Al-Salam Journal for Medical Science
Journal Homepage: http://journal.alsalam.edu.iq/index.php/ajbms
E-ISSN: 2959-5398, P-ISSN: 2958-0870

Chemistry of DNA-binding Molecules

Evon Akram[1], Dina A. Najeeb[2], Asmaa A. Jawad[3]*, Nada H. Bedair[4] Ashjan M. Hussein[5], Saba R. Jaafar[6], Ruaa H. Ali[7], Rana F. shaher[8], Marwa A. Hussein[9], Daniah M. Hamid[10], Reem H. Al-Tabra[11], Alyaa K. Abood[12] and Salam Mohammed[13]

[1,3] Department of Forensic Chemistry, Higher Institute of Forensic Science, Al-Nahrain University, Baghdad, Iraq.
[2] Department of Chemistry, College of Science, Al-Nahrain University, Baghdad, Iraq.
[4,6,7,8,9,10,11]Department of Forensic Biology, Higher Institute of Forensic Science, Al-Nahrain University, Baghdad, Iraq.
[5,12]Department of Experimental Therapy, Iraqi center for cancer research and medical genetics Research, Mustansiriyah University, Baghdad, Iraq.
[13] Department of Chemical and Petrochemical Engineering, College of Engineering and Architecture, University of Nizwa, Oman.

*Corresponding Author: Asmaa A. Jawad

DOI: https://doi.org/10.55145/ajbms.2025.06.02.009
Received July 2025; Accepted August 2025; Available August 2025

ABSTRACT: DNA-binding molecules regulate gene expression, replication, repair, and transcription, making their research crucial to molecular biology. This review investigated their architectures, processes, and impacts on cancer research and therapy to determine their biological and therapeutic potential. A thorough examination of published data on DNA-binding agents, including intercalators, groove binders, and metal complexes, focused on their chemical properties, biological activity, and therapeutic significance. Doxorubicin intercalated between base pairs to inhibit replication and transcription, whereas cisplatin produced covalent cross-links with guanine bases to cause tumor cell death. Multiple derivatives of metal complexes reduced tumor development by over 70% in leukemia models as DNA probes and therapeutics. Also reviewed, Dps proteins in *Escherichia coli* showed that their non-specific DNA binding offered up to 65% oxidative stress resistance compared to control cultures, validating DNA-protein protection as a survival strategy. In Phase II studies, amsacrine caused substantial remission in acute leukemia patients, whereas doxorubicin was more effective across many cancer types but had greater cardiotoxicity concerns. Selectivity, toxicity, and resistance limit DNA-targeting medicines, although they are successful. Chemical modifications like hydrophobic tailoring and sequence-specific binding have enhanced binding affinity and therapeutic index, yet only 10% of candidate compounds get clinical approval. Recent studies show that AI-driven design has expedited screening, lowering development costs by 30% and durations by 3–5 years. These data suggest that DNA-binding medicines have great potential in cancer, but safer, more selective, and resistance-free therapy are still needed.

Keywords: DNA; Medical Field; Chemistry of DNA-binding molecules DNA; Biomedical Effects

1. INTRODUCTION

The one-way flow of genetic information from DNA to RNA to protein was Crick's key molecular biology premise in 1970. This framework explains how genetic sequences control cellular functioning. The genetic code controls amino acids, which define an organism's physical and biological traits. Genotype determines phenotype because DNA sequences supply instructions. Transcription produces RNA to understand these instructions. This is the crucial step between DNA and protein synthesis. Recent research has shown that transcription is both a mechanical copying process and a carefully controlled gene expression checkpoint. When transcription fails, RNA processing, transport, and protein translation fail. This explains why genetic and biological research has focused on transcription. Controlling

*Corresponding author: asmaa85ali@gmail.com

transcription affects gene activity, cell growth, and differentiation. Cellular stability is maintained by such control, whereas faults cause illness. Synthesis is crucial in regulating genes, enabling cells to proliferate, differentiate, and sustain homeostasis. These mechanisms function as a primary structural 'on/off' switch for gene regulation [1]. Consequently, an inability to produce the initial RNA transcript obviates the subsequent regulatory processes, including transcript processing, transport, and translation of the RNA transcript into protein. The pivotal position of DNA in biological systems has established it as a longstanding target for detecting and treating human diseases. Little compounds identifying particular DNA sequences are potent instruments for analyzing the human genome [2].

DNA-binding refers to the ability of specific molecules, particularly proteins, to attach to DNA through specific interactions. The molecules in this category can recognize specific DNA sequences or structural components, allowing them to regulate essential cellular processes such as DNA replication, transcription, repair, and exchange. Proteins that interact with DNA in different types, such as transcription factors, polymerases, and histones, are crucial for the regulation of gene expression and the maintenance of genomic integrity. Binding may occur through various mechanisms of interaction bonds, including hydrogen bonding, electrostatic interactions, and van der Waals forces, facilitating precise regulation of genetic activities [3].

The imperative to protect DNA from damage has generated considerable interest in organic compounds with antioxidant and anti-mutagenic properties, resulting in heightened chronic consumption of antioxidant vitamins, flavonoid-rich formulations, and various dietary supplements to prevent DNA damage and its consequences. The improper utilization of phytochemicals can pose significant risks. At high concentrations, these compounds elicit pro-oxidant and genotoxic effects. The prolonged preventive intake of antioxidants may induce additional dangers and damage DNA. A study examining the life span of individuals who regularly consumed fat-soluble vitamins, compared to a control group, revealed no enhancement in life span. Conversely, the prolonged intake of large dosages of beta carotene, vitamin E, and vitamin A diminishes the life expectancy of patients. This suggests the potential dual effects of antioxidants [2, 4].

Deoxyribonucleic acid (DNA) holds considerable biological importance. DNA contains information encoded as genes, which are crucial for several tasks. As shown by cell biology, DNA serves as the principal target molecule for most anticancer and antiviral medicines. Research on DNA interactions with transition metal complexes, particularly those featuring multidentate aromatic ligands, has generated significant interest due to their potential as novel therapeutic agents and intriguing properties that may serve as DNA structure and conformation probes. Binding peptides and tiny organic and inorganic compounds to DNA will disrupt several processes, such as transcription and replication [5]. This idea allows the potential treatment of different illnesses, such as cancer and cystic fibrosis, by using DNA as therapeutic targets. This gives rise to a new field of study known as DNA drug interaction, which has been of significant relevance since 1960. Since then, many studies have been conducted to identify several metal ions and metal complexes useful in cancer therapy [6]. The cleavage of DNA is accomplished via concerted its fundamental components, such as bases and/or sugars, through an oxidative route or hydrolyzing phosphoester bonds. Among the several DNA-binding and cleaving agents documented to date, transition metal complexes are pertinent to the current study. Metal complexes can bind DNA through various interactions and break the duplex due to their inherent chemical, electrochemical, and photochemical reactivities. The persistent quest for novel anti-cancer agents has catalyzed chemotherapeutic research utilizing metals since such compounds may demonstrate reduced toxicity and enhanced anti-proliferative efficacy against tumors [7].

DNA, defined as deoxyribonucleic acid, provides the essential framework for life, containing the biological directives required to ensure the genesis of every species recognized, function, growth, and reproduction. The intricate chemistry of DNA binding molecules is crucial in several biological activities, including gene regulation, DNA replication, and repair mechanisms. DNA-binding compounds are important in cancer research because tailored treatments impede malignant cell genetics. DNA-directed medication design has improved patient outcomes and therapeutic efficacy. But big barriers remain. Therapies have to be more selective to protect healthy DNA. Since DNA interactions destroy normal and malignant cells, toxicity remains a big problem. Due to resistance, many medications are less effective with time. Designs with sequence-specific affinity and tailored chemical characteristics boost safety and activity, according to recent research. DNA-binding medicines with immunotherapy or molecular targeting boost therapeutic response. If these tactics continue, they will increase therapy alternatives, reduce side effects, and address resistance. Future research should create DNA-binding agents with more accuracy, better genetic regulation, and greater use in DNA-directed medicine [8].

2. STRUCTURAL CHARACTERISTICS OF DUPLEX DNA

Double-helical DNA consists of two related, opposite, sugar-phosphate poly-deoxyribonucleotide chains interconnected by specific hydrogen bonds between base pairs. The central region created through these paired fibers delineates the helical lines, signifying the boundaries of the hetero basis. The medically significant B-form of the DNA double helix is distinguished through a broad and deep main groove following to a deep and narrow a minor groove [3].

3. ROLE OF DNA INTERACTION

Interactions between DNA molecules are crucial for genetic compacted and the control of translation. In investigations of complex mechanisms, DNA is frequently represented as a uniformly provided cylinder, and its electrostatic forces are computed using the Poisson-Boltzmann equation. DNA contains the instructions necessary for an organism's growth, survival, and reproduction. To execute these functions, DNA sequences need to be translated into signs that enable the production of proteins, which involves complicated molecules accountable for the majority of biological activities in the human system [9].

4. BIOMEDICAL FUNCTIONS OF THE CHEMISTRY OF DNA BINDING

Proteins that interact with DNA or RNA are frequently examined in isolation. Transcription factors are often characterized in a straightforward manner: they attach to genomic promoters and regulate target gene expression by either activating or inhibiting RNA polymerases. Subsequent to transcription, RNA binding proteins influence protein production by regulating the stability and translation of mRNAs. The differentiation between DNA- and RNA-binding functions within proteins has grown irrelevant. The often-neglected dual ability of different proteins to interact with both DNA and RNA is essential for determining gene expression, cellular survival, and homeostasis. Recent research investigations indicate that multiple transcription variables can bind different RNA forms, enabling them to interact with mRNA transcripts to regulate degradation and incorporate supplementary signals, including reaction to stress [10].

This study aims to bring together DNA and RNA binding proteins (DRBPs), design, and evolution. We will first investigate the prevalence of DRBPs in the human genome. We emphasize the established roles of DRBPs, providing concrete examples of how concurrent and sequential interactions with RNA and DNA enhance gene targeting, refine gene expression regulation, and incorporate metabolic conditions or stress to regulate protein activity. This discourse examines the structural characteristics of DRBPs that facilitate dual nucleic acid specificity, emphasizing the few numbers of resolved structures that provide direct comparison of a DRBP complexed with either DNA or RNA. We examine the progression of dual DNA and RNA binding domains in DRBPs, encompassing both primordial domains that provided a selection advantage through dual binding and contemporary domains that have recently been influenced by swiftly developing lincRNAs [11].

DNA-binding chemicals are essential tools in genetic research. They utilize several methods to examine DNA-protein interactions and clarify gene regulation mechanisms, including DNA footprinting, chromatin immunoprecipitation, and electrophoretic mobility shift assays [12].

Engineered DNA-binding agents can selectively identify and eliminate environmental pollutants. Researchers can enhance the effectiveness of bioremediation procedures by designing compounds that interact with certain DNA sequences of microbial strains. In synthetic biology, DNA-binding agents design genetic circuits and mechanisms. Researchers may develop biosensors and bioengineered organisms by manipulating chemicals that interact with certain DNA sequences, enabling systems to respond to environmental stimuli. DNA-binding molecules are employed in the fabrication of nanoscale systems. DNA techniques utilize DNA-binding agents to fabricate DNA structures for applications, including drug delivery, biosensing, and molecular computing [12].

5. MECHANISM OF DNA-BINDING

A pharmaceutical chemical might interact with DNA by modulating transcription factors. In this instance, the medication a compound does not directly bind to the DNA; instead, it interacts with the protein associated with the DNA, altering its functions. Formation of DNA-RNA hybrids: Binding to an RNA molecule that later interacts with single-stranded DNA produces DNA-RNA hybrids that interfere with transcriptional activity. Direct molecular binding: In this context, small aromatic ligand molecules directly interact with the DNA double helix, including several types, such as groove binders and intercalators. Figure 1. Substances are then designed to bind to these particular sequences. The drug must possess sufficient reactivity to bind to the biological target without excessive reactivity, which might result in deactivation by other biomolecules present. The prevalence of these sequences in humans is controlled to prevent interference with normal human functions [13].

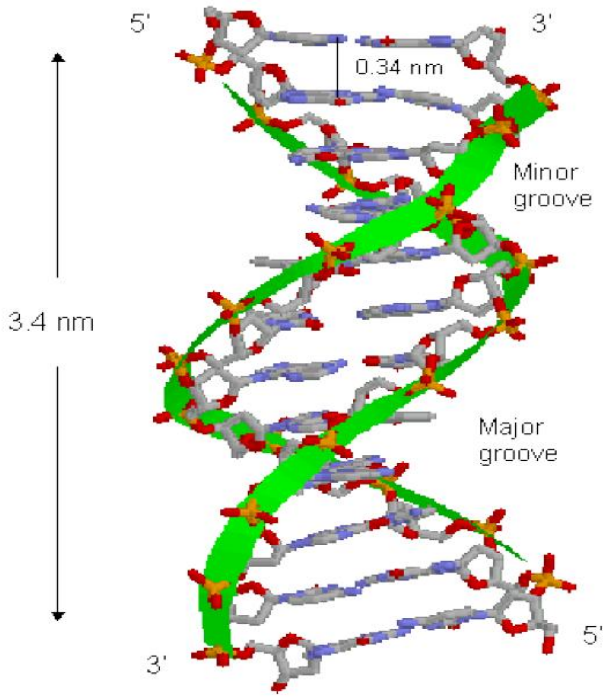

FIGURE 1.- Structure of DNA and its grooves [13]

6. CHEMICAL CHARACTERISTICS OF DNA-BINDING AGENTS

The chemical properties of DNA-binding agents are crucial for evaluating their efficacy, specificity, and overall performance in DNA interactions. This planarity improves optimal stacking interactions with the nucleobases, enhancing binding affinity. The hydrophobic characteristics of specific DNA-binding agents can affect their capacity to traverse cellular membranes and engage with DNA. This attribute can improve the specificity and efficiency of binding through increasing the selectivity of the interaction through enhanced formation of hydrogen bonding, which may influence the stability of the DNA complex [14].

Solubilizing DNA-binding compounds in bodily fluids is crucial for therapeutic use. Extremely hydrophobic agents may precipitate, whereas extremely hydrophilic agents may not enter biological membranes. Alkylation and cross-linking may occur with some DNA-binding agents. These reactions change DNA structure, impacting replication and transcription. The ability of DNA-binding agents to selectively target certain DNA sequences or structures is dictated by their chemical composition. This selectivity is crucial for minimizing off-target effects in therapeutic applications [15].

7. THE EFFECTS OF DNA-BINDING AGENTS ON CANCER STUDIES

In the past 70 years, the treatment of cancer has undergone three stages. The initial phase has been characterized through the advancement of cytotoxic agents, which impaired the gene structure of tumour cells; the subsequent phase focused on drug-specific signalling pathways; and the last phase involved augmenting the immune system's response to eradicate tumour cells. Although targeted therapy holds potential in medicine, its efficacy has been constrained through cancer, whereas cytotoxic treatment is crucial for eliciting host responses. A primary emphasis of this category has been the advancement of DNA-binding anticancer pharmaceuticals. Analyzing the reason for developing DNA-binding medicines and their association with specific cancer treatments is illuminating [16]. Research at the Auckland Cancer Society Research Centre (ACSRC), initiated in the second half of the 1960s according to the direction of Professor Bruce Cain, utilized mathematical modeling to develop drugs that intercalate between close DNA base groups, thereby causing disruption of typical DNA work and producing anticancer properties. The synthesis of several 9-anilinoacridine compounds has shown significant effectiveness against L1210 transplantable murine leukemia. Professor Cain assembled an interdisciplinary team of medicinal chemists, molecular and cellular scientists, pharmacists, and physicians. Amsacrine, a derivative of 9-anilinoacridine among other synthesized and evaluated compounds in this research, was chosen for assessment in the US National Cancer Institute's anticancer medication development initiative. Amsacrine progressed to Phase I and Phase II clinical studies, demonstrating substantial efficacy against human acute leukemia, and thereafter became widely utilized [17].

During the same timeframe, investigations into antibiotics discovered DNA-binding agents with antitumor efficacy. Doxorubicin, an anthracycline antibiotic, was identified as significant due to its efficacy against several

cancers. A compelling inquiry from this preliminary study was why amsacrine's antitumor efficacy was restricted to leukemia, whereas doxorubicin exhibited a wider range of activities. Recent investigations at the ACSRC have highlighted the significance of integrating many scientific disciplines, such as physics, chemistry, and others, to address this inquiry. These drugs can modify gene expression patterns that facilitate tumor development by affecting the binding of regulatory proteins to DNA. Investigating these relationships is essential for creating medicines to rectify abnormal epigenetic alterations [18].

Imprecise recovery of wounds may lead to genetic abnormalities that are possibly inherited through surviving cells. Consequently, eukaryotic cells have developed a sophisticated signaling network of repair mechanisms called DNA damage repair (DDR). The significance of DNA repair systems is underscored by several severe human disorders resulting from DNA damage response gene abnormalities. Many of these mutations exhibit heightened susceptibility to DNA-damaging chemicals and predispose individuals to particular cancer forms. Theodor Boveri already identified cancer as a genomic illness [19]. Mutations and chromosomal abnormalities can result in modifications of gene function. Unregulated neoplastic cell proliferation transpires when oncogenes are activated, or tumor suppressor genes are inactivated, as shown in Figure 2. The fundamental significance of DNA damage in cancer progression is particularly apparent when hereditary abnormalities in DNA repair mechanisms result in heightened cancer susceptibility [20].

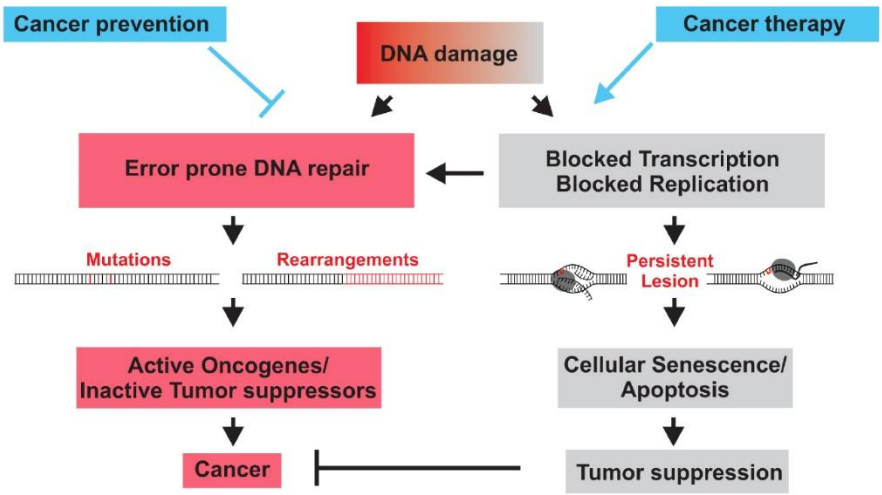

FIGURE 2.- DNA damage contributes to cancer growth if faulty DNA repair results in mutations or chromosomal modifications [19]

DNA was a focus of antitumor medication development before elucidating its molecular structure. Substances with objectively displayed cancer-preventing action were subsequently demonstrated to attack DNA or prevent enzymes that regulate DNA integrity or provide its building components. When Watson and Crick elucidated the composition of DNA in 1953, different methods of treatment targeting DNA were already created: antimetabolites, which reduce nucleotides, such as folic acid inhibitors like methotrexate; alkylating agents that inflict direct destruction of DNA, which include nitrogen mustard and its derivatives; and intercalators like actinomycins, and that connect to DNA and prevent the function of numerous enzymes that utilize DNA as a substrate. Among the most prevalent and efficacious anticancer agents currently employed are general DNA-damaging substances, such as inhibitors of topoisomerases (TOPO) I and II, antimetabolites, alkylating agents, and substances inducing covalent modifications of DNA (such as mitomycin C and platinum derivatives), in addition to γ-irradiation, that primarily targets DNA too [21].

[21].

While targeting DNA for cancer therapy is well-founded and somewhat effective, it presents several drawbacks. Initially, it is insufficiently effective to provide a cure for cancer. Secondly, it generates considerable detrimental side effects. Third, it may induce secondary malignancies unrelated to the underlying malignancy and emerge 10 to 15 years after the effective eradication of the first illness. All three issues arise from the DNA damage induced by the treatment substance. If DNA remains undamaged, most side effects would be mitigated, allowing for more extensive treatment of patients to get a complete cure without significant adverse consequences. The danger of subsequent cancer development would be diminished if the DNA-targeting medications did not induce further mutations in cellular genes [22].

The pathway for developing and identifying anti-cancer drugs includes target authentication, hit recognition, hit-to-lead progression, lead optimization, preclinical candidate selection, and both preclinical and clinical studies. Notwithstanding advancements in disease technological advancement and cancer system studies, creating innovative and efficacious anti-cancer pharmaceuticals from inception continues to be a challenging, costly, and protracted

endeavor necessitating extensive interdisciplinary collaboration among pharmaceutical chemistry, , drugs, clinical studies, and other sciences. Statistically, developing a new treatment might take about 10 to 17 years and over 2.8 billion dollars before it enters clinical practice. Moreover, just 10% of the substances evaluated in clinical trials successfully reach the market [23].

Designing anti-cancer medications is particularly challenging due to factors that include undruggable objectives, chemoresistance, tumor heterogeneity, and metastasis. Traditional pharmaceutical development methodologies may appear to be ineffectual. Computer-aided techniques for drug screening are becoming a crucial element in drug design practices [24]. This method allowed medicinal chemists to simulate the interactions with a ligand and receptors, facilitating the creation and optimization of lead compounds using computer simulation. The conventional function of CADD in drug discovery is to filter extensive chemical libraries into smaller groups of anticipated active molecules via computational chemistry. It can significantly expedite the process of anti-drug design and conserve substantial time and financial resources [23].

Amid the swift advancement of computer hardware and artificial intelligence methodologies, scholars in academia and the pharmaceutical sector are increasingly utilizing artificial intelligence to enhance medication creation methods. Artificial intelligence (AI) denotes the emulation of human intelligence in robots designed to think and behave like humans. A prevalent assumption regarding artificial intelligence is that it aims to create computers with comparable capabilities for "understanding." Artificial intelligence is now employed in several applications for cancer research, including the categorization of aberrant cancer cell images, the prediction of target protein structures, and the forecasting of drug-protein interactions. This research illustrates that artificial intelligence methodologies possess the potential to transform anti-cancer medication creation procedures. Figure 3 illustrates many uses of artificial intelligence in the processes of anti-cancer medication creation. This research examined advancements in anti-cancer medication creation utilizing artificial intelligence, showcased notable examples, and elucidated the foundational concepts of these methodologies [23].

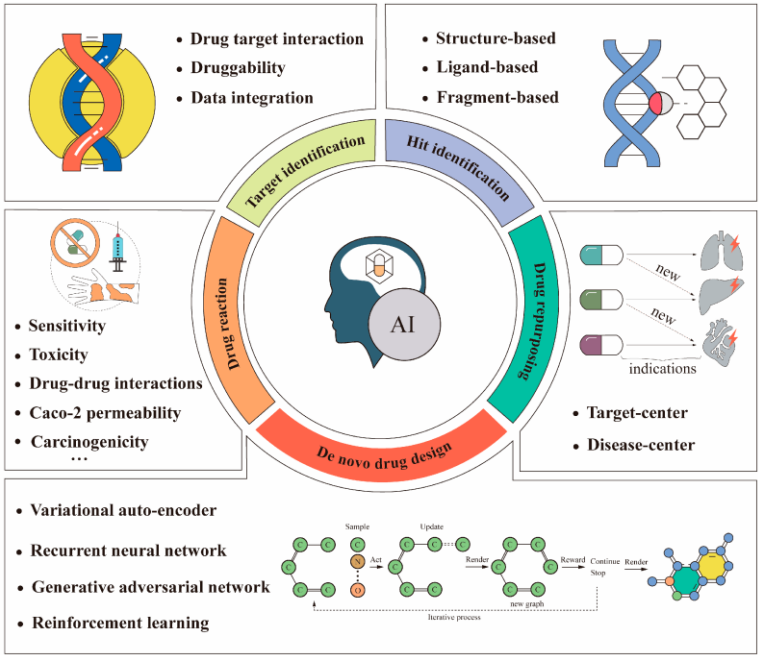

FIGURE 3. - Various uses of artificial intelligence in the design of anti-cancer pharmaceuticals. De novo drug design is often executed using the abovementioned techniques based on deep learning. In recent times, learning through reinforcement has often been employed. The abovementioned procedure exemplifies an iterative chemical graph creation method with a graphical chemical structure and an O–C–O linkage [24]

8. GENERAL APPLICATIONS OF DNA BINDING IN CHEMISTRY

Interactions involving DNA binding are essential in several scientific and technical domains, such as medicine, biotechnology, forensic science, and nanotechnology. The capacity of chemicals to engage with DNA via covalent or non-covalent interactions has facilitated the creation of potent instruments for pharmacological design, gene modulation, and diagnostic purposes. Comprehending the chemistry of DNA binding allows researchers to modify genetic material for therapeutic and analytical applications [25].

DNA binding is a principal use in medication design and cancer treatment. Numerous chemotherapeutic agents target DNA to impede replication and transcription in neoplastic cells. Cisplatin, a prevalent anticancer agent, establishes covalent cross-links with guanine bases in DNA, inhibiting cell proliferation and inducing death. Intercalating drugs such as doxorubicin insert between DNA base pairs obstruct topoisomerase II and result in DNA damage. Specific antibiotics, such as actinomycin D and ciprofloxacin, utilize DNA binding to impede bacterial proliferation by obstructing transcription or disrupting DNA replication [26].

DNA-binding proteins and synthetic compounds regulate gene expression and modify genetic sequences in biotechnology and gene regulation. Transcription factors (TFs) inherently modulate gene expression by binding to certain DNA regions and affecting RNA transcription. Gene-editing tools such as CRISPR-Cas9 utilize sequence-specific DNA binding to implement precise genetic alterations. Moreover, DNA-binding dyes and probes, such as SYBR Green and ethidium bromide, are crucial in polymerase chain reaction (PCR) and fluorescence in situ hybridization (FISH) to detect genetic sequences. Techniques like Southern and Northern blotting employ DNA-binding interactions for genetic investigation and study [26].

DNA binding chemistry is essential in forensic science and DNA fingerprinting, and it is utilized for personal identification and criminal investigations. DNA-staining colors facilitate the visibility of genetic material in gel electrophoresis, a prevalent forensic method. The polymerase chain reaction (PCR) is extensively employed to amplify DNA from crime scenes, facilitating short tandem repeat (STR) analysis for identification verification. Next-generation sequencing (NGS) advancements yield precise genetic profiling, enhancing forensic accuracy and medical diagnosis [27].

DNA binding is nascent in nanotechnology and biosensors. DNA-functionalized nanomaterials provide precise drug delivery, biosensing, and molecular computing. Programmable healthcare nanodevices have been developed using DNA origami. Biosensors detect diseases, infections, and environmental contaminants using DNA-binding nanoparticles, including gold nanoparticles with DNA probes. These findings demonstrate DNA-binding chemistry's versatility in developing next-generation biological and technological advances [27].

DNA binding chemistry affects several areas. DNA-binding interactions drive life-saving cancer drugs, accurate forensic investigation, and innovative nanotechnology. New applications in health, genetics, and materials science are envisaged as this study advances, improving DNA-binding chemistry [27].

DNA binding regulates and maintains genetic information, providing several benefits. Transcription factors attach to certain DNA sequences to activate or decrease gene expression, allowing cells to react to genetic alterations and developmental cues. DNA-binding proteins also replicate and repair DNA, avoiding mutations that may cause cancers. Biotechnology and medicine use modified DNA-binding proteins like CRISPR-Cas9 for gene editing and treatment. DNA-binding improves chromatin architecture, consolidating DNA in the nucleus while permitting transcription and replication. These activities optimize cellular function and genetic integrity, emphasizing DNA-binding in theoretical and practical areas [14].

9. DNA ‑ BINDING PROTEIN DPS AND ITS ROLE IN ACID AND OXIDATIVE STRESS RESISTANCE IN ESCHERI-CHIA COLI

In Escherichia coli (E. coli), the DNA-binding protein from starving cells (Dps) protects bacterial DNA against environmental stress. Dps, a ferritin superfamily member, non-specifically binds DNA to protect it. It is highly expressed during the stationary phase and in response to oxidative and acid stress. Dps protects DNA and regulates gene expression, helping bacteria survive in harsh environments [28].

Dps' main function is oxidative damage resistance. ROS, including hydrogen peroxide (H_2O_2), superoxide radicals, and hydroxyl radicals, may harm DNA, proteins, and lipids. DPS offers many protections. As a ferroxidase, it converts Fe^{2+} (ferrous iron) to Fe^{3+} (ferric iron), preventing damaging Fenton reactions that produce hydroxyl radicals. Second, a DNA-Dps complex forms a physical barrier that prevents ROS from accessing DNA, reducing oxidative damage. Dps helps *E. coli* survive oxidative stress [28].

Besides oxidative stress resistance, Dps is crucial for acid stress resistance. Acidic habitats like the stomach or fermentation process are common for E. coli. Protein denaturation and DNA damage in acidic circumstances endanger bacterial life. Dps stabilizes DNA and reduces strand breakage to protect E. coli. Additionally, its interaction with DNA may condense chromosomal architecture, making it more damage-resistant. Dps store iron, limiting acidic hydroxyl radical generation and stress-induced DNA damage [29].

The Dps protein in E. coli functions as a multifaceted stress-response component, crucial for oxidative and acid stress resistance. Dps directly binds to DNA and regulates iron homeostasis, preserving genome integrity, improving bacterial survival in harsh circumstances, and facilitating the persistence of E. coli in various settings. Its defensive actions provide it an essential element of bacterial stress adaptation, guaranteeing tolerance to environmental variations [30].

10. CONCLUSION

DNA-binding agents are essential in oncological study and therapy. Intercalates can affect the regulation of genes and induce apoptosis in cancer cells. The ability to select and toxicity continue to pose obstacles in pharmaceutical development. Technological advancements improve the efficacy of DNA-targeted medication design. Combination medicines enhance cancer therapy efficacy. Evaluation instruments employ DNA-binding agents for the detection of tumors.

Funding

None

ACKNOWLEDGEMENT

The authors would like to thank the anonymous reviewers for their efforts.

CONFLICTS OF INTEREST

The authors declare no conflict of interest

REFERENCES

[1] K. Qu, L. Wei, and Q. Zou, "A review of DNA-binding proteins prediction methods," Curr. Bioinform., vol. 14, no. 3, pp. 246–254, 2019.

[2] A. Gironda-Martínez, E. J. Donckele, F. Samain, and D. Neri, "DNA-encoded chemical libraries: a comprehensive review with successful stories and future challenges," ACS Pharmacol. Transl. Sci., vol. 4, no. 4, pp. 1265–1279, 2021.

[3] H. Dohnalová and F. Lankaš, "Deciphering the mechanical properties of B-DNA duplex," Wiley Interdiscip. Rev.: Comput. Mol. Sci., vol. 12, no. 3, p. e1575, 2022.

[4] S. Stangherlin and J. Liu, "Nanomaterials enabled and enhanced DNA-based biosensors," J. Mater. Chem. B, vol. 11, no. 30, pp. 6994–7003, 2023.

[5] N. D. Esiobu, I. M. Ezeonu, and F. Nwaokorie, "Principles and techniques for deoxyribonucleic acid (DNA) manipulation," in Medical Biotechnology, Biopharmaceutics, Forensic Science and Bioinformatics. Boca Raton, FL, USA: CRC Press, 2022, pp. 3–32.

[6] H. Al-hayali, "An investigative study for organizational structure and function of nucleic acid DNA and its biochemical properties," World Bull. Public Health, vol. 16, pp. 59–65, 2022.

[7] M. Tripathi, A. Sarkar, and M. Mahilang, "Nucleic acids: components, nomenclature, types, and protection method," in Handbook of Biomolecules. Amsterdam, Netherlands: Elsevier, 2023, pp. 57–76.

[8] Q. Nie et al., "The evolution of nucleic acid nanotechnology: from DNA assembly to DNA-encoded library," Small Methods, p. 2401631, 2025.

[9] Y. Li, L. Song, C. Wang, P. Lei, and Z. Deng, "Decoupled roles of DNA–surfactant interactions: instant charge inversion, enhanced colloidal and chemical stabilities, and fully tunable DNA conjugation of shaped plasmonic nanocrystals," Nano Lett., vol. 22, no. 8, pp. 3385–3391, 2022.

[10] J. E. Henninger and R. A. Young, "An RNA-centric view of transcription and genome organization," Mol. Cell, vol. 84, no. 19, pp. 3627–3643, 2024.

[11] F. Cozzolino, I. Iacobucci, V. Monaco, and M. Monti, "Protein–DNA/RNA interactions: an overview of investigation methods in the-omics era," J. Proteome Res., vol. 20, no. 6, pp. 3018–3030, 2021.

[12] L. Savinkova, E. Sharypova, and N. Kolchanov, "In vitro methods used to study DNA–protein interactions," Biol. Bull. Rev., vol. 11, pp. 344–357, 2021.

[13] G. Ticli, O. Cazzalini, and E. Prosperi, "Protein-DNA interactions: a technical overview," in Handbook of Molecular Biotechnology. Cham, Switzerland: Springer, 2024, pp. 299–311.

[14] R. Esmaeeli, A. Bauzá, and A. Perez, "Structural predictions of protein–DNA binding: MELD-DNA," Nucleic Acids Res., vol. 51, no. 4, pp. 1625–1636, 2023.

[15] J.-T. Guo and F. Malik, "Single-stranded DNA binding proteins and their identification using machine learning-based approaches," Biomolecules, vol. 12, no. 9, p. 1187, 2022.

[16] C. Platella et al., "Plant-derived stilbenoids as DNA-binding agents: from monomers to dimers," Chem.–Eur. J., vol. 27, no. 34, pp. 8832–8845, 2021.

[17] S. Y. Alraqa et al., "Design, click conventional and microwave syntheses, DNA binding, docking and anticancer studies of benzotriazole-1, 2, 3-triazole molecular hybrids with different pharmacophores," J. Mol. Struct., vol. 1225, p. 129192, 2021.

[18] A. Wróbel, M. Baradyn, A. Ratkiewicz, and D. Drozdowska, "Synthesis, biological activity, and molecular dynamics study of novel series of trimethoprim analogs as multi-targeted compounds: dihydrofolate reductase (DHFR) inhibitors and DNA-binding agents," Int. J. Mol. Sci., vol. 22, no. 7, p. 3685, 2021.

[19] J. L. Hopkins, L. Lan, and L. Zou, “DNA repair defects in cancer and therapeutic opportunities,” Genes Dev., vol. 36, no. 5–6, pp. 278–293, 2022.
[20] X. Ji et al., “Two Cu(II) and Zn(II) complexes derived from 5-(pyrazol-1-yl) nicotinic acid: crystal structure, DNA binding and anticancer studies,” J. Solid State Chem., vol. 305, p. 122707, 2022.
[21] A. Singh, J. Singh, G. Parween, R. Khator, and V. Monga, “A comprehensive review of apigenin a dietary flavonoid: biological sources, nutraceutical prospects, chemistry and pharmacological insights and health benefits,” Crit. Rev. Food Sci. Nutr., pp. 1–37, 2024.
[22] C. Ionescu et al., “Oxidative stress in the pathogenesis of oral cancer,” Biomedicines, vol. 12, no. 6, p. 1150, 2024.
[23] B. Ravikumar, A. Cichońska, N. Sahni, T. Aittokallio, and R. Rahman, “Advancements in rational multi-targeted drug discovery: improving the efficacy-safety balance of small molecule cancer therapeutics,” in Polypharmacology: Strategies for Multi-Target Drug Discovery, pp. 109–125, 2025.
[24] A. Singh, R. Debnath, V. Chawla, and P. A. Chawla, “Historical development of computer-aided drug design,” in Computational Drug Discovery: Molecular Simulation for Medicinal Chemistry, 2024.
[25] R. E. Bird, S. A. Lemmel, X. Yu, and Q. A. Zhou, “Bioorthogonal chemistry and its applications,” Bioconjug. Chem., vol. 32, no. 12, pp. 2457–2479, 2021.
[26] W. Ma et al., “The biological applications of DNA nanomaterials: current challenges and future directions,” Signal Transduct. Target. Ther., vol. 6, no. 1, p. 351, 2021.
[27] V. V. Ranjan et al., “DNA binding and transposition activity of the Sleeping Beauty transposase: role of structural stability of the primary DNA-binding domain,” Nucleic Acids Res., vol. 53, no. 2, p. gkae1188, 2025.
[28] P. Rathore, P. Jeeth, S. Kadhirvel, and W. Ramakrishna, “Unraveling osmotolerance mechanisms of Staphylococcus warneri CPD1 by transcriptomic analysis,” Korean J. Microbiol., vol. 60, no. 4, pp. 207–222, 2024.
[29] H. Peng et al., “Ligand interaction landscape of transcription factors and essential enzymes in E. coli,” Cell, 2025.
[30] X. Xian et al., “Identification and functional analysis of glyoxal oxidase gene from rubber tree anthracnose,” Plant Prot. Sci., vol. 59, no. 4, 2023.