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Research Article

Interaction of Co, Mn, Mg and Al with d(GCCCATGGC) and d(CCGGGCCCGG): a spectroscopic study

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Abstract. Spectroscopic study of the interactions of metal ions, Co, Mn, Mg and Al with d(GCCCATGGGC) and d(CCGGGCCCGG) revealed the following. Metal ions Mn, Al and Mg at the lowest concentrations enhanced the t_m of oligomers, whereas Mn and Mg at higher concentrations decreased the t_m. Co enhanced the t_m of oligomers at higher concentrations. The studies have also indicated that Mn at lower concentrations displaced EtBr fluorescence, Mg and Co at moderate concentrations and Al only at higher concentrations. Addition of Co, Mn, Mg and Al altered the bands of the circulars dichroism (CD) spectra of the oligomers in a concentration-dependent manner. The CD spectra of d(GCCCATGGGC) and d(CCGGGCCCGG) indicated B and Z forms of DNA, respectively, in contrast to the A form observed in the crystal structures. Mg and Co at different ionic strength induced Z–B transition in d(CCGGGCCCGG), while Al at higher concentrations induced a Z–A transition. Mn did not induce any transition. This is the first report to show that Al causes structural transitions in sequence-specific oligomers and has strong binding ability with GC-rich euchromatin oligomers.

Key words. DNA; interactions; transitions; spectroscopy; trace elements.

Metal ions are known to be involved in the stabilization of DNA strands and in the catalytic activity of DNA polymerases [1]. Transition metals such as Mn and Co at higher ionic strength are found to be mutagenic and carcinogenic and also change the handedness of their DNA [1–6]. Al is reported to be associated with neurological disorders [7] and causes cellular toxicity through its interaction with DNA in cells [8–9].

Many data are available on the effect of metal ions on the melting behaviour of genomic DNA, λDNA, poly (A-T) and poly (G-C) [10–12]. However, the precise mechanisms of binding of the metal ions to DNA are not yet clearly understood. Metal-binding studies on defined short sequences of DNA are also limited [13–16] and would be of interest in this connection.

Recently, the crystal structures of the two oligomers d(CCGGGCCCGG) and d(GCCCATGGGC) were solved in our laboratory. Both structures crystallize isomorphously and are found to adopt the A-DNA conformation in the crystals. They exhibit interesting changes in their local conformation which are brought about by base sequence and crystal-packing forces. We report here the melting behaviour and spectroscopic analysis of the metal ion interactions of Mn, Co, Mg and Al with the two deoxyoligonucleotides which were carried out to understand their structure in the solution

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Table 1. The influence of metal ions on t_m values (°C) of oligomers.

Metal/DNA	d(GCCCATGGGC) ratios					d(CCGGGCCCGG) ratios				
	Control	Mn	Al	Mg	Co	Control	Mn	Al	Mg	Co
Control	45	–	–	–	–	48	–	–	–	–
1:1	45	55	50	51	45	48	55	50	52	50
1:2	45	45	50	43	45	48	52	48	45	50
1:6	45	35	45	38	48	48	50	48	45	53
1:10	45	33	45	38	50	48	45	48	47	53
1:30	45	33	45	38	50	48	45	48	43	53

Table 2. The influence of metal ions on DNA-EtBr fluorescence.

Metal	d(GCCCATGGGC)			d(CCGGGCCCGG)		
	IC_{25}	IC_{50}	IC_{75}	IC_{25}	IC_{50}	IC_{75}
Al	2.5×10^{-4}	4.5×10^{-4}	6.5×10^{-4}	3.5×10^{-4}	6.5×10^{-4}	9.5×10^{-4}
Mg	5×10^{-6}	12.5×10^{-6}	22.5×10^{-5}	20×10^{-6}	10×10^{-5}	25×10^{-5}
Mn	2.5×10^{-7}	10×10^{-6}	30×10^{-6}	10×10^{-7}	25×10^{-6}	50×10^{-6}
Co	3×10^{-6}	10×10^{-5}	40×10^{-5}	12.5×10^{-5}	28×10^{-5}	50×10^{-5}

state. These sequences are found in several genomic DNA, promoter, heterochromatin and superhelical structures of the eukaryotic genome [17]. Human genomic organization has well-defined AT- and GC-rich DNA regions, generally designated, respectively, as heterochromatic and euchromatic DNA , or dark and light (R) G-bandings and cytogenetic banding 'flavours' in metaphase chromosomes [18]. Limited studies showed that Al causes cellular toxicity through interaction with heterochromatin regions of DNA [8], but provide no information on Al interaction with GC-rich euchromatin regions in DNA. The present study aims to show Al-specific interaction with biologically relevant GC-rich sequence-specific oligomers.

Materials and methods

The oligonucleotides d(CCGGGCCCGG) and d(GCCCATGGGC) were synthesized by the phosphoramidite technique using a 380B ABI automated DNA synthesizer. Deprotection of the oligonucleotide bases was carried out in the presence of ammonia at 55 °C for 12 h. The samples were ethanol-precipitated and freeze-dried.

Melting studies. The melting curves for d(CCGGGCCCGG) and d(GCCCATGGGC) (concentration of 2.5×10^{-5} M) were determined in 0.01 M Tris buffer (pH 7.4). Ultraviolet (UV) absorbance was recorded at 260 nm at different temperatures (1 °C/min, 15–75 °C) using a Gilford Response II UV spectrophotometer. t_m values were determined graphically from the percent hyperchromicity vs. temperature plots. The influence of metal salts $Al(NO_3)_3$, $MnCl_2$, $Co(NO_3)_2$ and $MgCl_2$ on t_m values was determined for a range of concentrations (2.6×10^{-6} M to 8.0×10^{-4} M). The precision in t_m values estimated from variance in three repeated experiments was ± 0.5 °C. To overcome the temperature-dependent Tris-buffer pH-induced melting temperature changes in DNA, the pH curve values of Tris buffer were deducted as background values from DNA and metal-DNA thermal curves using the thermal kinetic program available with the Gilford Response II UV spectrophotometer.

Circular dichroism studies. Circular dichroism (CD) spectra (210–320 nm) were recorded for d(CCGGGCCCGG) and d(GCCCATGGGC) (2.5×10^{-5} M) in 0.001 M Tris buffer (pH 7.4). The effects of the metal ion concentrations (2.6×10^{-6} M to 8.0×10^{-4} M) of $Al(NO_3)_3$, $MnCl_2$, $Co(NO_3)_2$ and $MgCl_2$ on the mean molar ellipticity values at 240 nm and 265 nm were calculated. The spectra were recorded on a Jasco J500 spectropolarimeter with 1 mm width and 5 mm cell length. The spectra at each concentration were averaged four recordings. Binding constant values were determined by the method of Formoso [19]. The metal/DNA ratios were molar ratios. DNA structures were characterized following the guidelines of Gray et al. [20].

Fluorescence studies. Fluorescence emission studies were carried out using equimolar quantities of d(CCGGGCCCGG), d(GCCCATGGGC) and ethidium bromide (EtBr) (2.5×10^{-5} M) solutions. The DNA:EtBr solutions were exited at 535 nm, and the emission was monitored at 600 nm using a JASCO J77 spectrofluorimeter. The effect of metal ion concentra-

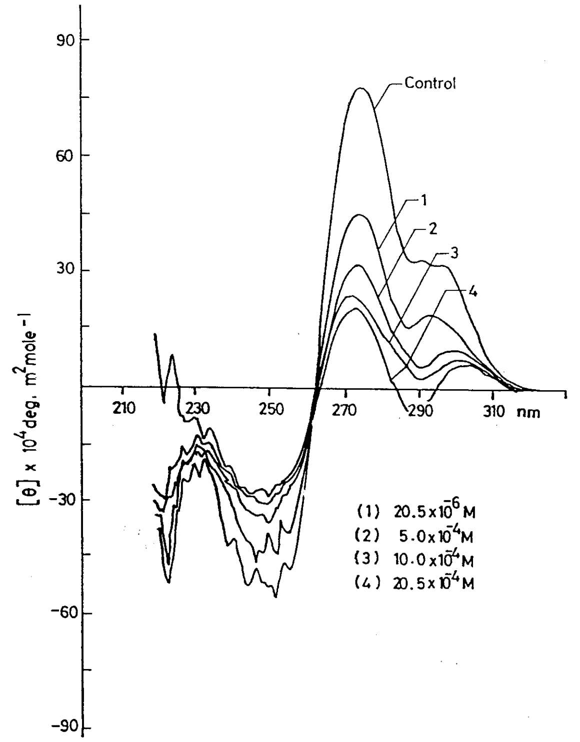

Figure 1. Effect of Al on CD spectra of d(GCCCATGGGC) in 0.001 M Tris buffer (pH 7.4). Control, 2.5×10^{-5} M DNA; 1, 20.5×10^{-6} M Al; 2, 5.0×10^{-4} M Al; 3, 10×10^{-4} M Al; 4, 20.5×10^{-4} M Al.

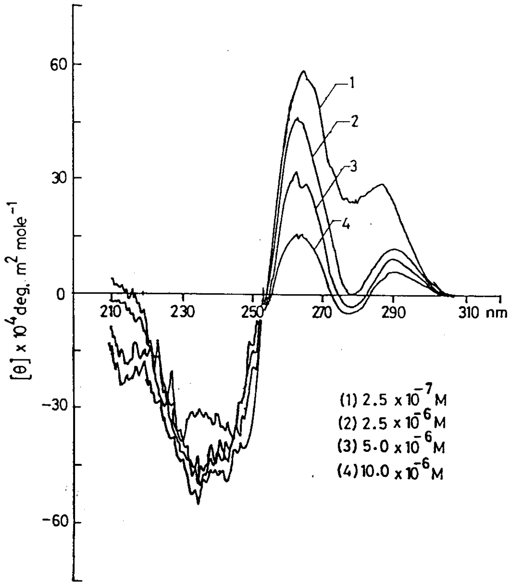

Figure 2. Effect of Mn on CD spectra of d(GCCCATGGGC) in 0.001 M Tris buffer (pH 7.4). 1, 2.5×10^{-7} M Mn; 2, 2.5×10^{-6} M Mn; 3, 5.0×10^{-6} M Mn; 4, 10.0×10^{-6} M Mn.

tions of $Al(NO_3)_3$, $MnCl_2$, $Co(NO_3)_2$ and $MgCl_2$ (2.5×10^{-6} M to 10.5×10^{-4} M) on the EtBr fluorescence was investigated.

Results

d(GCCCATGGGC)

Melting studies. The t_m value observed for d(GCCCATGGGC) was found to be 48 °C. Al at lower metal/DNA molar ratios (1 and 2) enhanced the t_m of the oligonucleotide by 50 °C and at higher ratios (>6) did not alter the t_m. Mn and Mg at 1:1 metal/DNA ratio enhanced the t_m value of d(GCCCATGGGC) by 10 and 6 °C, respectively, and at higher ratios the t_m decreased. Co at higher metal/DNA ratios increased t_m by 5 °C (table 1).

Fluorescence studies. Fluorescence emission spectra were monitored for equimolar concentrations of DNA:EtBr with and without metal ions. On addition of different concentrations of Al, Co, Mn and Mg to the d(GCCCATGGGC):EtBr solution, the fluorescence emissions decreased in a concentration-dependent manner. At high metal/DNA ratios (1:30), maximum reduction in fluorescence was observed (47% for Al, 40% for Mg, 57.6% for Mn and 53% for Co). The concentrations required to cause 25% reduction in EtBr fluorescence were 2.5×10^{-4} M, 5.0×10^{-6} M, 2.5×10^{-7} M and 30.0×10^{-6} M for Al, Mg, Mn and Co, respectively. The concentrations of metal that caused 50% reduction in fluorescence were 4.5×10^{-4} M, 12.5×10^{-6} M, 10×10^{-6} M and 10×10^{-5} M for Al, Mg, Mn and Co, respectively. Our observations show that Al displaces EtBr at higher concentrations (10^{-4} M), Mg and Co displace at moderate concentrations (10^{-6} M and 10^{-5} M) and Mn displaces at lower concentrations (10^{-7} to 10^{-6} M) (table 2).

CD studies. CD spectra of d(GCCCATGGGC) indicated the B form of DNA instead of the A form observed in crystals. Spectra observed had a negative band at 240 nm and a major positive band at 265 nm with a shoulder of broad positive band at 280 to 290 nm. On addition of increasing amounts of Al, Mg, Mn and Co to the oligonucleotide solution, the positive band observed at 265 nm decreased significantly, while the negative band observed at 240 nm increased (figs 1–4). Al at higher concentrations (20.5×10^{-6} to 20.5×10^{-4} M) altered the spectra significantly (20–80% decrease with respect to control DNA ellipticity value). In the case of Mn, lower concentrations varying from 2.5×10^{-7} M to 25×10^{-6} M caused a 15–90% decrease in ellipticity values at 265 nm (fig. 2). Co at different concentrations (2.5×10^{-6} M to 25×10^{-5} M) caused a 15–88% decrease in ellipticity values at 265 nm (fig. 3). Mg at moderate concentrations (5×10^{-6} M to 30×10^{-5} M) caused a 20–85% decrease in ellipticity

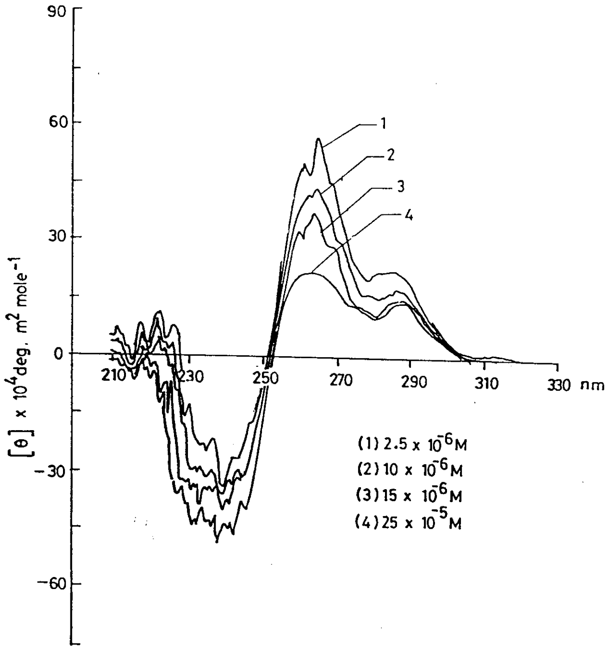

Figure 3. Effect of Co on CD spectra of d(GCCCATGGGC) in 0.001 M Tris buffer (pH 7.4). 1, 2.5×10^{-6} M Co; 2, 10.0×10^{-6} M Co; 3, 15.0×10^{-6} M Co; 4, 25.0×10^{-5} M Co.

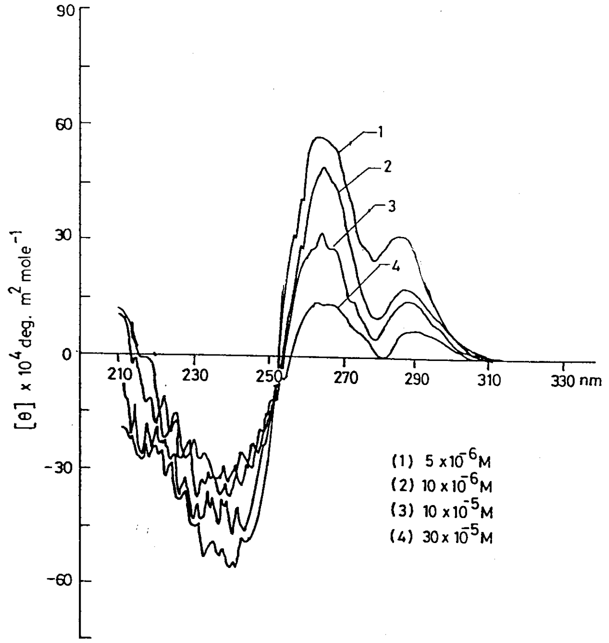

Figure 4. Effect of Mg on CD spectra of d(GCCCATGGGC) in 0.001 M Tris buffer (pH 7.4). 1, 5.0×10^{-6} M Mg; 2, 10.0×10^{-6} M Mg; 3, 10.0×10^{-5} M Mg; 4, 30.0×10^{-5} M Mg.

values at 256 nm (fig. 4). The binding constant values were found to be 4.8×10^6, 8.6×10^6, 3.8×10^6 and 4.0×10^6 for Al, Mn, Mg and Co, respectively.

d(CCGGGCCCGG)

Melting studies. The t_m value observed for d(CCGGGCCCGG) was 48 °C. Al at 1:1 metal/DNA ratios elevated the t_m to 50 °C and it did not alter the t_m at higher metal/DNA ratios, and the t_m remained the same as the control value. Mn at 1:1, 1:2 and 1:6 metal/DNA ratio elevated the t_m by 7, 4 and 2 °C respectively, while 1:10, 1:30 decreased the t_m by 3 °C. Mg at 1:1 metal/DNA ratio elevated the t_m to 52 °C, but at higher ratios, t_m decreased by 3–5 °C. Co elevated the t_m by 2–5 °C at 1:1 to 1:30 metal/DNA ratios (table 1).

Fluorescence studies. Fluorescence emissions spectra were monitored for equimolar concentrations of d(CCGGGCCCGG):EtBr in the presence and absence of metal ions. The concentrations required to cause a 25% reduction in EtBr fluorescence were 3.5×10^{-4} M for Al, 20×10^{-6} M for Mg, 10×10^{-7} M for Mn and 12.5×10^{-5} M for Co. The concentrations of metal that cause 50% reduction in EtBr fluorescence were 6.5×10^{-4} M, 10×10^{-5} M, 25×10^{-6} M and 28×10^{-5} M for Al, Mg, Mn and Co, respectively. Similarly for 75% reduction in fluorescence, the concentrations of metals required were 9.5×10^{-4} M, 25×10^{-5} M, 50×10^{-6} M and 50×10^{-5} M for Al, Mg, Mn and Co, respectively. Our observations indicate that EtBr displacements occur at relatively low concentrations of Mn (10^{-7} to 10^{-6} M), moderate concentrations of Mg and Co (10^{-5} M) and relatively high concentrations of Al (10^{-4} M) (table 2).

CD studies. CD spectra of d(CCGGGCCCGG) indicated a Z form of DNA (fig. 5). Mg at different concentrations (15×10^{-6} M to 7.5×10^{-4} M) caused Z–B transition (fig. 5). Co at higher concentrations (2.9×10^{-5} M and 5×10^{-4} M) converted the Z form of DNA to the B form of DNA (fig. 6). On the other hand, Al at higher concentrations (3.2×10^{-5} M to 5.0×10^{-4} M) converted the Z form of DNA to the A-form (fig. 7). Mn at different concentrations (5.0×10^{-5} M to 5.0×10^{-4} M) did not induce any transition except a decrease in ellipticity values at 260 nm (fig. 8).

Discussion

Upon interaction with metal ions, the DNA molecule shows significant changes in structure and conformation. The binding potential of metal ions to DNA is greatly influenced by the physicochemical properties of

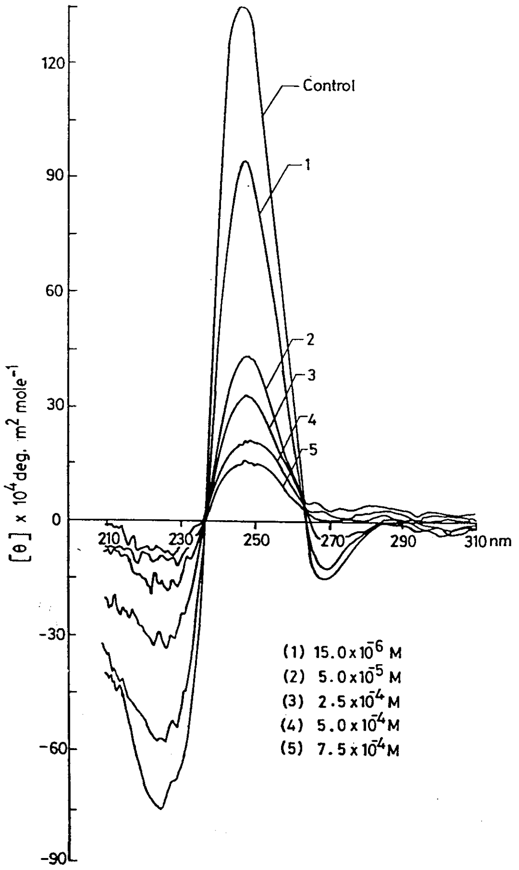

Figure 5. Effect of Mg on CD spectra of d(CCGGGCCCGG) in 0.001 M Tris buffer (pH 7.4). Control, 2.5×10^{-5} M DNA; 1, 15.0×10^{-6} M Mg; 2, 5.0×10^{-5} M Mg; 3, 2.5×10^{-4} M Mg; 4, 5.0×10^{-4} M Mg; 5, 7.5×10^{-4} M Mg.

the metal ions as well as the base sequence of the DNA. The divalent metal ions Mg, Mn and Co with, relatively small ionic radii, strongly interact with the DNA [16]. Although these metals are required for a number of biological functions, at higher concentrations they are reported to change the handedness of DNA [1–6]. Al has no established biological requirement and is implicated in many neurological disorders. Intranuclear accumulation of Al has been shown in the neurons of patients with neurodegenerative disease [7–8]. However, there are no reports on Al-induced changes in the handedness of DNA [21].

Mg, Mn and Al each have a coordination number of 6, their preferred geometries are octahedral and their biological ligands are oxygen, phosphates and carboxylates. Co has a coordination number of 4, tetrahedral logical ligands are oxygen, phosphates and carboxylates. Co has a coordination number of 4, tetrahedral geometries and its biological ligands are sulphur and thiolates. The solvent exchange rates $K_{ex(S-1)}$ for inner-sphere water molecules in metal ions are: Al (10^0); Mg (10^5); Co ($10^{5.5}$) and Mn ($10^{6.7}$) [22]. The order of increasing rate constants in acidic solution is Al < < Mg < Co < Mn. Ligand exchange rates take on special importance for Al because they are slow, and the system may not be at equilibrium. Mg, Mn and Co have exchange rates around 10^5 faster over Al. These differential characteristics of metals may play a crucial role in metal-DNA interactions [22].

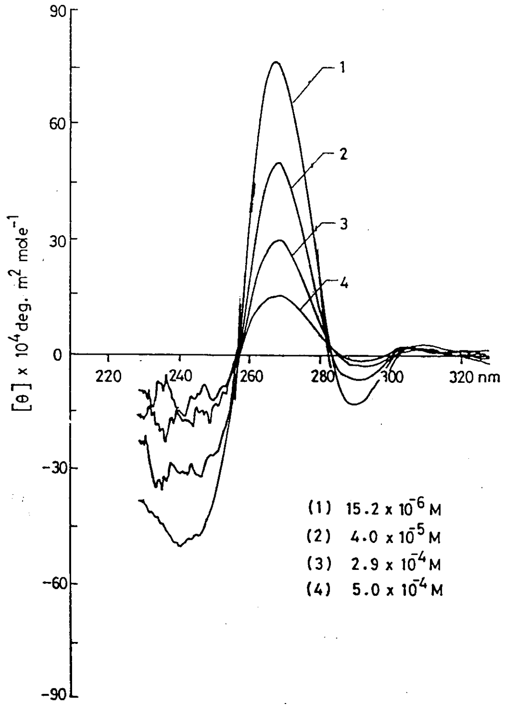

Figure 6. Effect of Co on CD spectra of d(CCGGGCCCGG) in 0.001 M Tris buffer (pH 7.4). 1, 15.2×10^{-6} M Co; 2, 4.0×10^{-5} M Co; 3, 2.9×10^{-4} M Co; 4, 5.0×10^{-4} M Co.

In the present study, we have studied metal ion (Al, Mn, Mg, Co) interaction with two biologically important oligomers. The two sequences, d(CCGGGCCCGG) and d(GCCCATGGGC), have little sequence similarity, but have a similar GC content (80%). The t_m values of the two sequences were 48 and 45 °C, respectively. The difference of 3 °C between the two values is significant and can be attributed to the presence of two hydrogen bonds in an *A-T* as compared with three in the G-C base pairing. The metal ions Mn, Mg and Al at the lower metal/DNA ratios (1:1) enhanced the t_m of both oligomers. But higher metal/DNA ratios (1:6, 1:10, 1:15) of Mn and Mg decreased the t_m of these oligomers. Al did not alter the t_m at higher metal/DNA ratios. Co enhanced the t_m of oligomers at all metal/DNA ratios studied. It was earlier reported that Al did not alter the t_m of DNA, and Mg was found to enhance the t_m of genomic DNA [10]. Rajan et al. [16] reported that Al did not alter the t_m of the DNA sequence

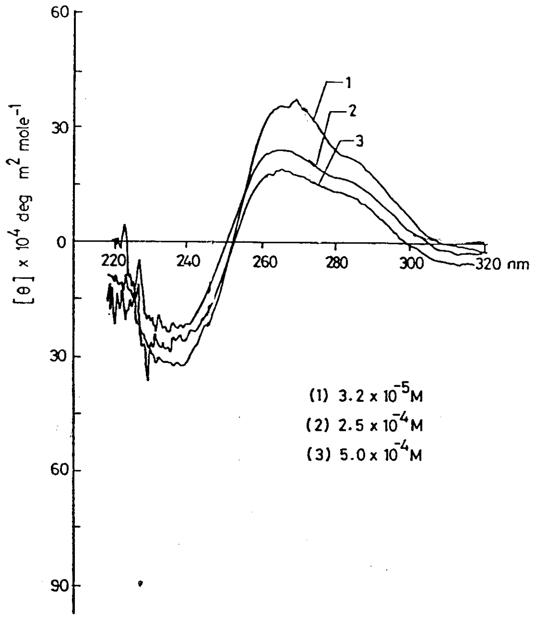

Figure 7. Effect of Al on CD spectra of d(CCGGGCCCGG) in 0.001 M Tris buffer (pH 7.4). 1, 3.2×10^{-5} M Al; 2, 2.5×10^{-4} M Al; 3, 5.0×10^{-4} M Al.

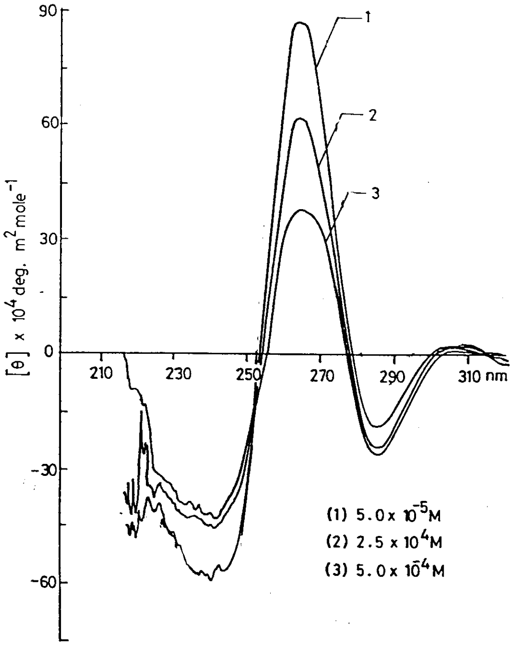

Figure 8. Effect of Mn on CD spectra of d(CCGGGCCCGG) in 0.001 M Tris buffer (pH 7.4). 1, 5.0×10^{-5} M Mn; 2, 2.5×10^{-4} M Mn; 3, 5.0×10^{-4} M Mn.

d(GCGTACGC) at both lower and higher metal/DNA ratios. Reports also indicated that lower concentration of Mn enhanced t_m and higher concentrations decreased t_m, while Co enhanced the t_m of genomic DNA irrespective of ionic strength [12]. In general, divalent metal ions bind with greater affinity as a result of higher charge. The binding of positively charged counterions by nucleic acids is a natural consequence of a polyanionic sugar-phosphate backbone. Metal ions alleviate electrostatic repulsion between phosphates, thereby stabilizing base pairing and base stacking. This is most clearly evidenced by the increase in melting temperature and hypochromism, respectively. In contrast, transition metals that have higher affinity for heteroatoms on the bases tend to lower base pairing and stacking. Thus, they destabilize the double helix, and t_m values come down. The alkali or alkali earth metals neutralize repulsive interactions between the negatively charged sugar-phosphate backbones and stabilize the interactions between base pairs. This further stabilizes the hydrogen bonding that pairs the two strands, resulting in higher melting temperatures and leads to enhanced base stacking with increased hypochromism [22]. The potential reactive sites found on the DNA molecule are (i) heterocyclic nitrogen atoms, (ii) exocyclic carbonyls on the purine and pyramidine bases and (iii) the phophate oxygens. PO_3^- and base binding have rather different consequences for the structure of the bound DNA. Generally PO_3^- binding stabilizes the double helix, while base binding causes the double helix to unwind. Electrostatic forces play a major role in the stability of double-stranded structures, and the double helix can be considered to be in equilibrium under two types of opposite forces. The flexibility of a double-stranded structure will increase with the ionic strength. In low ionic strength, the formation of an ion pair between the PO_3^- and the counter ion or anion and water shell plays a critical role in the interaction of metal with DNA. However, in the presence of high ionic strength, the negative potential will vanish very close to each PO_3^- group. Accordingly, the anions, which were excluded under low ionic strength, can penetrate the grooves of the double helix, together with the cations, facilitating van der Waals interactions with the bases. Changes in the melting profile of oligomers thus indicate that binding of metal ions to DNA affects the thermal stability of the oligomers in different ways based on metal ion charge, ionic radii and coordination potential [23].

Another very useful spectroscopic technique employed to study metal ion effects is the reduction of EtBr fluorescence. EtBr intercalates between the DNA bases and in doing so produces fluorescence [24]. In addition to intercalation, EtBr also shows phosphate binding. Fluorescence studies on metal/DNA interactions indicated that Mn reduces EtBr fluorescence at relatively low concentrations, Mg and Co at moderate concentrations and Al at higher concentrations. According to

Lepecq and Paoletti [24], EtBr at low salt concentrations shows a second mode of binding, which appears to be electrostatic binding of the cationic dye to negatively charged phosphate groups. Since metal ions show a greater affinity for phosphate groups, the displacement of EtBr from the bound PO_3^- sites might be the reason for the reduction in fluorescence emission. The effect of cations on the stability of the double helix may enhance the overall effect of metal ions in reducing fluorescence. Metal ions caused reduction in EtBr fluorescence in both oligomers which could not be attributed to a change in handedness of DNA because the metal ions induced transitional changes only in d(CCGGGCCCGG), and in the other oligomer there was no change in the handedness of DNA.

In the present study, the CD spectra of the d(CCGGGCCCGG) sequence indicated a Z form of DNA in solution. Divalent cations such as Mg and Co induced Z–B transition at higher ionic strength, while Mn did not promote any transition. Trivalent Al induced a Z–A transition in the above oligomer at higher concentrations. However, all four metal ions showed strong binding to the d(GCGTACGC) oligomer as evidenced by binding constant values, but these metal ions did not bring any structural transition from the B-DNA form. There are very limited studies in the literature on metal-induced transitions in sequence-specific oligomeric DNA. Previous studies on metal-induced conformational transitions in poly(G-C) and poly d(A-T) indicated the following trends. Divalent Co was found to cause B–Z transition in poly d(G-C), while Mg, Mn and Co at higher concentrations were also found to promote Z conformation in poly d(G-C) [25–28]. It has been reported that Tb, Eu, Mn, Co and trivalent complexes of group VIIIB metals (rhodium and ruthenium) are capable of inducing the Z-DNA conformation [29–31]. Devarajan and Shafer [32] reported that Mg at lower concentrations caused left-handed forms in poly(dG-m5dC), while higher concentrations induced right-handed conformations.The higher concentrations of Mg and cobalt hexamine were found to cause B–Z transitions in poly(dG-dC) [33]. Behe and Felsenfeld [34] reported that heavy metals cause B–Z transition in poly(dG-dC) and poly(dG-m5dC) in the presence of Na. Rajan et. al. [16] reported that Co, Mn, Mg and Al show a strong binding affinity to d(GCGTACGC), but CD spectra clearly indicated no structural transitions. The oligomer exhibited the B form of DNA. However, the addition of EDTA to the metal-DNA complexes of Co, Mn and Mg caused modified B-DNA structure with two positive peaks at 265 and 290 nm. Rossetto and Nieboer [6] reported that Pd, Al and Pt did not cause a sharp or well-defined transition in poly d(G-C). Although the interaction of divalent cations with DNA has been studied extensively [5–10], DNA complexation with trivalent cations is less well understood. It was shown that the interaction of Al with DNA produces several types of Al-DNA complexes depending on pH and metal ion concentration [21]. However, the exact cation binding site and the effect of Al interactions on DNA secondary structure have not been determined, particularly at low cation concentrations. Ahmed et al. [35] showed via FTTR spectroscopy studies that Al at low metal ion concentrations ($r = 1/80$, $1/40$) binds mainly to the backbone PO_2 group and the guanine N-7 site of the G-C base pairs (chelation). Evidence for cation chelate formation comes from major shifting and an intensity increase of the phosphate antisymmetric stretch at 1222 cm^{-1} and the mainly guanine band at 1717 cm^{-1}. The perturbations of A-T base pairs occur at high cation concentrations with major helix destabilization. Evidence for cation binding to A-T bases comes from major spectral changes of the bands at 1663 and 1609 cm^{-1} related mainly to thymine and adenine in-plane vibrations. A major reduction of the B-DNA structure occurs in favour of A-DNA upon trivalent cation coordination. Recently, Martin [36] indicated that the nitrogenous bases of DNA and RNA do not bind Al(III) strongly. The weakly basic phosphate group of DNA binds A(III) weakly, while the basic and chelating phosphate groups of nucleoside di and triphosphates do bind Al strongly. The reasons attributed for structural changes in DNA are metal specific binding sites on DNA (base nitrogen, phosphate oxygen). It is known that Mg binds to PO_3^- and the N7 atom of the nucleic acid base via a water bridge [37], while Mn binds to the PO_3^- and N7 site of the bases through the participation of a C_6-NH_2 group [36]. Co binds to the PO_3^-, C_6-NH_2 and C_5-OH groups of the bases [38], whereas Al binds only to the PO_3- moiety [10]. There are no definite mechanisms available in the literature to explain the role of metals in causing structural transitions. It has been suggested that reduction of DNA phosphate repulsion (charge screening) and polymer hydration state are important determinants of conformational and structural transitions in DNA [39]. Rossetto and Nieboer [6] propose that metals that bind to nitrogen bases facilitate DNA structural transitions. Drew et al. [40] propose that transition in DNA structures occurs by lowering the activity coefficient or the effective concentration of the surrounding water molecules. Daune [41] reported that metal ions cause the transition due to the formation of an ion pair between the phosphate group of DNA. The counterion as predicted by the electrostatic theories is accompanied by a distribution of electrical potential causing a rearrangement of water molecules around the ion pair. Some molecules of water were migrating from inside a closely packed hydration shell to the normal open structure of water.

Our studies on the interaction of Co, Mn, Mg and Al with d(GCCCATGGGC) and d(CCGGGCCCGG) indicate the strong binding of these metal ions to DNA with a structural transition in d(CCGGGCCCGG). Previously, our group reported that Al uncoils the superhelical state of DNA [9], and the present work provides a clue that Al may uncoil supercoiled DNA by possibly interacting with the above sequences, as they are widely present in supercoiled pockets of DNA. Further studies are required to explain the sequence-dependent effect of metal ions on DNA, which may enhance our knowledge of the role of metal ions in the structure and function of DNA.

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