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Metal Ions - Nucleic Acid Interactions: Mechanism and Biological Significance

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Abstract

This review's primary objective is to acquaint nucleic acid experimenters with the physical principles underlying interactions between nucleic acids and ions. But further research is needed to completely understand the specifics of how RNA interacts with metal ions. The fact that ion interactions with nucleic acids cannot be simply switched between similarly charged ions is support. Given that different structures are solved under a wide range of ionic circumstances, it is important to carefully consider the physiological significance of RNA-ion interactions, which primarily involve K^+ and Mg^{2+} cations. The analysis is made more challenging by the fact that the assignment is frequently imperfect and completed under unfavourable circumstances, which further restricts the generalization about the kinds of interactions these ions can have. What is known as an ion atmosphere is composed of ions that surround nucleic acids. The underlying behaviour of the ion atmosphere, however, is governed by physical principles that are different from the site binding principles with which biochemists are most familiar.

Keywords: DNA, Metal Ions, DNA-Metal Ion Interactions, Tris-HCI Buffer, DNA Binding Site.

1. Introduction

Nucleic acids basically are known as 'nuclein' as they extracted from the white blood cells present in pus by F. Miescher in 1869. The term nucleic acid was introduced 20 years following Miescher's discovery by another biochemist, Richard Altmann.

Two species of Nucleic Acid were found in nature.

a) DNA (Deoxyribose Nucleic Acid)
b) RNA (Ribose Nucleic Acid)

DNA is a very long thread like macromolecule made up of large no. of deoxyribose nucleotide, each composed of base sugar and phosphate group. DNA is generally double stranded as in case of many animal cells, but in some case, it is single stranded too, for example spherical shaped S13. Viruses, rod shaped F1 and M13 viruses etc. It can be linear or circular. The classic experiment of Avery in 1944demonstrated that DNA possess genetic information of all living organism except RNA. [1] The first model of DNA that explains the role of DNA as the hereditary was material was enunciated by Watson and Crick. [2-6]

- **Chemical Composition of DNA**

DNA is composed of heterocyclic aromatic base (purine and pyrimidine), sugar and phosphate group:

- **Bases:**

a) **Purines:** Adenine and Guanine (Composed of carbon and nitrogen) Adenine and Guanine are double ring ring bases called purine. Adenine has an amino group (- NH2) on the C6 position of the purine ring (carbon at position 6 of the purine ring). Guanine has an amino group at the C2 position and carbonyl group at the C6 position (Figure 1).

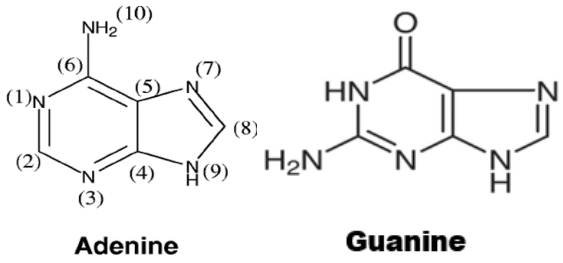

Fig 1

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b) Pyrimidines: Thymaine, Cytosine and Uracil (Composed of C and N)

Thymine, cytosine and uracil are the single ring bases called pyrimidines. Thymine contains a methyl group at the C_5 position with carbonyl group at the C_4 and C_2 position. Cytosine contain hydrogen atom at the C_5 position and amino group at C_4 position uracil is similar to thymine but lacks the methyl group at the C_5 position uracil is not found in DNA but it is componant of RNA. (Figure 2)

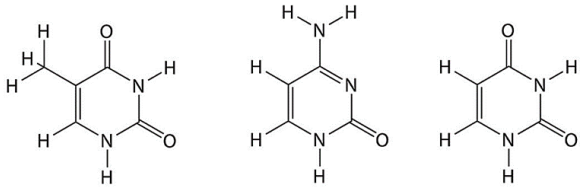

Fig 2

ii). Sugars

i). Ribose sugar is found in RNA.

ii). Deoxyribose sugar is found in DNA.

The sugar moiety of DNA is one of the more flexible and dynamic parts of the molecule. (Figure 3).

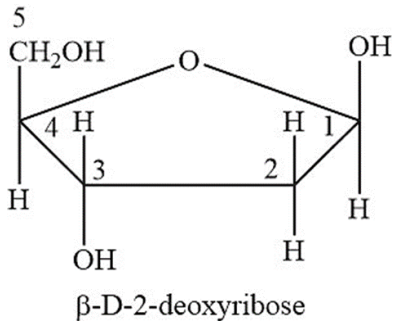

Fig 3

iii). Nucleosides and Nucleotides

Nucleotides – adenosine, guanosine, thymidine and cytidine are the terms given to the combination of base and sugar. The term nucleotide refers to the base, sugar and phosphate group in which the phosphate group is attached to the 5' carbon of the ribose. [4]

2. Resume of Relevant Literature

The human genome consists of about 100,000 different genes in association with the regulatory region as the thread of life and in chemical terms a deoxyribonucleic acid (DNA). The genetic alphabets comprising of the four bases, two purines, A and G and two pyrimidines, T and C joined together by deoxyribose phosphate linkages makeup this thread- The molecule that determines the life processes in a living cell. The present knowledge of the structure of this DNA and other biomolecules as well as their mutual interaction would be the prerequisite to study life processes what follows is a brief review of the same.

i). DNA: Structure

The correct structure of double helix DNA was first deduced by J. D Watson and F.H. Crick 1953 (6). Their double helix model of DNA structure was based on two major kinds of evidences:

a) One of which was Chargaff rule (7) - when the composition of DNA from many different organism was analysed by E. Chargaff and colleagues.
Chargaff point out that the concentration of thymine was always equal to the concentration of the adenine and the concentration of the cytosine was always equal to the concentration of guanine. This strongly suggested that thymine and adenine as well as cytosine and guanine were present in DNA with some fixed relationship. Of course, it also necessitated that the total concentration of pyrimidines (T and C) always equal to the total concentration of purines (A and G).

b) Franklin, Gosling, and Wilkins (8, 9, 10). The cross pattern in the fibre diffraction method of DNA by Franklin and Gosling as well as Wilkins indicating clearly the helical structure of the molecule. According to this method the geometric shape of the DNA is a right-handed helix. Watson and Crick (6) used this information to deduce a model for the structure of DNA. According to this model. The diameter of the helix is 20 A and the distance between adjacent base pairs along with helix axis is 3.4 A. There are 10 residues per helical turn and the intrastrain phosphate-phosphate separation is 7 A. The base pairs are perpendicular to the helix axis. Watson and Crick may be pointed out, had not only given the structural model but went on to show how this model explains the role of DNAs in the life processes. It was only two decades later, in 1978 that Vishwaamitra *et al*. (12) and Sanger (11) gave the first-evidence for the W.C. base pairing scheme from the crystal structure of the tetranucleotide (dA-dT)2

ii). Hydrogen Bonding and Base Stacking Hold the DNA Double Helix Together

A hydrogen bond is a short, noncovalent, directional interaction between a covalently bound H atom (donor) that has some degree of positive charge (due to attachment to a nitrogen or oxygen atom) and a negatively charged acceptor atom. In the A.T base pair are two hydrogen bonds (figure 4) that are separated by 2.82 and 2.92 A.

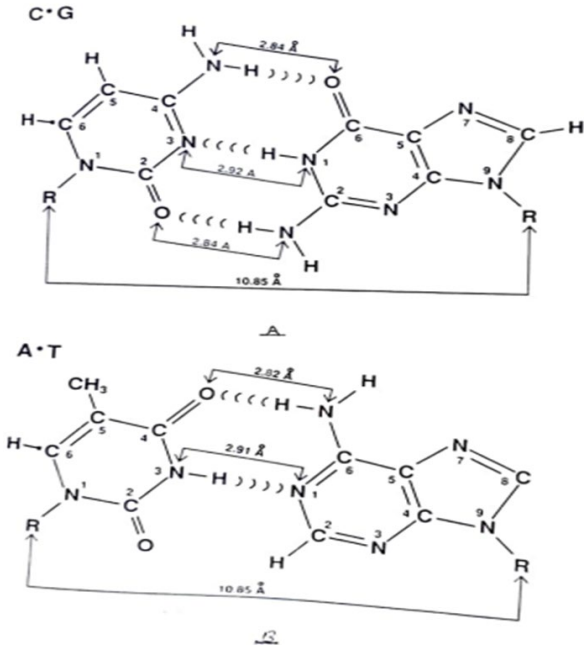

Fig 4

iii). DNA: Interactions

Nucleic acid are rarely found alone for any biological function, they have to interact with metal ions, proteins, ligands etc. these interactions are mainly of the following types

- DNA-metal ion interaction
- DNA-protein interaction
- DNA-ligand interaction

DNA – Metal Ion Interaction:

DNA forms compounds with various ions of metal through interaction. The process of DNA replication, transcription, m-RNA translation, etc. all are dependent upon the interaction of metal ions with nucleic acids. If metal -ions contact with bases rather than groups of phosphates, however, they can potentially destabilize the double helical structure of DNA. The affinity for base complexation compared to phosphate binding improves from left to right in the order: Mg^{+2}, Ni^{+2}, Cd^{+2}, and $Cu^{(+2)}$. The Tm doubles with the addition of $Mg^{(+2)}$, showing increased stability of the double helical helix. $Cu^{(+2)}$, on the other hand, significantly decrease and the Tm which encourages the change into the random coiled condition. $Cu^{(+2)}$, on the other conjunction, additionally encourages renaturation. Phosphate oxygen, ribose hydroxyl, base ring nitrogen, and keto substitutions are the four distinct binding sites provided by nucleotides for a metal ion. The coordination of metals is not done by amino groups. Alkaline earth cations prefer phosphate oxygen and sugar hydroxyl over base nitrogen, although transition metals bind to both of these compounds.

Table 1: Occurrence of Metal Ions in the Human Body, in the Blood Plasma, and in Intracellular Fluid [3]

Cation	Total Concentration in Body (g/70 Kg)	Blood Plasma (m mole/litre)	Intracellular (m mole/litre)
Na	100	142	10
K	140	4	160
Ca	1100	3	1
Mg	35	1	13
Fe	4	0.018	-
Cu	0.15	0.016	-
Zn	3	0.018	-
Mn	0.02		
Co	0.001		
Mo	≤0.001		

Table 2: Metal Ions Interacting and Crystalizing with nucleic Acid Constituents and Preferred Binding Sites.

Alkaline Li, Na, K, Rb, Cs
Alkaline earth Mg, Ca, Sr, Ba
Transition metals Mn (+2), Ru (+3), Os (+4 as osmate), Co (+2), Ni(+2), Pd (+2), Pt (+2),Cu(+2), Ag(+1), Au(+3), Zn(+2), Cd(+2), Hg(+2)
Preferred binding sites:
Base keto oxygen and ring nitrogen
Phosphate oxygen
Sugar hydroxyl

The affinity of metal ions for nucleotide binding sites is rather specific, complexation to purine N7 accommodating sixfold coordinated metals whereas Pyrimidine N3 allows only lower coordination numbers. In purine bases, imidazole nitrogens are better ligands than pyrimidine nitrogens.

Nucleic acids contain four different potential sites for binding of metal ions-(Figure 5):

i). Negatively charged phosphate oxygen atoms
ii). The ribose hydroxyls
iii). The base ring nitrogens
iv). Exocyclic base keto groups

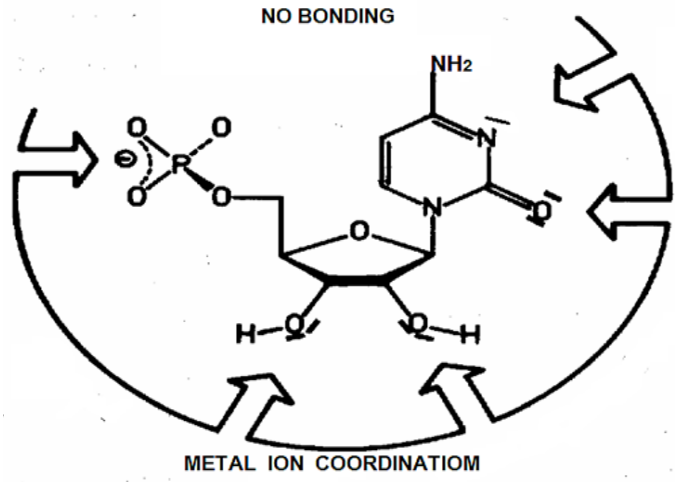

Fig 5: Schematic description of metal ion coordination sites on a nucleotide

i). **Phosphate Groups:** In living cell, the bivalent metal ions are coordinated to the phosphate groups of nucleotides. These can in general bind to all the metal ions to form complexes between positively charged metal ion and negatively charged phosphate oxygen's. [10]

ii). **Sugar Hydroxyls:** The Pentose ring of nucleotide is a poor ligand for metal coord1ination.

iii). **Heterocyclic Nitrogen of Base:** Since these atoms carry lone electron pairs, they are good ligands for Alkali and transition metals and also for alkaline earth cations. :

Table 3: -Matalation site on the nucleoside.

Compounds	Common Coordination Site	Additional Site
Adenosine	N7	N1
Guanosine	N7	O6, N1
Uridine	N3	O2, N4
Cytidine	N3	N2, OH

iv). **Base Keto Substituent:** These are able to contribute to complex formation with metal ions. In pyrimidine nucleotides, direct metal ion binding to O2 (Cytosine) or to O2, O4 (Thymine, Uracil) takes place. In contrast, in the purine systems guanine and hypoxanthine, O6 is generally not involved in direct metal binding, probably because N7 is a better ligand and simultaneous coordination of N7 and O6 would lead to unfavourable geometry (28).

Condensation of DNA

One of the very important aspects of DNA structure itself is the deoxy sugar-phosphate backbone in which the bases are attached to give a strand which intertwined with another complementary stand, in which for every A there is a T to pair with and vice-versa and every C pairs with a G and vice-versa and this long chain single molecule occupies each cell. To take the example of a human cell, it has 4.6 x 10° bp having a length of 1.8 meters occupying a spheroid of 0.06 um diameter nucleus and controls life itself. It is obvious that DNA is somehow packed into this small volume and the compaction or condensation or packaging is understood to be mediated by other molecules. Mainly identified as proteins.

The molecular function takes place within the nucleus of this flexible system. Although, a one-to-one correlation is not available on the way in which these molecules play their role.
As we know that DNA is made up of thousands of base pair in each organism whether it is prokaryote or Eukaryote. So, they can't remain as it is as long strands of polynucleotide in the nucleus because the size of the nucleus is not So big so that these long strands of base pairs can remain in it as it is. So, their condensation is necessary. It occupies less space. The inorganic cation (43) Co (NH,)Å* and cationic polypeptide (44-46) such as polyline and histone HI. Eukaryotic chromosome undergoes condensation and condensation cycle at cell division, whereas the DNA of prokaryotic is never cycled in this way. This constitute specific difference between prokaryotes and eukaryotes as a result of which the DNA of the latter can be, replicated continuously in fast growing culture. During interphase, the chromosome are decondensed and cannot be distinguished under the microscope. Using the experimental trick, however, it 1s possible to induce the condensation of chromosome in all three stages of interphase. Mitotic cells fused to interphase cells are able to induce premature chromosome condensation in the interphase nuclei. During metaphase, chromosomes are highly condensed chromosome easily appear within the cell under the microscope. Condensed chromosome does not synthesize RNA(47,48).
As already stated most DNA in living organism is present in highly packed state with positively charged species such as histone or polyamine serve to stabilize the conformation by neutralizing electrostatic repulsion. This condensation protects the DNA from various enzymes and external danger like radiation. Besides histones and polyamines, condensation of DNA is also induced by Poly (Lys), Poly (Lys-Ala), divalent metal ions and the inorganic cation Co (NH.)3* etc.. Monovalent cations condensation is implicated in the stability and multivalent cations such as polyamine, spermine (4°) or spermidine (3*) stabilise the DNA double-helix (generally in its B form) and lead to its precipitation (50-52). Ethanol which is used as a precipitate in the purification of DNA induce condensation at controlled conditions (53,54). The neutral polymer, poly (eth1ylene glycol) produces a supra molecular structure in the presence of salt. The resulting structure has been termed as PSI. DNA (y DNA) (The acronym for polymer and salt induced). DNA condensation is also induced by anionic polymer such as polyepitope, polyglutamate and anionic peptides found int the capsid of bacteriophage T4 (56).
Electron microscopic technique were used by many research groups study the morphology of condensed particles. In general, two types o morphology have been observed Toroid's and rods. Marx and Ruben (59) have shown by frees etch electron microscopy, that DNA is toroid condensates circumferentially wrapped, each DNA molecule winds several times around the toroid's parallel to the helix axis. Erickah *et al*. (60) formed this coiling as homogenic coiling because only one DNA helix is continuously bending unlike the plectonemic structure in native supercoiled DNA. They suggested a change in the form of angle between consecutive base pairs in such a manner that the conformation of the helix inside the coiled structure is more like the C-form than B form(61).
Rod type structures form when small nucleotides are associated perpendicular to the helix axis or due to the specific band in long nucleic acid at different regions. The formation 0f particular structure toroid or rod was found to be independent of the condition in which the condensation was induced. Toroid formation in preferred over rod shape in most of the cases studied. The condensation of nucleic acids can result into two structures p +) and p () which are characterised by the appearance of very intense band in the C.D spectra in the 260-300 nm region, the signs indicating whether the bands are in the positive or negative region. Change *et al*. suggested that the unusual optical properties of o state many originate from a cholesteric or twisted nematic liquid crystalline structure and Leman presented detailed microscopic evidence for this arrangement. The cholesteric structure comprising the major ordered arrangement of DNA consists of a layer of parallel double helix stacked together with a slight twist between the layers so that the helix axis in the successive layers are not parallel but rotated through a small angle relative to each other. Repetition of this rotation generates a supramolecular helical array, whose asymmetry affords the anomalous optical activity. The tailing of the C.D at >300 nm is also suggested to be a proof of the liquid crystalline nature of DNA. (63)

Packaging the giant DNA Molecule into the Chromosome

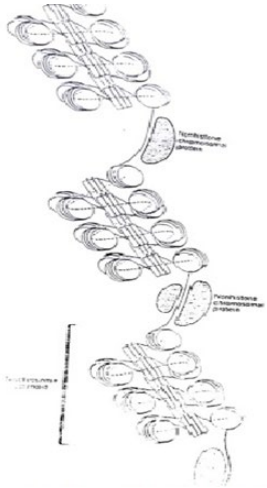

Fig 6: Between successive solenoids, nucleosome-free DNA may be solenoid with nonhistone chromosomal proteins

Each DNA molecule in packed in a separate chromosome and the total genetic information stored in the chromosome of an organism.. Isolated chromatin found to consist of series of elliptical "beads joined by thin threads. This bead of chromatin subunit is called nucleosome. Nucleosome are the fundamental organisational unit in eukaryotic cell (Nucleus). The nuclear DNA is highly compacted through its association with histone proteins (65). At the first level of organisation nucleosome are formed by the association of DNA molecule and protein. Each nucleosome contains eight histone molecule, two copies each of H2A, H2B, H3 and H4. The histone forms a core of nucleosome in which the 2 nm thick molecule of DNA is wound to form a left-handed super helix of diameter 10.8 nm and pitch 2.8 nm.**(Figure 6)** The DNA makes two turns around the histone Core. Each turn consists of about 83 base pair. Successive nucleosomes are connected by linker DNA. Linker DNA are the susceptible to nuclease attack after partial nuclease digestion of chromatin and appear 200 nucleotide pair length of DNA is found in association with each nucleosome (produced by cleavage in each linker region).
After extensive nuclease digestion, a 146-nucleotide pair long segment f DNA remains present in each nucleosome. This

nucleosome reside (1) structure is called the nucleosome core (Figure 6). The complete chromatin subunit consists of nucleosome core and linker DNA, an average of one molecule of histone HI and the associated non histone chromosomal proteins

The histone core is an octamer consist of two each of 4 histone molecules (H2A, H2B, H3 and H4). The DNA forms nearly two complete turns around the core. The fifth histone (H1) interacts with the DNA at its entry and exit point on the nucleosome. Although the structure of histone 0ctamer and nucleosome core partial is now well documented and understood. Nucleosome arrays interacts with linker histone to form a highly folded transcriptionally repressive 30 nm diameter chromatin fibre and with different chromatin associated protein to form other type of specific functional chromosomal domains. The structure form by linker stone containing nucleosome arrays after they fold into highly condensed, higher ordered 30 nm fibre has long been sought but still remain unsolved.

At least 3 level of condensation are required to package the 10 to 105 um of DNA in a eukaryotic chromosome into a metaphase structure.

i). The first level of condensation involves packaging DNA as a super coil. (DNA folding in prokaryotic cells and formation of solenoid in eukaryotic cells. is called supercoiling) into nucleosome. This produces the 100 Å diameter interphase chromatin fibre. This clearly involves an octamer of histone molecule, two each of H2A, H2B, H3 and H4.

ii). The second level of condensation involves an additional folding and/or supercoiling of the 100 Å nucleosome fibre to produce the 300 Å chromatin fibre characteristic of mitotic and meiotic chromosome. H1 is involved in this supercoiling of 100 Å nucleosome fibre to produce the 300 Å chromatin fibre.

iii). Finally, the non-histone chromosomal protein form a scaffold that is involved in condensing the 300 Å chromatin fibre into the tightly packed metaphase chromosome. This third level of condensation appear to involve the segregation of segment of giant DNA molecule present in eukaryotic chromosome into independently supercoiled domains or loops.

3. Objectives of the Work

i). To study about the interaction between metal ions and nucleic acids: The main aim of this work is to understand why metal ions interact with nucleic acids like DNA and RNA and explains the type of coordination between metal ions and nucleic acid molecules and their effect on their structure and behaviour

ii). To identify the binding sites of metal ions in nucleic acids: The other crucial significant of this study is to find the exact position where metal ions combine in DNA molecules. Metal ions may bind with phosphate groups, nitrogen atoms, oxygen atoms, or nucleic acid.

iii). To study about the different types of interactions: This work also aims to invest different route by which metal ions bind with nucleic acids, such as electrostatic interaction, coordination bonding, intercalation, and groove binding.

iv). To study the medicinal importance of metal–nucleic acid interactions: Another objective is to understand the role of metal ions and metal complexes in medicine. Many metal-based drugs interact with DNA and show anticancer, antimicrobial, and antiviral activities. Studying these interactions may help in the progression of new and better medicines.

v). To investigate the hazardous effects of toxic metals on nucleic acids: This study also aims to describe the study how toxic metal ions like lead, mercury, and cadmium damage DNA and RNA molecules. These harmful effects may cause mutations, genetic disorders, and other diseases. Understanding metal toxicity is important in health and environmental studies.

vi). To study the experimental methods used in metal ion–nucleic acid research: Another objective is to understand different analytical and experimental techniques used for studying these interactions. Methods such as spectroscopy, potentiometry, X-ray crystallography, electrophoresis, and computational studies help in finding binding sites and structural changes. [63-65]

4. Material and Methods

The various DNA samples and reagents used during the course of study are:

i). Calf Thymus DNA
ii). Sodium phosphate buffer
iii). Tris-HCI buffer
iv). Different monovalent cations
v). Different divalent cations

These all chemicals are of analytical grade.

vi). Stock solution of Calf Thymus DNA - 1.3 mg/ml in distilled water (9610 uM conc.) These stock solutions were stored in the refrigerator at 4°C.

UV-Absorption Spectroscopy

Molecules absorb light. The wavelengths that are absorb the efficiency of absorption depend on both the structures environment of the molecules, making absorption spectroscopy or useful tool for characterizing both small and large macromolecules.

Theory of the Absorption of Light by Molecules

Light in its wave aspect, consists of mutually perpendicular electric and magnetic fields which oscillate sinusoidally as they are propagated through space.

$$E = \underline{hc}/\lambda = hv$$

The energy E of the wave is in which h is Planck's constant, C is the velocity of light, & is the wavelength and v is the frequency. When such a wave encounters a molecule, it can be either scattered (i.e., it's direction of propagation changes) or absorbed (i.e., its energy is transferred to the molecule). If the electromagnetic energy of the light is absorbed, the molecule is said to be excited or in an excited state, A molecule or part of a molecule that can be excited by absorption is called a “chromophore". This excitation energy is usually converted into heat (Kinetic energy) by the collision of the excited molecule with other molecules e.g., a solvent molecule). With some molecules it is remitted as fluorescence. In both cases, the intensity of the light transmitted by a collection of chromophores is less than the intensity of the incident light. An excited molecule can possess anyone of a set of discrete amounts (quanta) of energy described by the laws of quantum mechanics. These amounts are called the energy levels of the molecule. There are electronic energy levels, vibrational levels and rotational

levels present which are usually described by an energy level diagram. The lowest electronic level is called the ground state and all others are excited states.

The absorption of energy is most probable if the amount absorbed corresponds to the difference between energy levels. This can be expressed by stating that light of wavelength & can be absorbed only if:

$$\lambda = hc/E_2\text{-}E_1$$

in which E_1, is the energy level of the molecule before absorption and E_2, is an energy level reached by absorption. A change between energy levels is called a "transition". A plot of the probability of absorption versus wavelength is called an "absorption spectrum" and absorption spectroscopy refers to the gathering and analysis of absorption. The probability of absorption at a single wavelength is characterized by the "molar absorption coefficient" at that wavelength. If light of intensity I passes through a substance (which may be in solution) of thicknessed (in cm) and molar concentration C, the intensity I of the transmitted light. Obeys the Beer Lambert Law: in which E is the molar absorption coefficient. Absorption data are reported either as % transmission (100 × I/I) or, more commonly, as the absorbance, A, (log 1/1,). When d = 1 cm, A is commonly called O.D, or optical density, in which the subscript I tells the wavelength at which the measurement was made. Optical density is convenient because it equals E × C. In some cases, if C is high, E appears to be a function of C and it can be said that Beer's law is violated.

The most common use of absorbance measurements is to determine concentration. This can be done if the absorption coefficient is known and Beer's law is obeyed. For example, for double stranded DNA, an O.D260 nm =1 corresponds to 50 ug/ml. Because Beer's law is obeyed to at least O.D = 2.

The DNA spectra in different cation type before and after heat treatment were recorded in the range of 200 nm - 320 nm with Schemadzu, 260 spectrophotometers (Ambedkar Centre for Biomedical Research (A.C.B.R.), Delhi University).

The concentration of oligonucleotide was determined spectrophotometrically using extension coefficient calculated by nearest - neighbour method.

i). Samples were prepared separately by taking known concentration of DNA. (pH = 7.4) with buffer + different concentration of cation types.
ii). The spectra were recorded in the range of 320 nm - 200 nm.
iii). Peak-position at 260 mm was recorded for each separate spectrum for different monovalent and divalent cation solution.
iv). Finally, overlay of one complete set of spectra of one cation type was recorded and printed.

Quartz cuvettes of one cm path length and siliconized coming glassware's were preferred for use in order to avoid absorption of molecules on to the glass surface.

1. Results and Discussion

With the aim of understanding possible mechanism of DNA condensation, we have investigated the interaction of monovalent and divalent cations at different concentrations with DNA in aqueous solution at physiological ph. UV-absorption spectroscopy has been used to monitor various condensation on states of DNA. The DNA samples included Calf Thymus DNA (CT DNA) and a single stranded deoxyribonucleotide with a conserved sequence from the genes of various organisms. The DNA samples with and without the metal ions were divided into three groups depending on sample preparation. The first group of samples were prepared directly using the stocks, stored at 4°C, after bringing them to room temperature. Such samples are called as "Before Heat treatment." The second group of samples are prepared like first group samples but after preparation, they were subjected to slow heating by placing them in boiling water for about 5 minutes and subsequently cooling back to room temperature. We called them "samples with Heat treatment." Third group of samples were subjected to heating at 100°C for five minutes and then immediately transferring them in an ice bath, thus giving them "cold shock" and were called by the same name, significance of such preparation was that in the first group samples, we assume that the cations interacted only to the nature state of DNA. While in case of "Heat treated" samples the tons interact with the denatured state i.e. when both the strands go apart as a result of Liam case of "cold shock" samples, we assume that the ions interact with the double strand region as well as the single strand loop regions. Which were generated as a result of random base pairing (zipping up of bases). The monovalent cations (Na^+ and K^+) and divalent cations (Mg^{2+} $Ca^{2+}$$Ba^{2+}$) were supplied as chloride salts. The solution containing monovalent cations contained 20 mM Sodium phosphate buffer (pH = 7.4), this was done to avoid precipitation of divalent cations in sodium phosphate buffer.

Interaction of Monovalent Cations: Chloride salts of sodium and potassium were used at 50,100,200 and 500 mM concentrations. (Figure 7) shows the UV absorption profiles of the three groups of samples which differ in mode of preparations, marked is the metal ion concentration on each curve. The effect of monovalent cations on the stability of Calf Thymus DNA Was investigated by UV absorption spectroscopy, monitoring the hyper or hyperchromicity of DNA at 260 nm. A general trend is found in all the samples with Na and K salts that the absorbance decreases with the first addition of 50 mM Sodium or potassium salts. This was expected as DNA gets stabilized by interaction with positively charged ions which reduces he repulsion between the negatively charged strands. Further, addition of ions, till 200 mM increases the stability, shown absorbance in almost all the sample of both the cation types. The "cold shock" sample showed a pronounced effect on the spectrum at 500 mM Potassium ion. This concludes that the neutralization of phosphate negative charge is done more efficiently by potassium than sodium in the case of DNA which has random coil or loop regions. Over all observation is that the high concentration of monovalent cations, either destabilize the DNA or (> 500 mM) condense the DNA in the form of aggregates.

By measuring the hyper- or hyper chromaticity of DNA at 260 nm with UV absorption spectroscopy, the impact of monovalent cations on the stability of calf thymus DNA was examined. The absorbance generally reduced after the initial addition of 50 mM sodium and potassium salts in all the samples with Na and K salts. This was anticipated since the interaction of positively charged ions with DNA stabilizes it and lessens the attraction between the negatively charged standards. Additionally, the stability is increased by the addition of ions up to 200mM as evidenced by the decline in 260 nm absorbance. It has been noted that practically all samples of both cations types exhibit increased absorbency at

the maximum salt concentration utilized (500mM). [4, 8, 9, 13, 14]

Table 4: Effect of monovalent cation by the decrease in absorbance at 260 nm. It is observed that the highest concentration used (in 500 mM) of the salt showed an increase in.

	Concentration Mm	Na^+	K^+
Before	0	0.366	0.402
Heat	50	0.346	0.337
Treatment	100	0.308	0.346
	200	0.208	-
	500	0.418	0.385
After Heat	0	0.496	0.406
Treatment	50	0.378	0.304
	100	0.340	0.303
	200	0.346	-
	500	0.446	0.252
Cold Shock	0	0.548	0.448
Treatment	50	0.437	0.357
	100	0.367	0.347
	200 500	0.437 0.464	- 0.619

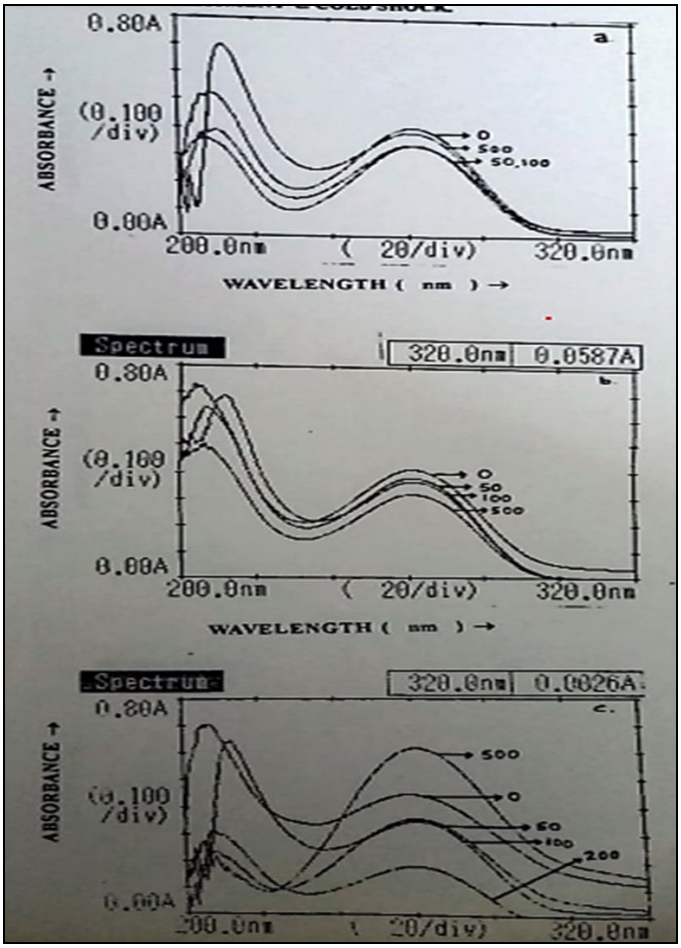

Fig 7: U.V absorption profile of the g three groups of sample containment K^+ (KCl) as indicated in mm concentration : a before heat treatment, b. after heat treatment, c. cold shock [15]

Interaction of Divalent Cations: The chloride salts of divalent cations (Mg^{2+}, Ca^{2+}, Ba^{2+}, Zn^{2+}) were used at 10, 15, 20, 30 mM concentrations. The UV absorption spectra of DNA samples with different cation type. Among the various metal ions used, Mg^{2+} Ca^{2+}, $Ba^{2+}$and the alkaline earth metals (IA group) while the Zn^{2+} (II B) is transition metal ion. The spectra of DNA containing Mg^{2+} and Ba^{2+} metal ions show a common pattern of effects on DNA, in heat treated and cold chock samples. It is clear that a big decrease in absorbance at 260 mm. In the presence of 30 mM cation (Mg^{2+} Ba^{2+}) is due to precipitation of DNA, which was seen by naked eye. While a concentration of 10 mM cation stabilizes DNA, which is seen by a decrease in absorbance than compared to spectra without 'O' salt.

The behaviour of the same metal ions was found different in each case with the DNA samples called without heat treatment. Here at 30 mM concentration, the absorbance at 260 nm exceeds the absorbance of spectra indicated as 'O' salt. This is only possible if $Mg2^+$ and Ba^{++} destabilized the DNA at said concentration. [12]

6. Conclusion

In conclusion, the interaction of metal ions with nucleic acids is a highly important area of study in bioinorganic chemistry, molecular biology, and medicinal chemistry. Metal ions play a significant role in maintaining the structural stability, conformation, and biological functions of DNA and RNA. Essential metal ions such as Na^+, K^+, Mg^{2+}, Ca^{2+}, and Zn^{2+} help stabilize nucleic acid structures and participate in important biological processes including replication, transcription, translation, and enzyme activity. Nucleic acids contain several potential metal-binding sites such as phosphate oxygen atoms, nitrogen atoms, carbonyl oxygen atoms, and hydroxyl groups, which allow different types of interactions including electrostatic attraction, coordination bonding, intercalation, and groove binding.

In addition, toxic heavy metals like Pb^{2+}, Hg^{2+}, and Cd^{2+} can damage nucleic acids, causing mutations, oxidative stress, and various diseases. Therefore, understanding these interactions is important not only for biological and medicinal applications but also for environmental and toxicological studies.

Modern analytical and spectroscopic techniques such as X-ray crystallography, NMR spectroscopy, electrophoresis, potentiometry, and computational modeling have profoundly improved our understanding of metal ion binding and nucleic acid structure. Furthermore, metal–nucleic acid complexes are finding increasing utilizations in nanotechnology, biosensors, biochips, and diagnostic systems.

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