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Linear and Circular Dichroism Characterization of Thionine Binding Mode with DNA Polynucleotides

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ABSTRACT

The binding mode of thionine (3,7-diamino-5-phenothiazinium) with alternating and non-alternating DNA polynucleotides at low binding ratios was conclusively determined using linear and circular dichroism spectroscopies. The binding to $[poly(dG\text{-}dC)]_2$ and poly(dG)·poly(dC) was purely intercalative and was insensitive to ionic strength. Intercalative binding to $[poly(dA\text{-}dT)]_2$ is observed at low ionic strength, but a shift of some dye to an non-intercalative mode is observed as the background salt concentration increases. With poly(dA)·poly(dT), intercalative binding is unfavourable, although some dye molecules may intercalate at low ionic strength, and groove binding is strongly promoted with increasing concentration of background salt. However, stacking with bases is observed with single-stranded poly(dA) and with triplex poly(dT)∗poly(dA)·poly(dT) which suggests that the unusual structure of poly(dA)·poly(dT) precludes intercalation. Thionine behaves similarly to the related dye methylene blue, and small differences may be attributed either to the ability of thionine to form H-bonds that stabilize intercalation or to its improved stacking interactions in the basepair pocket on steric grounds.

KEYWORDS

DNA binding; phenothiazine dyes; intercalation; minor groove binding

INTRODUCTION

Phenothiazinium dyes (Figure 1) are widely used in biology for histological cell staining due to their metachromic behaviour [1] and have also found utility as redox transducers in biosensors [2]. Due to their photochemical activity in biological systems [3-5], they have potential applications in photodynamic therapy and this feature makes them suitable agents for photodecontamination of pathogens, for example when treating blood for transfusions [6]. Their biological activity is related, at least in part, to their nucleic acid binding properties. The most well-studied dye of this family is Methylene Blue (MB) which is full methylated on the exocyclic amines. We previously published comprehensive linear and circular dichroism studies of MB interactions with DNA and polynucleotides [7-9], which demonstrated intercalation of MB with most duplex DNA sequences as well as triplex poly(dT)∗poly(dA)·poly(dT) [10]. However, non-intercalative binding occurred with poly(dA)·poly(dT), and also with $[poly(dA\text{-}dT)]_2$ at high ionic strength. Calculations by Rohs *et al.* [11] and Nogueira *et al.* [12] have indicated that MB has a preference for a minor-groove location in alternating AT sequences, with an angle between the dye transition moment and the helix axis that can produce zero linear dichroism signal, and this provides a theoretical underpinning of our observations with $[poly(dA\text{-}dT)]_2$. With $[poly(dG\text{-}dC)]_2$, modelling agrees with spectroscopic results that intercalation is favoured [13,14].

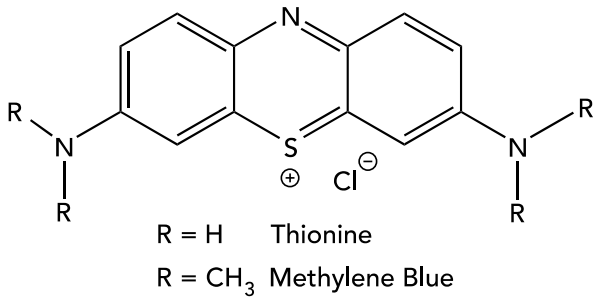

Figure 1. Structures of the phenothiazinium dyes used in this study.