic power towards DNA B-Z transition

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A novel porphyrin-based molecular probe ZnTCPPSpm4 with catalytic, stabilizing and chiroptical diagnostic power toward DNA B-Z transition.

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Abstract

In this work we have designed a new zinc(II) porphyrin with four spermines conjugate in the meso positions, *meso*-tetrakis-(4-carboxysperminephenyl)porphyrin, ZnTCPPSpm4) with the aim of acting as a chiroptical probe for the Z-form of DNA, a high energy transient conformation of DNA. In addition to *monitor* by Electronic Circular Dichroism chiroptical response the formation of Z-DNA in the presence of micromolar concentration of spermine, this porphyrin based molecular probe is also able to *catalyze* and *stabilize* this important DNA structure. The ZnTCPPSpm4 conjugate represents a perfect example of single molecule, which possesses all these three properties at the same time. The increased stability of Z-DNA in the presence of this derivative opens possibility for further studies on the mechanism of B- to Z-DNA transition, and on the design of new probes with improved efficiency.

Keywords: porphyrin derivative • Z-DNA • Circular Dichroism • B-Z transition • chiroptical probe • supramolecular chemistry

DNA containing an alternation of purine and pyrimidine repeats has the potential to adopt the Z conformation, one of the most intriguing structures besides A- and B-DNA.[1-3] Z-DNA is a left handed double helix, in which purines adopt a *syn*- conformation while pyrimidines are in *anti*-conformation. Because the Z-form is a transient high energy structure, which without stabilization, spontaneously relaxes into the more stable B conformation, it is therefore difficult to study its biological role and to characterize the mechanism and kinetics of the B-Z transition. [4-6] Indeed to date the B-Z conversion mechanism remain an unsolved issue, and among the several postulated processes the most widely accepted is the "zipper model" that involves a two-stages B-Z transition.[4] Indeed, although the discovery of proteins that bind to Z-DNA with high affinity and specificity suggests that Z-DNA can exist *in vivo*, the biological role of this left-handed helix remains almost unknown yet.[7-10] *In vitro*, the B-Z transition is observed in the presence of molar or millimolar concentrations of NaCl, $NiCl_2$ or other transition metal complexes like $[Co(NH_3)_6]^{3+}$, as well as micromolar concentrations of spermine.[11-18]

Although promotion of the B to Z transition requires only low concentrations of spermine, much higher concentrations are necessary for observing its stabilization effect. Yet the processes of induction and stabilization of Z conformation as well as its sensitive detection have remained challenging issues.

For this reason, it is desirable to design efficient and versatile probes, which promote these processes and contribute to a better understanding of the formation mechanism of this important DNA structure.

In recent years, there is an increasing interest to meso-substituted porphyrins and their metal-derivatives as chirality reporters.[19-26] These molecules appear very attractive due to their unique spectroscopic and geometric properties. Non-covalent interactions of water-soluble porphyrins with DNA, have been studied and well characterized in past years.[27-30] One of their advantages is that they are Electronic Circular Dichroism (ECD) silent but become ECD active upon binding to DNA and show an induced ECD in their absorption region, as a specific spectroscopic signature of the chirality of the "host" molecule. The zinc(II) derivative of the tetra-cationic meso-tetrakis-4(N-metlhylpyridyl)porphine (ZnTMPyP) has been utilized as a chiroptical probe for detection of left-handed Z-DNA.[22,31] Crucial for the specific recognition by ZnTMPyP is the axial binding of the central zinc to N7 of guanines which in the Z form are no longer shielded, compared to the B-form.¶ Therefore porphyrins are arranged on the face of Z-DNA[32] and by that exhibit a

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