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Analytical Study Interaction Studies Of Deoxyribonucleic Acid With Metal Complexes And Their Mechanism

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Deoxyribonucleic acid (DNA) is a biopolymer consisting of each nucleotide and, through Watson Crick hydrogen bonds, is combined with two other nucleotide monomers in polymer chain. Through phosphodiester connections, those nucleotides inside strands are connected to the 3' carbon of a sugar of a nuclear fibre by the hydroxyl group in the phosphate group, which forms an ester bond with the phosphate of another 5' end of the nuclear sugar carbon, and eliminates a molecule of water. The following three fundamental building components, such as an aromatic planar derivative of a pyrimidine (thymine & cytosine)/purine base (adenine & guanine), sugar deoxyribose, and a group of phosphates, constitute a nucleotide monomer. B-DNA is the most frequent type of conformational helix of the dsDNA base pair (Shamsi & Kraatz 2012) (Table 1.5).

Table 1.5 Some features of DNA forms: A, B and Z forms

Geometry attribute	A-form	B-form	Z-form
Helix sense right	Right-Handed	Right-Handed	Left-Handed
Repeating Unit	1bp	1bp	2bp
Rotation / bp	32.7°	34.3°	60°/2
Mean bp / turn	11	10.5	12
Pitch /	28.2 A°	33.2 A°	45.6 A°

turn of helix	(2.82 nm)	(3.32 nm)	(4.56 nm)
Nucleotide phosphate to phosphate distance	5.9 Å°	7.0 Å°	C: 5.7 Å° G: 6.1 Å°
Diameter	23 Å° (2.3 nm)	20 Å° (2.0 nm)	18 Å° (1.8 nm)

DNA and RNA play a key function in live cell systems, and for many natural, synthesized organic compounds, they represent the most essential cellular target. In particular, anticancer, antiviral and antibacterial medicines function as carriers of hereditary information encoded as genes and used by the transcripts and replication to biosynthesize enzymes and proteins (Ma et al. 2012; Singh et al. 1992 and Sparks & Scholz 2009). DNA is often copied and transcribed by DNA and RNA polymerases in the nucleus carrying genetic information. While certain other biological targets in tumour cells, such RNA, enzyme or protein, are widely considered to be the main objective for many anti-cancer medicines (Reddy & Shilpa 2011). The study of the interaction of DNA is thus of primary significance for the creation and development of drugs. In addition, DNA cleavage may be seen as an enzyme reaction involving several biological processes as well as biotechnological genetic material manipulation. It has a broad range of applications in bio-organic, molecular and medical design applications etc (Reddy & Shilpa 2011). Since nucleic acid and biomolecular interactions are complex, knowledge on comparable reactions with tiny molecules needs to be collected. It is observed that bioactive ligands with a low molecular weight also identify and interact with DNA. These ligands and their metal complexes have the extraordinary biological power to bind cell-based DNA and cause single or two stranded breaks with high efficiency (Reddy & Shilpa 2011). The interactions between transitional metal complexes and DNA have been attractive because of their significance in cancer and molecular biology (Yang et al. 2008). However, three major activities in prokaryotic and eukaryotic cells are involved. Eukaryotic cells have nuclei (e.g. human animals, plants, fungus and insects) and are without nuclei (e.g. bacteria). A large size (diameter range: 10-100 µm) of eukaryotic cells with much more DNA/proteins than prokaryotic cells (diameter range: 0.1-5.0 µm). Linear DNA in eukaryotic cells and smaller circular DNA in prokaryotic cells. The complete ribosome / mRNA complex attaches to the outer membrane of the endoplasmic reticule in eukaryotic cells (ER). They manufacture polypeptides and the newly produced polypeptide

for further liposome vesicle transport and secretion outside the cell may be stored within the ER.

(i) Transcription

Transcription is the initial stage in the gene expression in which a certain sequence of DNA with the aid of the RNA polymerase enzyme has been transcribed into the RNA (ssmRNA/coding or sensory strand). In biology, transcription is also a process of replicating the gene DNA sequence in the comparable RNA alphabet. However, a gene is transcribed in three phases: initiation, elongation and termination. In the initiation phase, RNA polymerase enzymes are linked to a particular DNA sequence, termed a promoter, and then the DNA strands are separated and the single-stranded transcription template generated. Promoter area is a specially identified active location of dsDNA to bind or support RNA polymerase enzyme. While dsDNA opens at the promoter area, a transcription process may begin using the RNA polymerase enzyme. During transcription, the RNA enzyme synthesises the additional RNA strand 5'-AUGAUCUCGUAA-3' direction from the 3'-ACCATCAGTC-5' direction single-strand DNA template. Genetic data are recuperated by Ribonucleic acid (RNA) from DNA and used for the synthesis of proteins in the body, which are also influencing all biological processes and play a key part in the production of hormones, enzymes, structural proteins (Figure 1.5).

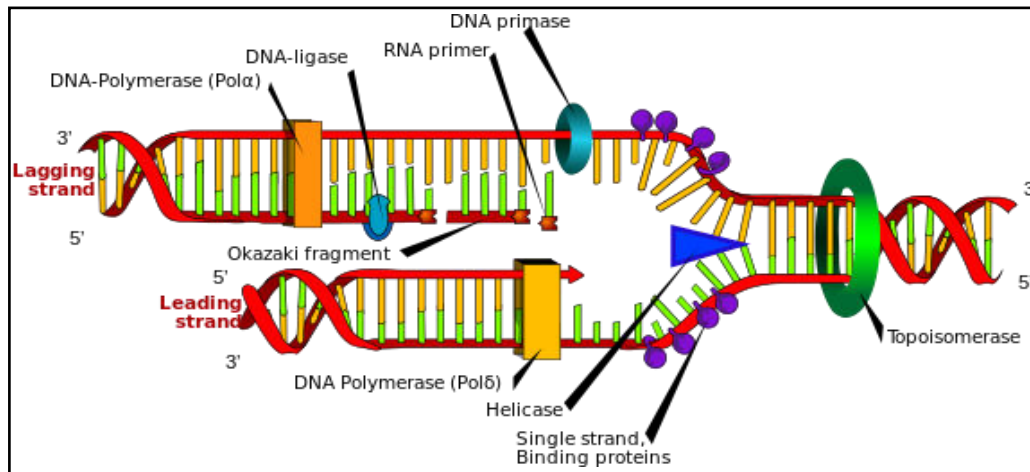
(ii) Replication

The DNA is responsible for its own regeneration (dna self replicates) and is a biological process in which two comparable DNA copies are generated from the base pair of the DNA. This process is founded on biological legacy in all living things. These strands are split by a single strand DNA helicase enzyme during replication. Each strand of the original DNA molecule serves as a model for its counterpart creation, known as semi-conservative replication. The procedure takes place in three stages (a). Initiation: beach septic tissues in presence of helicase that catalyses hydrolysis of Adenosine Triphosphate (ATP) and utilises this energy to disconnect strands during répllication by breaking the hydrogen link between base pairs. In the meanwhile, DNA topoisomerase enzyme cleaves the phosphodiester connection between nucleic acids on a regular basis (Schoeffler & Berger 2008). This process is reversible and the phosphodiester bond may thus be reformed when the enzyme is removed from the DNA strand. There are also two kinds of topoisomerases, which may be distinguished on mechanical and structural grounds. The topoisomerase enzymes of type I create a one-beach break at a time, while the topoisomerase enzymes of type II (DNA Gyrase)

produce a coordinated dual beach break. The single stranded DNA fragments are bound with protein and the short RNA primers nucleotide sequence (b). Elongation: DNA polymerase III enzymes connect DNA fragments (okazaki fragments identified by Reiji Okazaki) in sequence order to template strands as well as assist in revision and remediation of new strands. (c). Termination: the DNA ligase controls the arrangement for the DNA fragment by filling the gaps and closes the nick in double stranded DNA. In the meanwhile, DNA polymerase I helps remove the RNA primers and balance the gaps (Figure 1.5).

(iii) Genetic translation

The translation of genetic information takes place in the live cell system from RNA to protein. During transcription, DNA creates messenger RNA (mRNA) in the nucleus of the cell. The mRNA serves as a template to translate the protein production. The transcribed gene, on the other hand, can encode non-coding RNAs such as ribosomal RNA (rRNA), transmission of RNA (tRNA)/enzyme RNA molecules known as ribocids and of small RNAs such as microRNA, small interfering / silencing (siRNA), piwi-interacting RNA (piRNA), small nucleolar RNA (SnoRNA), small nuclear RNA (snARN), extracellular RNA (exRNA), etc. The ribosome is used to manufacture the amino acid protein in all living cells as a sophisticated molecular mechanism and the RNA helps synthesise and control the proteins process. Ribosomes and tRNA are performed together in the cytoplasm of eukaryotic cells to convert the mRNA into a protein. This process is referred to as genetic translation. While the many individual DNA sequences were transcribed with the support of several RNA polymerase enzymes into RNA molecules, the vast numbers of proteins may be produced in live cells. In addition, the ribosomes assemble around the target mRNA and the first tRNA (first mRNA codon) is connected at the start of the amino acid chain. When a stop codon is achieved, the polypeptide is released by the ribosome. Numerous medications such as anisomycin, clindamycin, streptomycin, erythromycin, puramycin, tetracycline, cycloheximide, and chlororamphenicol suppress prokaryotic cell translation. However, owing to the prokaryotic ribosomes, the adverse effects may mostly decrease from the eukaryotic ribosome in structure (Figure 1.5)



**FIGURE DNA TRANSCRIPTION, REPLICATION AND GENETIC TRANSLATION
PROCESS**

In addition, single/divalent metal cations play significant structural and physiological roles in all living cells (Izatt et al. 1971). They also help to stabilise the DNA structure via phosphodiester coordination (Neidle 2008). The multivalent cation interaction between two phosphate strands of B-DNA was established by Rouzina and Bloomfield in 1998. As a consequence, the phosphates on both strands are interacting strongly with the groove. This induces groove closure and the bending of DNA into the cationic molecule (Figure 1.6) (Bloomfield & Rouzina 1998).

Mechanism: How a medication molecule may interact with the DNA are various: I Transcription factors control: the medication molecule does not interact directly with the DNA. They initially attach to the protein, which then interacts with the DNA base pair when the functions change. (ii). Forming DNA-RNA hybrids. Binding to an RNA molecule that binds in turn to single stranded DNA hybrids that generate DNA-RNA hybrids that impede transcripts. (iii). Direct molecular binding: The tiny medication molecules attach directly to a double helix DNA. In general there are two types of interactions between DNA and metal ions, (a) ligand/complex-mediated relationships via the H-bound, π - α interaction between a complex metal and DNA base pairs by intercalation or shape-selective groove bonding and (b) direct metal ion bonding with DNA that involve the interaction between the filled orbital of the nucleo-base ligand with the appropriate emp interaction (Barton & Lolis 1985).

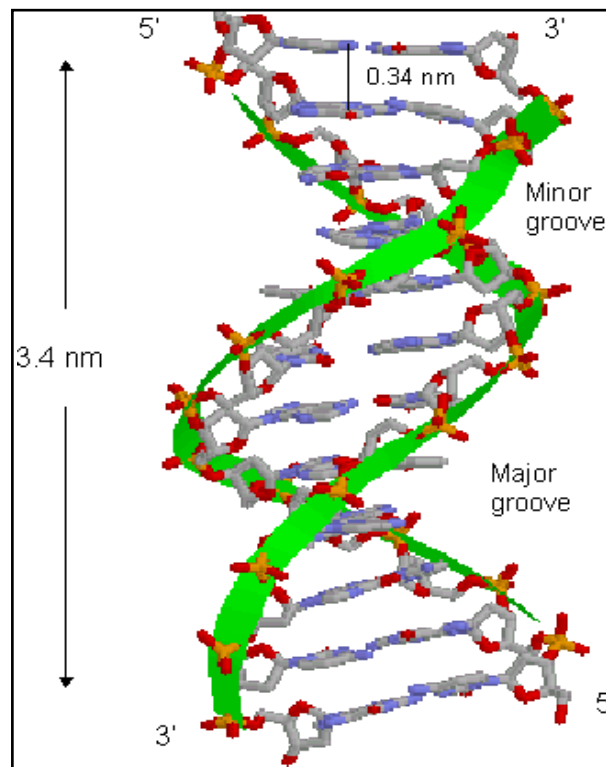


Figure 1.6 DNA structure and its grooves

1.9.1 Radical Scavenging Abilities Towards DPPH (DPPH•)

The Brand-Williams (Brand-Williams et al. 1995) technique created and uses the stable free radical DPPH, which has a deep purple colour and can be detected spectrophotometrically. In the presence of molecules able to transport an electron or to donate hydrogen, the DPPH becomes bright yellow in an aqueous solution. Due to the fast, easy and cheap technique, the radical capability for scavenging in medical and food technology is extensively measured (Arnab et al. 2010). However, they may also affect the absorption at the same wavelength in certain limits because of steric hurdles during the interaction of small molecules with biomolecules and carotenoids (Karamac et al. 2011).

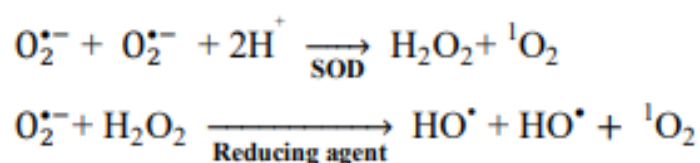
1.9.2 Radical Scavenging Abilities Towards Hydroxyl (• OH)

Hydrogen peroxide has high oxidising characteristics. It consists of numerous oxidising enzymes such as SOD. The Ruch technique is used to evaluate the free radical scavenging capability of H₂O₂. OH• Scavenging is the most important antioxidant activity owing to extremely high reactivity and severe oxidation characteristics. While hydroxyl radical

intensities in cells rise, they may contribute to toxicity in live cells (Mandade et al. 2011). The OH• radicals produced in the presence of reduced transition metals/H₂, and the reduced form of dioxygen, cause cell damage in vivo according to the Fenton reaction (Duan et al. 2007) OH• is most essential antioxidant activity owing to its extremely high reactivity and oxidation characteristics; OH• interacts with a variety of biomolecules, including amino acids, lipids, sugars and nucleotides. It ends up damaging the live cells. Therefore, the OH• production prevention method plays an important function in the preservation of living systems (Wang et al. 2008).

1.9.3 Radical Scavenging Abilities Towards Superoxide (O₂•⁻)

Superoxide dismutase (SOD) is an essential antioxidant that protects all living cells and acts as a catalytic for discharge into ordinary molecular oxygen or H₂O₂ of superoxides radically anion. During the respiratory chain process, superoxide anion radical is generated as a by-product of oxygen metabolism. Excess O₂•⁻ should be rapidly eliminated from the biological system because of toxicity. The SOD helps to avoid excess O₂•⁻ radicals to protect live cells.



The radical reaction of OH• to O₂•⁻ also produces the excited molecular oxygen. The superoxide is a comparatively low oxidant compared to nitrogen oxide and hydroxyl oxidative species (Miguel et al. 2014). Superoxides are also known to promote lipid peroxidation as a consequence of the production of H₂O₂, generating hydroxyl radical precursors (Sun et al. 2010). Even though superoxide anion radicals themselves are not reactive to biomolecules and are more potent in the formation of the SAOO and ONOO⁻. During mitochondrial respiration, the radical superoxide anion is generated by various enzymes such as nicotinamide Adenine Dinucleotide Phosphate Oxidase (NADPH), monooxygenases, xanthine oxidases (XO) and cyclooxygenases in significant amounts for destroying pathogens. The dominating superoxide anion radicals cause the biological system to suffer from many damaging alterations. Hydrogen is donated to superoxide radicals by antioxidants, resulting in detoxification, suppression of lipid oxidation propagating phases and peroxidant reactions.

1.9.4 Radical Scavenging Abilities Towards Nitric Oxide (NO•)

The radical nitric oxide is an important chemical mediator that is caused by endothelial cells, macrophages and neurons and involved in the control of many physiological processes. NO is manufactured via three nitric oxide synthase isoforms, endothelial NOS, neural NOS and inducible NOS (iNOS). Nitric oxide is produced by enzymes in the vascular endothelial cells, neural cells and phagocytes of amino acid L-arginine. NO THE supports diseases such as cancer, Alzheimer's disease, AIDS, arthritis and so forth. While NO intensity grows, division of the DNA, cell damage and neural cell death in the human body may occur (Dawson et al. 1992). NO is unstable in aerobic circumstances, producing intermediate reactions with oxygen NO_2 , N_2O_4 , and N_3O_4 . The stable products nitrite and nitrate (Maccocci et coll. 1994) and peroxynitrite likewise generated by interacting with superoxide were synthesised in this process. These compounds are genotoxic and the deamination of guanine, cytosine and adenine is mainly mediated by N_2O_3 . Chronic exposure to radical nitric oxide is associated with many carcinomas and inflammatory diseases, including diabetes of young people, multiple sclerosis, arthritis and ulcerative colitis. The toxicity of NO can rise significantly when it combines with radical superoxide and forms a highly reactive peroxynitrite anion (ONO^-) (Boora et al. 2014).

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