**Interaction of Oxaliplatin with DNA: A Theoretical Study**

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Abstract:

Recent studies on the structure and dynamics of nucleic acids reveal that salt and solvent can cause the DNA helix to change shape. This adaptability causes DNA to fold either smoothly or by abruptly changing the chain direction and creating kinks. Theoretical study regarding theinteraction of drug Oxaliplatin and its enantiomeric analog with DNA duplex is presented in the current study by using an amended Zimm and Bragg theory, to explain the melting behavior and heat capacity of DNA with and withoutdrg binding. The experimental models of Malina et al. (1983) were used for the study. Half width and the sensitivity parameter (H/σ) have been used to analyse the transition's sharpness. The different metrics, including the transition profile, transition sharpness, heat capacity curve, and half widths, are in good agreement with the experimental results for oxaliplatin binding. For a better understanding of bimolecular interaction, this theoretical approach can be used, which has implications for the process of developing new drugs.

Keywords:  heat capacity, nucleation parameter, DNA binding, transition profile, intercalation, minor groove

1. **Introduction**

Deoxyribonucleic acid is commonly abbreviated as DNA. DNA is polymer composed of two [polynucleotide](https://en.wikipedia.org/wiki/Polynucleotide), which form a double helix by coiling around each other. All known organisms and many viruses have genetic information in the DNA that is essential for their development, functioning, growth, and reproduction. Both DNA and [ribonucleic acid](https://en.wikipedia.org/wiki/Ribonucleic_acid) (RNA) are [nucleic acids](https://en.wikipedia.org/wiki/Nucleic_acid). Nucleic acids along with proteins, lipids, and complex carbohydrates (polysaccharides) are four major categories of macromolecules that are necessary for all known forms of life.The two DNA strands are composed of simple monomeric units called nucleotides. Therefore these strands are also called polynucleotides [1,2]. Nucleotide is made up of deoxyribose a kind of pentose (five carbon) sugar, a phosphate group along with one [nitrogen-containing](https://en.wikipedia.org/wiki/Nitrogenous_base) [nucleobases](https://en.wikipedia.org/wiki/Nucleobase) ([cytosine](https://en.wikipedia.org/wiki/Cytosine) [C], [guanine](https://en.wikipedia.org/wiki/Guanine) [G], [adenine](https://en.wikipedia.org/wiki/Adenine) [A] or [thymine](https://en.wikipedia.org/wiki/Thymine) [T]).

An alternating sugar-phosphate backbone is created when the nucleotides are linked together in a chain by covalent bonds (also referred to as the phosphodiester linkage) between the sugar of one nucleotide and the phosphate of the next nucleotide. To create double-stranded DNA, the nitrogenous bases of the two distinct polynucleotide strands are joined by hydrogen bonds in accordance with the base pairing principles (A with T and C with G). The two DNA strands are antiparallel because they move in directions that are opposite to one another.

RNA strands are made using DNA strands as a template. DNA nucleotides are switched for their equivalent bases, with the exception of thymine (T), for which RNA substitutes uracil. This process is known as Transcription. These RNA strands function as the translation machinery for the genetic code, which specifies the order of amino acids in proteins.

DNA is arranged into long scaffolds within eukaryotic cells known as chromosomes. These chromosomes are replicated in the course of DNA replication prior to the regular cell division, giving each daughter cell a complete set of chromosomes.

The majority of the DNA in eukaryotic creatures (animals, plants, fungi, and protists) is stored as nuclear DNA inside the cell nucleus, while some is also stored as mitochondrial DNA or chloroplast DNA.[3] Prokaryotes, such as bacteria and archaea, store their DNA in the cytoplasm, in the form of circular chromosomes. DNA is compacted and arranged within eukaryotic chromosomes by chromatin proteins like histones. These compacting structures direct how DNA interacts with other proteins, assisting in regulating which parts of the DNA are transcribed.

**1.1 Base Pairing**

Each type of nucleobase on one strand of a DNA double helix links with just one type of nucleobase on the other strand. Complementary base pairing is the technique we achieve here. Adenine forms two hydrogen bonds with thymine and cytosine forms three hydrogen bonds with guanine only and purines form hydrogen bond with pyrimidines. This type of binding in two nucleotides across the double helix (from six-carbon ring to six-carbon ring) is called a Watson-Crick base pair. High GC content DNA is more stable than low GC content DNA.

A unique type of base-pairing is called a Hoogsteen base pair, which involves hydrogen-bonding a 6-carbon ring to a 5-carbon ring.[4] Since they are not covalent, hydrogen bonds are simple to break and reassemble. Thus, a mechanical force or high temperature can be used to tear apart the two strands of DNA that make up a double helix like a zipper.[5] This base pair complementarity is crucial for DNA replication because it ensures that every piece of information in a DNA helix's double-stranded sequence is reproduced on every strand. All of the functions of DNA in organisms depend on this particular, reversible connection between base pairs.[6]

**1.2 Grooves**

The grooves are the voids that are adjacent to the base pair which are capable of providing binding sites. Other strands may be found tracing the voids, or grooves, between the strands. These voids are adjacent to the base pairs and may provide a [binding site](https://en.wikipedia.org/wiki/Binding_site). The grooves are not equal in size because the strands are not symmetrically positioned in relation to one another. The minor groove measures 12 Å (1.2 nm) in width, whereas the main groove measures 22 Å.[7]

The major groove has a wider width than the minor groove, making it easier to access the bases' edges there. Therefore, the sides of the bases exposed in the main groove are frequently in contact with proteins like transcription factors that can bind to specific sequences in double-stranded DNA.[8] Although the odd DNA conformations in this condition vary from cell to cell, the major and minor grooves are always designated to represent the differences in breadth that would be evident if the DNA were twisted back into the standard B form.

**1.3 Functions of DNA**

The two major functions of DNA are as follows:

**1.3.1** **Transcription:**

Ribonucleic acid, or RNA, extracts data from the DNA and uses it to produce proteins in the body. Proteins play a variety of roles in all bodily functions such as receptors, enzymes, transporters, structural proteins, hormones, regulators, etc.

**1.3.2** **Replication:**

DNA replicates itself. As discussed earlier Adenine (A), thymine (T), guanine (G), and cytosine (C) are the four nucleotides that make up each strand of the double-helix structure of DNA. These nucleotides are linked together by phosphodiester linkages within a strand. A and C develop two hydrogen bonds with T and three hydrogen bonds with G, respectively, to hold the two strands together mainly by Watson-Crick hydrogen bonds. Pairing of the bases AT and G-C Proteins and tiny molecules can specifically recognise DNA sequences by combining hydrogen bond acceptor/donor sites that are present on either the major groove or minor groove.

**1.4 Interaction of drug with DNA**

For cells to survive and grow, as well as for the efficient operation of every biological process, transcription and replication are crucial. DNA begins transcription or replication only after receiving a signal which is often in the form of a regulatory protein attaching to a specific area of the DNA. Therefore, if a tiny molecule can match the binding specificity and potency of this regulatory protein, DNA function can be artificially regulated, blocked, or activated by binding the molecule rather than the protein. This artificial/natural tiny molecule can therefore operate as a medication when activating or inhibiting DNA function whenever it is necessary to treat or manage a disease.

Depending on which spot the medicine is targeting, DNA activation could cause DNA replication or result in the production of more of the necessary protein. DNA inhibition would limit protein replication or synthesis and would result in cell death. Despite the possibility of both of these activities, DNA is typically targeted in an inhibitory mode to kill cells for antitumor and antibiotic action.

Both covalent and non-covalent bonds are used by drugs to bind to DNA. DNA covalent binding is irreversible, completely inhibits DNA activities, and always results in cell death. A well-known covalent compound called cis-platin (cisdiamminedichloroplatinum) is used as an anticancer medication. The chloro groups in cis-platin react with the nitrogens in DNA bases to form an intra/interstrand cross-link.

Most non-covalently bound drugs fall into one of the following two categories:

**1.4.1 Minor groove binders**

Minor groove binding drugs are typically designed like crescents, which complement the groove's shape and make binding easier by encouraging van der Waals interactions. These substances can also form hydrogen bonds with bases, most frequently with the N3 and O2 of adenine and thymine. Drugs that bind to minor grooves primarily bind to A/T rich sequences. A/T groove regions are narrower than G/C groove regions, and this preference is likely due to better van der Waals contacts between the ligand and groove walls in this region as well as the steric hindrance presented by the C2 amino group of the guanine base in the latter. This preference is in addition to the designed propensity for the electronegative pockets of AT sequences. Lexitropsins and imidazole-pyrrole polyamides, two synthetic polyamides with a focus on the G-C and C-G regions of the grooves, have been developed, though.

Small molecules will be helpful tools in molecular biology and, possibly, in human medicine if they can bind with high affinity to any predefined DNA sequence in the human genome. To rationally manage the sequence specificity of minor groove-binding polyamides including N-methylimidazole and N-methylpyrrole amino acids, pairing rules have been created. [9]

Perhaps the most well researched minor groove binding substance to date is the dye Hoechst 33258. Recent research has taken a look at how this dye interacts with a self-complementary dodecanucleotide [d(CGCAAATTTGCG)2, A3T3] [10-12].

Raman *et. al* [13] have designed and synthesized novel [tyramine](https://www.sciencedirect.com/topics/chemistry/tyramine%22%20%5Co%20%22Learn%20more%20about%20tyramine%20from%20ScienceDirect%27s%20AI-generated%20Topic%20Pages) derived [Schiff base](https://www.sciencedirect.com/topics/chemistry/schiff-base), 3-4-dimethoxybenzylidene-4-aminoantipyrinyl-4-aminoethylphenol(L) and a series of its transition metal complexes of the type, ML2Cl2 where, M = Cu(II), Ni(II), Co(II) and Zn(II). Electronic absorption spectroscopy, viscosity testing, cyclic voltammetry, and molecular docking analysis were used to examine the binding characteristics of these complexes with calf thymus DNA (CT-DNA). The findings show that DNA interact by metal(II) complexes through minor groove binding. Comparing the complexes to the free ligand, antifungal and antibacterial activities were improved.

S009-131, a coumarin-chalcone hybrid, has been shown to have anti-proliferative and anti-tumor effects by inducing apoptosis. Sarkar *et. al* [14] examined the role of the DNA damage signalling pathway in the S009-131-induced death of cancer cells. They demonstrated that S009-131 damages DNA by potentially binding to the minor groove, which activates ATM and DNA-PK but not ATR earlier in the DNA damage process by phosphorylating them.

**1.4.2 Intercalators**

These have stacking planar heterocyclic groups between neighbouring DNA base pairs. The complex is thought to be stabilised, among other things, by drug-DNA base interactions known as "stacking." Intercalators significantly alter DNA's structural integrity. Considering the medication metabolism and severe side effects, non-covalent binding is often favoured over covalent adduct formation. However, a significant benefit of covalent binders is their strong binding capacity. With binding constants in the nanomolar range, proteins are big molecules that bind to DNA quite strongly. Using tiny non-covalent binders to attain equivalent specificity and affinity has been challenging and continues to be a significant obstacle in the development of medicines for DNA.

Although intercalators are a significant class of DNA interacting ligands, there have been very few thorough thermodynamic investigations characterising these interactions. There is still a dearth of comprehensive thermodynamic information on intercalation processes, with the exception of the daunomycin-DNA interaction, which has been well researched in all respects. Hopkins and Wilson were some of the first people to document a change in the heat capacity of an intercalation process.[15]

To see DNA and DNA interactions in vivo and in vitro, DNA intercalators are frequently utilised as fluorescent probes. They are well known to disrupt DNA stability and structure, which can affect how proteins process DNA. Wuite et al. measure the kinetics of DNA intercalation using the mono- and bis-intercalating cyanine dyes SYTOX Orange, SYTOX Green, SYBR Gold, YO-PRO-1, YOYO-1, and POPO-3 in order to elucidatr perturbation  by combining single-dye fluorescence microscopy with force spectroscopy.[16] They demonstrated that a significantly tension-dependent dissociation rate primarily controls their DNA-binding affinity. By adjusting DNA tension, intercalating species, and ionic strength, these rates can be adjusted over a span of seven orders of magnitude. The effect of intercalators on strand separation and enzymatic activity is reduced by optimising these rates.

Riahi *et. al* [17] used FTIR, CD, fluorescence spectroscopy techniques, and molecular modelling to explore the intercalation of the anticancer medication doxorubicin (DOX) and its analogue N-(trifluoroacetyl) doxorubicin (FDOX) with DNA duplex. While there were no DNA structural changes with FDOX contact, DOX intercalation with a partial B to A-DNA transition caused significant changes in DNA structure to be seen.

A strong anticancer medication called mitoxantrone (MTX) is used to treat specific cancers. For the first time, Fathi *et. al* [18] use spectral fluorescence spectroscopy and SPR (surface plasmon resonance) based techniques to explore the intercalation of anticancer drugs into DNA. This research demonstrates that the primary binding force for intercalating MTX to DNA is hydrogen bonding.

Barone *et. al* [19] used Density functional theory (DFT) to computationally analyse the intercalation of the anticancer drug daunomycin into six stacks of Watson-Crick DNA base pairs (AT-AT, AT-TA, GC-AT, CG-TA, GC-GC, and GC-CG). Their findings indicate that while hydrogen bonds between daunomycin and hetero atoms in the minor groove of AT base pairs play a significant role in the computed and experimentally observed sequence specificity as well as the overall stability of the intercalation complexes.

**1.5 Crosslinking in DNA**

When different exogenous or endogenous substances interact with two DNA nucleotides, a covalent bond is created between them. This process is known as crosslinking of DNA. This crosslink can happen within the same strand of double-stranded DNA (intrastrand) or between the opposing strands (interstrand). These adduct cause cell death by interfering with biological processes including DNA replication and transcription. Nevertheless, these crosslinks can be removed by excision or recombination mechanisms.

Additionally, DNA crosslinking is advantageous for chemotherapy and apoptosis targeting of cancer cells as well as for studying how proteins interact with DNA.

* + 1. **Crosslinking agents**

Many characterised crosslinking agents have two independently reactive groups that can each bind to a DNA nucleotide residue inside the same molecule. These substances are divided into exogenous and endogenous categories based on where they came from. Chemicals and substances, both natural and manufactured, that come from environmental exposures like drugs, cigarette smoke, or vehicle exhaust are known as exogenous crosslinking agents such as Nitrogen musterd, Cisplatin, Mitomycin C, Psoralen etc.. Compounds and metabolites that enter a cell or organism through cellular or biochemical processes are referred to as endogenous crosslinking agents such as Nitrous acid, Bifunctional Aldehydes etc.

**1.5 Oxaliplatin**

In present study the stability of Oxaliplatin-DNA duplex has been examined theoretically which is a cisplatin exogenous cross linking agent. Oxaliplatin is one of the drug in the class of chemotherapy known as alkylating agents. Oxaliplatin functions by binding to a DNA strand within the cancer cell. Oxaliplatin [trans- (R,R)- 1,2-diminocyclohexaneoxaloplatinum] and its enantiomer[trans- (S,S)- 1,2-diminocyclohexaneoxaloplatinum] marketed as Eloxatin is a platinum based antineoplastic agent used in cancer chemotherapy.

It is a new third-generation platinum compound which is effective in the treatment of advanced ovarian and colorectal malignancies. With low haematotoxicity and moderate, controllable gastrointestinal toxicity, it has shown to have an excellent safety profile. The peripheral sensory neuropathy brought on by oxaliplatin, characterised by distal and perioral dysaesthesia, is generally regressive between treatment cycles and is brought on or made worse by the cold. The majority of the time, this cumulative dose-limiting toxicity reverses within a few months of medication cessation [20]. It has a large diaminocyclohexane (DACH) moiety, which kills cancer cells primarily by causing transcriptional inhibitory (DACH)Pt-GpG intrastrand cross-links. [21]



**Figure 1 (a) Chemical Structure of Oxaliplatin**



**Figure 1 (b) Chemical Structure of Oxaliplatin [Pt(R,R-DACH)]2+**



**Figure 1 (c) Chemical Structure of [Pt(s,S-DACH)]2+**

Since the introduction of cisplatin [cis-diamminedichloridoplatinum(II)], only [cis-diamminecyclobutanedicarboxylatoplatinum(II)] (carboplatin) and [(1R,2R-diamminocyclohexane)oxalatoplatinum(II)] (oxaliplatin) have acquired universal approval and reached widespread clinical use [22]. Compared to cisplatin, carboplatin is less toxic and can be administered at significantly higher doses. Sadly, carboplatin continues to only be effective against tumours that fall within the same spectrum as cisplatin [23]. While oxaliplatin has showed potential for use in some cisplatin-resistant tumours when delivered in combination with 5-fluorouracil or folinic acid [24]. It has not yet shown any significant advantages over cis platin or carboplatin when used as a single agent. The biological effects of third generation platinum anticancer drug oxaliplatin and traditional cisplatin are thought to differ due to downstream mechanisms that distinguish between DNA adducts of each. The fact that oxaliplatin can more effectively generate DNA adducts in their biological effects is what accounts for these various biological consequences.

The differential scanning calorimetry (DSC) of oxaliplatin and its Enantiomeric analog ([Pt(R,R-DACH)]2+ and [Pt(s,S-DACH)]2+)has been published by Malina *et. al*[25]. The chemical structures are shown in figure 1(a), 1 (b) and 1 (c). Their work described recognition by the HMG domain protein and DNA polymerization across the significant 1,2-GG intrastrand cross-link created by cisplatin and oxaliplatin. Since the system remains cooperative after the binding therefore modified Zimm and Bragg theory [26] have been used to study the effect of binding of oxaliplatin and its enantiomer with DNA in the present study.

1. **Theoretical approach to study the binding of Oxaliplatin with DNA**

Calorimetric analysis of the complex formed between oxaliplatin and DNA by Malina *et. al* suggests that that the melting transitions of both the platinated and unmodified duplexes are fully reversible, Each transition shows negligible changes in the heat capacities between the initial and final states. However, in spite of these the duplex remains highly cooperative so the co-operative transition hypothesis can be applied to clarify the melting profile and temperature dependability of thermodynamical parameters including heat capacity. The modified Zimm and Bragg theory had been thus adopted. The Ising-Model, which was developed to examine the ferromagnetic transition in linear chains of spins, is a foundation for all theories. A residue in a long polymer chain can exist in either an ordered or disordered form; much like a spin can exist in either a spin up or spin down state. Due to the finite nature of interactions, a one-dimensional system is unable to demonstrate any sort of phase transition; consequently the Ising model has been modified by incorporating the boundary state. The first ordered state in a sequence of ordered states is this boundary state. Once the residue transitions, maintaining it in the second state is simpler. Now, different states U can each have a different partition function assigned to them.

One can create an Ising matrix for an ordered and disordered state of a two-phase system using the theory. The Ising matrix, as was previously addressed [27–33] and by Zimm and Bragg [26] can be represented mathematically as follows;

 M =

Where the equivalent base pair partition functions contributions in the three states are fr, fh, and fk. such as  ordered, or disordered and boundary or nucleation. The values of M's eigenvalues are provided by:

 λ3=0 …..(1)

 Because we are working with a finite system, the impact of the starting and end states becomes crucial. The following provides the first segment's contribution to the partition function:

U = (fr1/2,0,0) .....(2)

 When the last segment's state is represented by column vector V,

 …..(3)

 N-segment chain's partition function is provided by

Z = UMN-1V …..(4) The matrix T consists of the column vectors only. It diagnolizes M and is given by

 …..(5)

Where: …..(6)

When the values of M from Equation 5 are substituted, we obtain:

T =

Similarly, the matrix equation yields T-1 as follows:

 …..(7)

Where,

When we again use the values of M from equation 1 in equation 7, we obtain;

 …..(8)

These are the normalisation constants:

And C3 = 0 …..(9)

  If Λ = T-1MT be the diagonalized form of M, the partition function can be written as:

Z = UTΛN-1T-1V …..(10)

 The partition function is as follows once the values from equations 1, 2, 3, 6, 8, and 9 are substituted in equation 10:

 …..(11) In disoedered form, the fraction of the segments is given by

 The solution to the aforementioned equation is:

 …..(12)

Where

, , ,

Here, s is the propagation parameter in this case, and it is considered to be one for simplicity. In reality, it is discovered to be very close to unity in the majority of systems.

The total absorption can be expressed as follows if Ar and Ah represent absorbance in the disordered and ordered states, respectively:

…..(13)

 It is simple to extend this formalisation to specific heat. The changes in molar enthalpy and entropy during the transition from state I to state II are related to the specific heat. Free energy and internal energy are derived from well-known thermodynamic relations such as and respectively. We obtain the specific heat by differentiating internal energy with respect to temperature.

 .....(14)

 Where  H is the molar change in enthalpy about the transition point and S represents entropy, which is equal to

 .....(15)

 Where Tm is the transition temperature, and

With

Where, and 

The nucleation parameter σ measures the energy released or expanded at the formation of the initial state of ordered/disordered state. It's got related to do the lengths of uninterrupted sequences. Using Nernst-Lindemann approximation [19], the volume heat capacity Cv has been transformed into the constant pressure heat capacity Cp.

( …..(16)

 Where A0 is a constant often of universal value [3.9×10-9 (Kmol)/J-1] and Tm is the melting temperature.

1. **Discussion**

 **3.1 Transition Profile**

 Since DNA's structure is still quite cooperative after oxaliplatin binds to it, the two-state theory of order-disorder transition holds true. In order to account for the ordered (bound-ed/unbounded) and disordered states that coexist at the transition point, the Zimm and Bragg theory is modified. The nucleation parameter and total change in enthalpy/entropy, which together define the transition, are the main thermodynamic forces that propel it. Base pairs in the context sequence may also influence the transition. The energetics of transition will depend on the strength of all hydrogen bonds and non-bonded interactions with changing context sequences, assuming that intrastand crosslinking does not significantly disrupt the surrounding base pair stacking. The distortion at the crosslink location spans at least four pairs of guanine residues, which are not connected to their equivalent cytosin residues by hydrogen bonds. The transition is more abrupt the lower the nucleation parameter's value. All of this is considered when calculating the change in enthalpy using the differential scanning calorimeter (DSC) [23]. A reduction in the total transition enthalpy of the duplexin occurs concurrently with the drug-induced decrease in the thermal stability of the duplex. The change in enthalpy is greater in case of [Pt(S,S-DACH)]2+ -DNA duplex. Unmodified DNA melts at 332.109 K The melting temperatures of the DNA saturated with the drugs [Pt(R,R-DACH)]2+  and [Pt(S,S-DACH)]2+  are 321.477 K and 318.493 K, respectively.

 Table 1 lists the various variables giving transition profiles that best match experimental findings in GG Intrastrand crosslink of antitumor Oxaliplatin and Its Enantiomeric Analog. To determine how acute the transition is, we use a sensitivity parameter with the symbol ΔH/ σ and half width. It can be seen that the transition is sharpest in the case of an unbounded state.

 The variation in heat capacity with temperature is calculated and plotted in Figures 2, 3 and 4. Figure 2 gives transition profile for unmodified DNA while figure 3 and 4 gives transition Profile for binding of DNA with [Pt(R,R-DACH)]2+ and [Pt(S,S-DACH)]2+ respectively. Solid curve represents experimental values taken by Malina *et. al* [24] while the ӾӾӾӾ represents calculated values. Slight changes at the tail ends are due to the fact that various disordered states are present that cannot be uniquely defined. The presence of small helical segments in the random coil state can also cause a variation. In case of λ- transition the sharpness s better in unmodified state than the modified state, as expected.

**Table1.Transition parameters for WP762 binding to DNA**

|  |  |  |  |
| --- | --- | --- | --- |
| **Parameter** | **DNA** | **[Pt(R,R-DACH)]2+ -DNA** | **[Pt(S,S-DACH)]2+ -DNA** |
| Tm(K) | 332.109 | 321.477 | 318.493 |
| ΔH( Kcal/mol) | 96.8 | 59.9 | 56.7 |
| σ | 0.012 | .00095 | .009 |
| No. of segments N | 66 | 66 | 66 |
| Sensitivity parameter(ΔH/σ) | 8.06×103 | 63.05×103 | 6.30×103 |

**Figure 2 Heat capacity and transition profile of unmodified DNA**

**Figure 3 Heat capacity and transition profile of DNA bounded with oxaliplatin enantiomer [Pt(R,R-DACH)]2+**

**Figure 4 Heat capacity and transition profile of DNA bounded with oxaliplatin enantiomer [Pt(S,S-DACH)]2+**

**3.2 Heat Capacity**

 The second derivative of the free energy is used to describe the structural and dynamical states of a macromolecular system [32]. By employing scaling factors, which are very close to unity (and only slightly more than one in the case of heat capacity curves) it was almost possible to make the theoretically and experimentally determined heat capacity profiles coincide. The slight variation in experimental and calculated data may arise due to the fact that only one dimensional linear chain has been considered. The three dimensional structure is even more complicated which results in much more complex calculations.

 A closer look at these thermodynamic parameters reveals several intriguing characteristics: First, crosslinking formation of [Pt(R,R-DACH)]2+ or [Pt(S,S-DACH)] 2+ reduced the thermal stability of duplex. [Pt(S,S-DACH)] 2+ s crosslinker reduced DNA melting temperature more effectivelt than [Pt(R,R-DACH)] 2+ 's crosslinker. Second, the enthalpy of duplex dissociation significantly decreased as a result of crosslinker creation by DACH complexes. In contrast to its unmodified cousin, the duplex is enthalpically destabilised by the intrastrand Crosslinker of these platinum complexes. It's interesting to note that compared to its R,R counterpart, the intrastrand crosslinker of [Pt(S,S-DACH)]2+ produced in this latter sequence thermodynamically destabilised the duplex much more.

1. **Conclusion**

One of the goals of conducting biophysical studies of drug-DNA interactions is to develop design techniques for novel compounds with therapeutic or biotechnological applications is. In this paper, we have made an effort to demonstrate how in-depth thermodynamic studies might be an effective instrument for delivering knowledge that can direct such initiatives.

Thus, in addition to affecting the transition enthalpy and the melting temperature, drug binding also affects the features of the transition, as shown by the change in transition breadth in both experimental and computed data. Dynamical and thermodynamic behaviour are directly influenced by the kind and strength of interactions. This technique can be used to investigate a polymer's biodegradability. The biomedical sector can use the results of the current study to better understand the stability of drug interactions with nucleic acids as well as drug-DNA interactions at the bimolecular level.

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