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ASSESSMENT OF THE MODE OF DNA BINDING BY FEW ANTI-CANCER DRUGS

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ABSTRACT

The present study will focus on the with the aim of understanding the molecular interactions responsible for their therapeutic activity. DNA is an important cellular target for several anti-cancer agents, and their binding may occur through intercalation, groove binding, electrostatic interactions, or covalent association. Selected anti-cancer drugs will be investigated using suitable spectroscopic and biophysical techniques to determine their binding characteristics, affinity, and interaction mechanism with DNA. Changes in absorption and fluorescence spectra, binding constants, and thermodynamic parameters will be evaluated to characterize drug–DNA interactions. Molecular docking and structural analysis will further be employed to identify the preferred binding sites and interaction patterns. The findings will provide valuable information regarding the relationship between chemical structure and DNA-binding behavior of the selected drugs. The study will contribute to a better understanding of their molecular mechanism of action and may support the rational development and optimization of more effective anti-cancer therapeutic agents.

Keywords: DNA binding; Anti-cancer drugs; Drug–DNA interaction; Intercalation; Groove binding; Spectroscopic analysis; Binding affinity.

INTRODUCTION

Because anti-cancer medications may halt cell-cycle progression and cancer cell death by interfering with DNA's structure and function, DNA is a prime biological target. A number of anti-cancer medications work by interacting with DNA in various ways, such as via electrostatic interactions, covalent bond formation, intercalation between base pairs, minor- or major-groove binding, and so on. How these interactions play out determines how therapeutic drugs work biologically, how selective they are, and how harmful they are. To better grasp how anti-cancer medications work molecularly, it is crucial to comprehend the manner of DNA binding. This research will use suitable spectroscopic and biophysical methods to evaluate the DNA-binding behaviour of several anti-cancer medications. We will characterise drug-DNA interactions by evaluating changes in fluorescence and absorption characteristics, binding constants, and thermodynamic parameters. Drug development and treatment optimisation may benefit greatly from the insights gained from molecular docking and structural analysis, which will aid in the identification of preferred binding sites and interaction patterns.

REVIEW OF LITRETURE

Mohammed, Sameer et al., (2025) The classifications, mechanisms of action, and historical development of anticancer medication therapy are all covered in this paper. The review focuses on the shift from conventional to targeted therapies, including immunotherapies, hormone treatments, tyrosine kinase inhibitors, monoclonal antibodies, conventional chemotherapeutic agents, and new approaches such as CART cell therapy and nanotechnology delivery systems. Medications that target cancer work by inhibiting tumour growth, regulating the cell cycle, or inducing DNA damage.next-generation sequencing has made great strides in understanding angiogenesis, To conquer these obstacles, a variety of approaches are being considered, such as medication resistance and the need for precise dosing and targeting in order to provide therapeutic benefit with less side effects. The article discusses DDS for anticancer drugs and notes recent innovations in drug delivery methods and molecular targeting methodologies. To improve treatment and overcome challenges in cancer therapy, personalised medication development has advanced, with an emphasis on tumour genetic analysis. With the goal of improving patient outcomes and expanding access to cutting-edge treatment alternatives, this study compiles and analyses the available information on ongoing innovative initiatives.

Zafar, Aasma et al., (2025) The fact that cancer is still the second biggest killer in the globe is a huge problem for public health all around the world. It is still necessary to enhance treatment approaches and get a better knowledge of tumour biology, even if science and technology have come a long way. Surgery, chemotherapy, radiation therapy, and hormonal therapy are the four conventional cancer treatment procedures that are the subject of this study. The main approach of tumour removal, surgery, has advanced with the use of robotic systems and fluorescence-based technologies, which have increased accuracy and decreased collateral damage. With the advent of 3D technology, improvements in focus and intensity control have allowed radiation therapy to advance, enhancing both the diagnostic and treatment processes. Synthesised derivatives of naturally occurring compounds have increased cytotoxicity against cancer cells, marking a significant step forward in the history of chemotherapy. Restricting growth or causing regression, hormonal treatment has become an essential tactic treating hormone-dependent malignancies. Regardless of these developments, there are still obstacles to overcome for every method. Complete tumour removal is a challenge for surgeons because tumours are so diverse. Drug resistance and adverse effects are challenges in chemotherapy. Radiation treatment has challenges related to pinpoint accuracy and restricted availability in some areas. Hormonal treatment has side effects that affect people's quality of life and may lead to resistance. By tracking the development of these time-honoured cancer treatments, this study sheds light on their achievements and points the way toward potential new avenues of investigation. We want to highlight the modalities' significance in modern oncology and find ways to enhance cancer treatment tactics by analysing them.

Yasir, Huzaifa et al., (2024) The unique interactions between metal-based medicines and their biological targets give them great potential as powerful anticancer agents. New insights into the complex chemical interactions between metal-based anticancer drugs and their cancer cell therapeutic targets are presented in this study. Structure dynamics, functional results, and binding processes are elucidated using state-of-the-art computational and experimental approaches. Further, the study clarifies the exact mechanisms of action of these medications, how well they work, and possible future directions for improving cancer treatment tactics and creating tailored metal-based treatments that effectively fight different types of cancer.

Chen, Zhen et al., (2024) For the treatment of EGFR-mutant (EGFRm) non-small cell lung cancer (NSCLC), there is an immediate need for the development of efficient techniques to handle the acquired resistance to osimertinib, a third-generation EGFR inhibitor. Doxorubicin and etoposide, two DNA topoisomerase II (Topo II) inhibitors, worked synergistically to reduce cell survival, increase DNA damage and apoptosis in osimertinib-resistant cells, slow the growth of tumours resistant to osimertinib, and postpone the emergence of resistance to osimertinib that had been acquired, according to this study. From a mechanistic standpoint, osimertinib reduced Topo IIα levels in EGFRm NSCLC cells by promoting FBXW7-mediated proteasomal degradation, which led to DNA damage induction. However, these effects were lost in osimertinib-resistant cell lines that had elevated levels of Topo IIα. Additionally, most tissue samples from NSCLC patients who experienced relapse after treatment with an EGFR tyrosine kinase inhibitor showed increased Topo IIα levels. Restoring sensitivity to osimertinib-induced DNA damage and death in osimertinib-resistant cell lines was achieved by knocking down TOP2A, while resistance to osimertinib was given by forcing expression of an ectopic TOP2A gene in sensitive EGFRm NSCLC cells. Based on these findings, it is scientifically justified to target Topo II in order to control acquired resistance to osimertinib, since Topo IIα inhibition is crucial for mediating the therapeutic effectiveness of osimertinib against EGFRm NSCLC.

Bhosale, Mrinalini et al., (2022) An essential part of the medication's distribution mechanism is the interaction between the drug and proteins. Because of its high binding affinity and abundance in the human body, human serum albumin (HSA) has become an important therapeutic ingredient. There are a lot of publications on medication interactions with HSA because of its importance in the pharmacokinetics of several medicines. It is vital to examine the binding properties of these cancer medicines with HSA since it might bind to them. In this study, we review the binding characteristics of a few anti-cancer medications by analysing their HSA binding sites in detail. Site I of Sudlow's hierarchy in subdomain II A has a higher drug binding capacity than site II.

MOLECULAR INTERACTIONS BETWEEN SELECTED ANTI-CANCER DRUGS AND DNA

An essential biological mechanism for the prevention of cancer cell growth is the interaction between anti-cancer medicines and DNA. DNA has several possible binding sites that might

interact with medicinal substances by means of covalent or non-covalent forces. The chosen anti-cancer medications' chemical make-up, charge, functional groups, and three-dimensional arrangement will dictate the character of these interactions. In order to assess their biological activity and therapeutic potential, it is crucial to comprehend these interactions. Various methods of interaction between DNA and anti-cancer medications have been proposed, such as covalent attachment, electrostatic association, groove binding, and intercalation. In most cases, intercalative chemicals will alter the structure of DNA and impede its replication and transcription by inserting their planar aromatic rings between neighbouring DNA base pairs. When interacting with nucleotide bases, groove-binding medications will use hydrogen bonding, van der Waals forces, and hydrophobic interactions. They will occupy either the minor or major DNA grooves.

Particularly for positively charged pharmacological compounds, which may bind to the negatively charged DNA phosphate backbone, electrostatic interactions play a substantial role in DNA binding. It is possible for some anti-cancer drugs to create DNA adducts, cross-links, or strand damage by forming covalent connections with nucleophilic sites on DNA bases. These changes have the potential to disrupt DNA processing normally and trigger apoptotic pathways in cells. A number of variables, including ionic strength, pH, temperature, drug concentration, and DNA conformation, will impact the robustness and selectivity of drug-DNA interactions.

This research aims to identify the optimal way of interaction between DNA and a subset of anti-cancer medicines. Observations of variations in absorption and fluorescence, as well as other spectral features, may shed light on the processes involved in complex formation and binding behaviour. Possible binding locations and the main molecular forces at work may be better understood with the use of complementary molecular docking studies. The combined analysis will provide light on the ways in which the chosen medicines' structural characteristics impact DNA recognition and binding. This data will be helpful in understanding how they work and might lead to the creation of anti-cancer drugs that target DNA more specifically and with more efficacies.

SPECTROSCOPIC ASSESSMENT OF DRUG–DNA BINDING INTERACTIONS

By tracking changes in the optical characteristics of the drug, DNA, or both, spectroscopic methods provide useful ways to study the interaction between anti-cancer medications and

DNA. The current investigation will use spectroscopic analysis to learn more about the properties and binding behaviour of certain anti-cancer medications with DNA. Initially, we will utilise UV-Visible absorption spectroscopy to look at how the drug absorption spectra change as we add more and more DNA. Signs of drug-DNA complex formation, such as changes in absorption maximum and variations in absorption intensity, may be used to differentiate between possible binding types.

To supplement these methods, we will also use fluorescence spectroscopy to look for variations in fluorescence intensity that correspond to DNA binding. Binding features may be uncovered by analysing fluorescence quenching or enhancement, which may reveal interactions between the drug molecules and DNA. To further understand whether the chosen medications mostly interact via intercalation or groove binding, we will conduct competitive binding assays where applicable, utilising well-established DNA-binding probes. Observations of altered fluorescence patterns after complex formation may potentially give light on the drug's immediate surroundings.

In order to assess the strength of the drug-DNA connection and to estimate the binding constants, appropriate binding models will be applied to the experimental data. In order to comprehend the motivating factors at work in the interaction, it is possible to calculate thermodynamic parameters, such as changes in enthalpy, entropy, and Gibbs free energy. Consequently, the drug-DNA binding behaviour may be thoroughly evaluated and the likely interaction mode can be determined by combining the spectroscopic findings. These results will help fill gaps in our knowledge of the molecular mechanisms of action of some anti-cancer medications and their promise as DNA-targeting therapeutic agents.

CONCLUSION

To better understand the molecular mechanism of action of some anti-cancer medications, it is necessary to determine how these compounds attach to DNA. Intercalation, groove binding, electrostatic association, and covalent contact are some of the ways these medications interact with DNA that will be studied. In order to learn about the binding affinity and interaction strength, as well as any changes that occur throughout the creation of the drug-DNA complex, spectroscopic studies are essential. We can learn more about the driving factors behind the chosen medications' DNA associations by analysing binding constants and thermodynamic characteristics. By determining potential binding locations and

particular molecular interactions, molecular docking and structural analysis will supplement the results of the experiments. The correlation between pharmacological structure and DNA-binding activity will be better understood as a consequence of the combined findings. In sum, the research will help shed light on the molecular processes of some anti-cancer therapies and might lead to better DNA-targeting anti-cancer medications via improved design, optimisation, and development.

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