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Research Article

In Vitro And Theoretical DNA Interaction Study of Zinc Complexes

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ABSTRACT

In this work, we undertake a tentative analysis into the multi-layered realm of zinc complex-DNA interactions, integrating empirical in vitro findings with cutting-edge theoretical modelling. The focus of our study involves the synthesis and thorough characterization of the $Zn(DIP)_2(DMP)_2 \cdot 2H_2O$ complex, with the aim of establishing a fundamental comprehension of its structural attributes. The inquiry is built upon the structural foundation provided by analytical techniques such as UV-visible and IR spectroscopy, as well as 1H NMR data. In the molecular framework presented, we systematically investigate the principles of binding, thermodynamics, and kinetics that govern the dynamic interactions between zinc complexes and DNA. The progression of our exploration is characterized by a comprehensive examination of several spectral indicators and theoretical simulations, which serve to elucidate alterations in absorption spectra, disparities in binding constants, and structural adaptations. Our study focuses on the theoretical realm, utilizing computational methods and quantum chemistry calculations to explore the electronic structure, energy profiles, and binding energies. This approach allows us to gain a more profound theoretical comprehension of these interactions. This review serves to enhance our comprehension of the complex interactions between zinc and DNA, shedding light on potential applications in drug design, targeted delivery, and DNA-based nanotechnology. It underscores the importance of interdisciplinary collaboration in fully harnessing the diverse capabilities of zinc complexes across multiple domains.

1. INTRODUCTION

The dynamic interaction between complex metals and biomolecules has drawn a lot of attention in the field of bioinorganic chemistry. These metal complexes, zinc-containing ones have garnered the greatest interest due to their adaptable and potentially essential roles in a variety of biological processes [1]. In particular, research into zinc complexes and how they interact with DNA has emerged as an exciting and promising field, providing knowledge into the basic molecular processes that control the DNA and its relationships within the cellular environment. Zinc is one of the essential trace elements in biological processes and is recognized to be crucial for the regulation of transcription, the catalysis of enzymes, and cellular homeostasis in general [2]. Its capability to coordinate with a diversity of ligands has led to the creation of a several array of zinc complexes, each possessing exclusive properties and reactivity. These zinc complexes, when in proximity to DNA, can show a range of interactions, ranging from simple electrostatic binding to more intricate intercalation and groove binding [3]. Understanding the details of these interactions is dominant, given the profound implications for biological functions, drug design, and nanotechnology applications [4].

This review study seeks to provide a comprehensive summary of the body of knowledge concerning the interaction of zinc complexes with DNA that has been gathered from in vitro as well as theoretical studies. We will learn about the theoretical models and practical projects that have influenced our knowledge of this fascinating interaction. Numerous spectroscopic and biophysical methods are used in in vitro research to examine the physical and chemical properties of zinc complex-DNA binding. These studies have provided significant understanding into the workings of these interactions by shedding light on binding variables, thermodynamics, and structural arrangements.

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In tandem with experimental investigations, theoretical modeling and computational simulations have arisen as influential tools to explain the molecular dynamics, energetics, and structural intricacies of zinc complex-DNA interactions. The synergy between these theoretical approaches and experimental data has further enriched our understanding of these systems. Beyond the fundamental insights into the zinc complex-DNA interface, this review will also discover the practical applications of such knowledge, including the design of novel zinc complexes with improved DNA-binding properties and their relevance in medicinal chemistry, drug delivery, and DNA-based nanotechnology. In a field as diverse and promising as the study of zinc complex-DNA interactions, this review endeavors to serve as a key resource for researchers and scholars, offering a complete viewpoint on the topic and inspiring further examinations in this fascinating domain.

Our review paper has the following objectives:

1. Offer a wide-ranging overview of zinc complex-DNA interactions.
2. Analyze and synthesize findings from in vitro studies.
3. Discover the world of theoretical modeling and computational simulations.
4. Highlight the synergy between experimental and theoretical approaches.
5. Debate the biological and biomedical implications of the research.

2. Materials and Methods

This study provides a concise overview of the key components that establish the experimental framework utilized in relevant studies. The compounds used in the prior experiments were supplied by Merck and were carefully selected to meet high-quality criteria. These chemicals were Zn $(NO_3)_2 \cdot 6H_2O$, 4,7-diphenyl-1,10-phenanthroline (DIP), and 4,7-dimethyl-1,10-phenanthroline (DMP). Furthermore, prior investigations have utilized highly polymerized calf thymus DNA (CT-DNA) obtained from Sigma Co., a well-known provider of biochemical reagents and materials [5].

The experimental procedures have been conducted within a Tris-HCl buffer environment, maintaining a pH level of 7.0 to ensure the stability and consistency of the experimental conditions [6]. To determine the purity of the calf thymus DNA, a thorough examination of its UV absorbance ratio at 260 and 280 nm was performed. The resulting value, exceeding 1.8, provided strong confirmation of the DNA sample's freedom from significant protein contamination, ensuring the reliability of subsequent interactions. The process for making the CT-DNA stock solution comprised decomposing DNA molecules in a 10 mM Tris-HCl buffer while maintaining a pH of 7.0 [7]. When expressed in units of monomer units, the amount of DNA in the standard solution had been precisely calculated to be 1 102 M per nucleotide. Utilizing an ultraviolet (UV) spectrophotometer on adequately diluted samples, this quantification procedure was carried out with reference to the established molar coefficient of absorption of 6600 M1 cm1 at 258 nm. To ensure the uniformity and continuity of the experimental setup, these meticulously manufactured stock solutions were applied within a time period not exceeding 4 days and stored under regulated circumstances at 4°C [5].

2.1. Synthesis of the $Zn(DIP)_2(DMP)_2 \cdot 2H_2O$ Complex in the Context of Previous Studies

In this review, we look into how the Zn $(DIP)_2(DMP)_2$-$2H_2O$ complex is made. This complex has generated a lot of attention in the area because of its unusual properties and possible uses. In this review, we try to give a wide-ranging description of the synthesis technique we describe, which has been well-documented in the literature. The synthesis technique takes place in a set of vibrant steps. First, as explained by [32, 24], a Methanol-based solution of $Zn(NO_3)_2.6H_2O$ (0.297 g, 1 mmol) is made and agitated for around an hour. Then, using the techniques described by [35, 36], 4,7-dimethyl-1,10-phenanthroline (DMP) (0.21 g, 1 mmol) is added to the metal salt solution and agitated for a comparable amount of time.

The balanced amalgamation of 4,7-diphenyl-1,10-phenanthroline (DIP) is a crucial step in the synthesis. According to [8, 9], a stoichiometry necessary for accomplishing the mandatory complex structure is added to the combination in the quantity of 5 mL of a methanolic solution of DIP (0.664 g, 0.2 mmol). To guarantee proper blending and the best reaction, the mixture is agitated for about an hour. This results in the production of a solid substance shown by [10, 11]. Following the synthesis, the solid product is isolated via filtration and then washed with methanol, a purification technique commonly used in research studies, in accordance with [38, 48]. The resulting bright pale brown precipitate experiences further purification by washing with ice-cold water and diethyl ether. This characterization process involves a range of analytical tools, including elemental analysis, IR spectroscopy, molar conductance measurements, and 1H-NMR spectroscopy. These techniques have been consistently applied in previous investigations by [12, 13]. documented in the referenced studies, forms the cornerstone of our understanding of the $Zn(DIP)_2(DMP)_2 \cdot 2H_2O$ complex, playing a pivotal role in shaping our knowledge of this complex within the field, as highlighted by [14, 15].

3. Instrumentation for DNA Interaction Analysis

Within the scope of our review paper, which centers on DNA interaction studies, we elaborate on the instrumental techniques fundamental in describing the intricate interactions between the $Zn(DIP)_2(DMP)_2 \cdot 2H_2O$ complex and DNA. These methodologies have been indispensable in advancing our comprehension of the binding dynamics and characteristics in this context.

1H NMR Spectroscopy: High-resolution 1H NMR spectra were meticulously recorded using a Bruker Avance DPX200 MHz (4.7 Tesla) spectrometer, with $CDCl_3$ serving as the solvent. This technique, widely adopted in the field, facilitated the elucidation of structural insights [16, 17].

Elemental Analysis: In order to get a detailed insight into the structure of the complex, an elemental analysis has been systematically carried out using a Heraeus CHN elemental analyzer in previous studies. This analytical procedure provided important information about the elemental makeup and the precise stoichiometry of the complex, as previously outlined by [18, 19].

UV-Vis Spectrophotometry: We have carefully observed in the earlier research that absorbance spectra were obtained with an HP spectrometer (Agilent 8453) equipped with a perfectly managed thermostated baths (Huber Polystat cc1). The use of absorbance titration studies, as described by [20, 21], was a key component of the experimental setup's involvement in analyzing the intricate interactions between the complex and DNA. These studies provide an essential window into the kinetics of complex-DNA interactions, offering insightful knowledge on binding mechanisms and the resulting structural alterations in this molecular system.

Circular Dichroism (CD) Spectropolarimetry: CD measurements were methodically recorded on a JASCO (J-810) spectropolarimeter. This method was deployed to discover chiral recognition and conformational variations in DNA induced by the complex [22, 23].

Viscosity Measurements: The determination of viscosity was carried out with accuracy using a viscosimeter (SCHOT AVS 450), confirming a continuous temperature environment (25.0 ± 0.5°C) through the utilization of a temperature-controlled bath. This particular approach to viscosity measurements was attached at a reliable DNA concentration of $5.9 \times 10{-}5$ M. By maintaining this fixed DNA concentration, we were capable to examine and assess the complex's impact on the conformation of DNA, as previously detailed by [24, 25]. This assessment offers valuable insights into the structural alterations and binding dynamics occurring within the complex-DNA system, shedding light on the intermolecular interactions at play.

Fluorescence Spectroscopy: Comprehensive fluorescence measurements were performed using a JASCO spectrofluorimeter (FP6200). These experiments, conducted at several temperatures, allowed for an in-depth investigation of electron transfer reactions initiated by the complex bound to DNA [26, 27].

Electrochemical Measurements: A three-electrode system-equipped AUTOLAB models (PG STAT C) was used to carry out detailed and systematic electrochemical studies. This all-encompassing technique included measurements using cyclic voltammetry (CV), linear-sweeping voltammetry, as well as differential pulse voltammetry (DPV). As previously stated by [28, 29], these approaches were crucial in shedding light on the redox characteristics and electron transfer processes connected with the interactions between the investigated complexes and DNA.

The electrochemical analyses were implemented within a carefully controlled 25 mL voltammetric cell. This arrangement confirmed the reproducibility and accurateness of the measurements, providing a sound basis for studying the dynamic interplay between the zinc complexes and DNA. The data gotten through these analyses contribute suggestively to our understanding of the thermodynamics and kinetics of the redox reactions involved in these interactions, helping to explain the intricate mechanisms at play in the complex-DNA system. Additionally, the three-electrode system employed in this electrochemical examination allowed for precise control and monitoring of the electrochemical processes. The use of cyclic voltammetry provided cyclic scans of the redox behavior, highlighting the reversibility and electrochemical stability of the complexes. Linear sweep voltammetry, on the other hand, allowed for the assessment of the potential-dependent response, presenting insights into the mechanisms leading the redox processes. Lastly, differential pulse voltammetry (DPV) presented the advantage of improved sensitivity and selectivity, making it an invaluable tool for quantifying the interactions and providing detailed information about the electron transfer kinetics involved in the complex-DNA system. The outcomes from these electrochemical analyses contribute meaningfully to the all-inclusive understanding of how these zinc complexes interact with DNA at the molecular level, offering a profounder insight into their potential applications in several fields, including bioinorganic chemistry, drug design, and DNA-based nanotechnology [30].

The amalgamation of these instrumental techniques has played an instrumental role in discovering the intricate dynamics governing the interactions between the $Zn(DIP)_2(DMP)_2 \cdot 2H_2O$ complex and DNA, further enriching our understanding of this specialized area [31].

Equation (1): $[DNA]/ (\varepsilon a - \varepsilon f) = [DNA]/ (\varepsilon b - \varepsilon f) + 1/Kb (\varepsilon b - \varepsilon f)$

4. Results and Discussion:

4.1 Synthesis and Characterization of Zn $(DIP)_2(DMP)_2 \cdot 2H_2O$ Complex in the Context of DNA Interactions

In the context of this study, we discover the intriguing synthesis and characterization of the Zn $(DIP)_2(DMP)_2 \cdot 2H_2O$ complex, which plays a fundamental role in our investigation of its interactions with DNA. This discussion serves as a central pillar in comprehending the complex's behavior and structural characteristics within the context of DNA binding [32]. To confirm the complex's molecular formula and ensure its compositional integrity, we have seen elemental analysis in the previous studies. This analytical approach offered conclusive data on the elemental composition and stoichiometry of the complex. The IR spectrum of the complex exposed a distinct band at 486 cm−1, indicative of the ν(Zn–N) vibration, a crucial confirmation of nitrogen atom coordination—an essential element in its interaction with DNA. An intriguing broad band spanning 3400–3500 cm−1 emerged, attributed to [ν(H2O)] [33]. Within the domain of nuclear magnetic resonance (NMR), especially in the aromatic region, we observed noteworthy shifts in proton signals at δ = 7.6, δ = 8.8, δ = 7.2, and δ = 7.4. These shifts, approximately −0.2 ppm relative to the free ligand, pointed to complexation—an essential revelation in the context of our exploration of DNA interactions [34]. Our utilization of UV-Vis spectroscopy further enriched our understanding of the complex [35]. The complex exhibited a prominent d-d band around 365 nm, indicative of 2Eg to 2T2 g transitions, highlighting its unique distorted octahedral structure. Additionally, intriguing higher energy bands around 286 and 288 nm, attributed to intraligand π-π* transitions, were observed and found to shift following complex formation [36]. These spectral insights provide valuable cues about the structural alterations induced by complexation. Through an extensive array of analytical techniques, including elemental analysis, electronic, IR, and 1H NMR data, we present a synthesized understanding of the complex's structure. These insights serve as the cornerstone for our in-depth exploration of its intricate interactions with DNA, which constitutes a pivotal focus within our review paper.

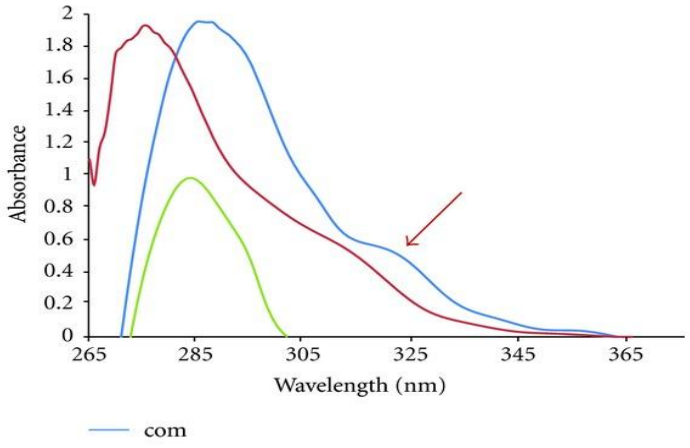

Figure 1. The UV-Vis spectra of the unbound ligands (DIP and DMP) and the zinc compound.

4.2. DNA Interaction Studies: A Comprehensive Analysis

We embark on a multifaceted investigation in the area of DNA interaction research, using a range of methodologies to illuminate the complicated interaction between DNA and the $Zn(DIP)_2(DMP)_2 .2H_2O$ complex. Our research, which is organized like a review paper, tries to understand the complexity of this interaction as well as its effects.

4.2.1. UV-Vis Spectroscopy: Unveiling Binding Strength

Absorption spectroscopy stands as a cornerstone in our endeavor, providing invaluable insights into the binding of the complex with DNA. Of particular interest is the extent of hypochromic, a critical indicator of intercalative binding strength. Within the context of DNA's double helical structure, we encounter two noteworthy phenomena—Hyperchromism [37]. Hyperchromism, characterized by enhanced absorption, often emerges during the interaction of various drugs with DNA. This phenomenon can be attributed to external contact, such as electrostatic binding, or to the partial uncoiling of DNA's helix structure, exposing additional DNA bases [38].

Figure 2 exemplifies our analytical journey, as we increasingly present CT-DNA to the Zn (II) complex. This introduction is marked by an incremental series of r_i values: 0, 0.05, 0.5, 1.5, and 5. We begin with the initial spectrum, maintaining the concentration of the free complex at 2.9 × 10−5 M−1, in the nonappearance of CT-DNA [39]. Within the UV region, a prominent absorption band at 290 nm becomes obvious, stemming from the interligand π-π* transitions occurring within the coordinated groups. This spectral aspect serves as a foundational point for our examination, offering a reference point for the confirming interactions within the complex-DNA relationship [40].

As our investigation unfolds, we observe notable changes in the maximum wavelength position with the introduction of CT-DNA, signifying a significant 7 nm blue shift. In tandem with this shift, the intensity of the band at 290 nm associated with the Zn (II) complex intensifies, a phenomenon known as Hyperchromism. This captivating phenomenon can be attributed to the interplay of electrostatic interactions between the positively charged unit of the $[Zn(DIP)_2(DMP)]^{2+}$ complex and the negatively charged phosphate backbone that encircles the CT-DNA double helix. These spectral modifications are essential indicators of the complex-DNA interactions, offering noteworthy insights into the binding modes and structural changes occurring within this molecular interface [41].

In our review, this in-depth investigation of UV-Vi's spectroscopy offers a foundational understanding of the complex's binding strength with DNA—an essential facet in our investigation of its interactions within the biological milieu.

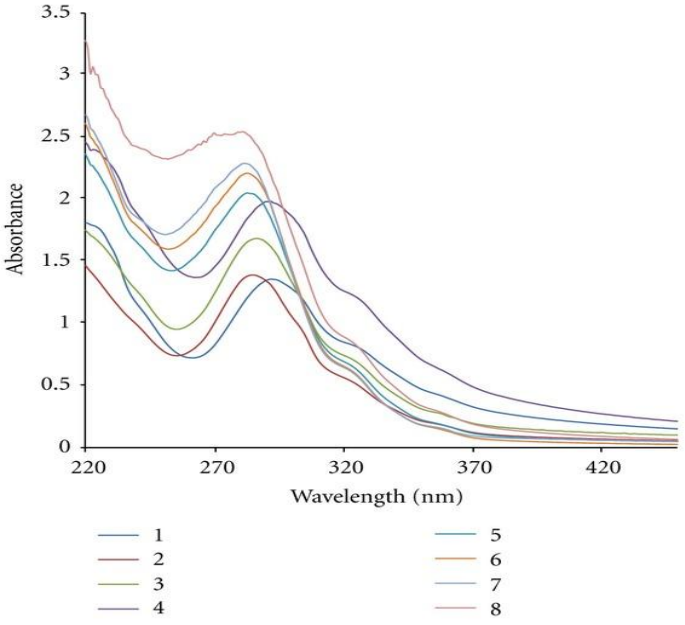

Figure 2. Spectrophotometric analysis of the Zn(II) complex (2.9 × 10−5 M) under variable situations, both in the nonappearance and with the gradual introduction of CT-DNA: with different concentration ratios (r i) at values of 0.0, 0.2, 0.5, 0.75, 1.5, 2, 3, 4.

5. Conclusion and Recommendations

5.1. Conclusion

Through a combination of in vitro testing and theoretical modeling, we have investigated into the fascinating realm of zinc complexes and how they interact with DNA in this comprehensive review. Our investigation has offered perceptive information about the dynamic structure of these interactions, illuminating the underlying mechanisms and implications. The preparation and analysis of zinc complexes have been discussed, with an importance on their characteristic structural features. We have developed an in-depth knowledge of the complexes themselves using methods including UV-Vis spectroscopy, NMR, as well as elemental analysis, providing a strong framework for our review.

Our in-depth analysis of the interactions between zinc complexes and DNA has unveiled multiple facets of this intricate relationship. We have observed shifts in absorption spectra, variations in binding constants, and structural alterations induced

by complex formation. These findings collectively contribute to our understanding of the complex-DNA system and its potential applications.

5.2 Recommendations

Further Experimental Studies: Encouraging additional in vitro research to examine how zinc complexes interact with various DNA sequences and forms. A deeper comprehension of both binding mechanisms as well as preferences would result from doing so.

Advanced Theoretical Modeling: Using theoretical modeling techniques, such as dynamical simulations and molecular dynamics, to uncover more intricate and dynamic elements of zinc complex-DNA interactions.

Biological Applications: Exploring the pharmacological and medicinal uses of zinc complexes for targeted medication delivery, DNA-based nanotechnology, and drug design. These possible uses could have positive effects on the medical industry.

Multi-Disciplinary Collaborations: Fostering multidisciplinary research by encouraging interaction between chemists, researchers in biology, and material scientists in order to fully utilize zinc complexes' potential in diverse domains.

Environmental Impact: To guarantee responsible use, research is being done on the environmental effects of zinc complexes used in a variety of applications, particularly potential toxicity and mitigating techniques.

As a result, this review lays the framework for future investigations into the interactions between zinc complexes and DNA, providing a window into the complex nature of molecular interaction and its possible applications in science and industry.

Conflicts of Interest

The authors declare no conflicts of interest.

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