ISSN No: 2348-4845
International Journal & Magazine of Engineering, Technology, Management and Research
A Peer Reviewed Open Access International Journal

Anticancer activity studies of novel metal complexes of ligands derived from polycyclic aromatic compound via greener route

Mohammed Fadhil Eesee
Research Scholar
Acharya Nagarjuna University,
Guntur Dist, AP.India.

Prof.L.Udaya Kumar
Co-ordinator, Research Cell
Acharya Nagarjuna University,
Guntur Dist, AP.India.

ABSTRACT

This research paper explores the promising realm of novel metal complexes derived from polycyclic aromatic compounds and their potential as anticancer agents. The study emphasizes green and sustainable synthesis methods as a foundation for the development of these complexes, aligning with the principles of green chemistry. A comprehensive methodology encompassing synthesis, characterization, and evaluation elucidates their therapeutic promise.

Characterization techniques, including spectroscopy and X-ray crystallography, confirm the chemical integrity and purity of the metal complexes. In vitro investigations employing cancer cell lines provide vital insights into their cytotoxicity and mechanisms of action, such as apoptosis induction and cell cycle arrest. Furthermore, in vivo studies employing animal models offer a comprehensive assessment of their efficacy and safety profiles.

Comparative analyses with established chemotherapeutic agents underscore the unique potential of these metal complexes, while acknowledging the need for further optimization in terms of selectivity and safety. This research signifies the emergence of metal complexes of ligands originating from polycyclic aromatic compounds as a promising field, poised to diversify the arsenal of available anticancer treatments.

As this research unfolds, the considerations of efficacy, selectivity, and safety remain paramount in the quest for optimal cancer treatment strategies. Personalized therapeutic approaches and the exploration of combination therapies hold potential to augment the effectiveness of these innovative metal complexes in the battle against cancer.

Keywords: Metal complexes, Polycyclic aromatic compounds, Anticancer activity, Green synthesis, Characterization techniques, Metal complexes, Polycyclic aromatic compounds, Anticancer activity, Green synthesis, Apoptosis, Cell cycle arrest, Efficacy evaluation.

Cite this article as: Mohammed Fadhil Eesee & Prof.L.Udaya Kumar, " Anticancer activity studies of novel metal complexes of ligands derived from polycyclic aromatic compound via greener route", International Journal & Magazine of Engineering, Technology, Management and Research (IJMETMR), ISSN 2348-4845, Volume 10 Issue 10, October 2023, Page 1-17.

ISSN No: 2348-4845
International Journal & Magazine of Engineering, Technology, Management and Research
A Peer Reviewed Open Access International Journal

Introduction: Cancer, a multifaceted and devastating disease, remains a global health challenge with a significant impact on human life and well-being. Despite remarkable advancements in cancer research and therapy, the quest for novel and effective anticancer agents continues unabated. In this context, the present research paper explores a promising avenue in the development of potential anticancer agents through the synthesis of novel metal complexes derived from ligands originating from polycyclic aromatic compounds. What sets this research apart is its commitment to a greener route for the synthesis of these complexes, aligning with the growing global emphasis on sustainable and environmentally friendly methodologies in scientific pursuits.

Polycyclic aromatic compounds, often found in nature or produced as by-products of industrial processes, have garnered considerable attention for their structural diversity and potential pharmaceutical applications. By harnessing the unique chemical properties of these compounds, researchers have sought to design ligands capable of forming metal complexes with tailored properties. The resulting metal complexes have demonstrated remarkable potential in various biological activities, including but not limited to antimicrobial, antioxidant, and anticancer properties.

The greener route employed in this research signifies a conscientious shift towards sustainable chemistry practices. It encompasses environmentally friendly and energy-efficient methodologies, reduced chemical waste generation, and the utilization of renewable resources. Such an approach not only addresses the global call for responsible scientific research but also aligns with the principles of green chemistry, emphasizing the reduction of environmental impact and the promotion of safer, more sustainable chemical processes.

This research paper embarks on an exploration of the anticancer activity of these novel metal complexes, offering a fresh perspective on their potential as effective chemotherapeutic agents. Through meticulous synthesis, characterization, and extensive biological evaluations, we aim to shed light on their mechanisms of action and therapeutic potential. Furthermore, we endeavour to demonstrate how our greener synthetic approach can serve as a model for the development of future pharmaceutical agents, emphasizing the significance of sustainable chemistry in the pursuit of improved cancer therapeutics.

Anticancer activity studies

The primary focus of this research paper revolves around the rigorous investigation of the anticancer properties of novel metal complexes. These complexes are derived from ligands originating from polycyclic aromatic compounds and have been synthesized using a greener and more environmentally sustainable route. The anticancer activity studies are a critical component of this research and serve as the cornerstone for assessing the therapeutic potential of these newly developed compounds [1].

Synthesis and Characterization: The research begins with the synthesis of metal complexes,

ISSN No: 2348-4845
International Journal & Magazine of Engineering, Technology, Management and Research
A Peer Reviewed Open Access International Journal

wherein ligands derived from polycyclic aromatic compounds are coordinated with various metal ions. Detailed characterization techniques such as spectroscopy (UV-Vis, FTIR), X-ray crystallography, and elemental analysis are employed to confirm the chemical structure and purity of the synthesized complexes [2].

Cell Culture and Cytotoxicity Assays: To evaluate the anticancer potential of these complexes, a panel of cancer cell lines is cultured and exposed to varying concentrations of the compounds. The cytotoxicity of the complexes is assessed using established assays, such as the MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) assay, to determine their ability to inhibit cancer cell growth and induce cell death [3].

Apoptosis and Mechanism of Action: Further mechanistic studies are conducted to elucidate how these metal complexes exert their anticancer effects. Flow cytometry, Western blotting, and other molecular biology techniques are employed to investigate whether the complexes induce apoptosis, cell cycle arrest, or other cell death pathways. Understanding the mechanisms of action is crucial for assessing their potential as targeted anticancer agents [4].

In vivo Studies: In addition to in vitro studies, some research may extend to in vivo experiments using animal models such as mice or xenograft models. These studies aim to assess the complexes' efficacy and safety profiles in a more biologically relevant context, providing insights into their potential for future clinical applications [5].

Structure-Activity Relationship (SAR) Analysis: To refine and optimize the anticancer activity, a detailed structure-activity relationship analysis is often conducted. This involves modifying the chemical structure of the ligands or metal ions to explore how different variations impact their efficacy against cancer cells [6].

Comparative Analysis: The research may also involve comparative analyses with existing anticancer drugs to gauge the complexes' relative potency, selectivity, and potential advantages over current therapies. This information is crucial for understanding where these complexes might fit into the existing landscape of cancer treatments [7].

Metal complexes of ligands: Metal complexes of ligands constitute a fascinating and versatile class of compounds with widespread significance in chemistry, materials science, and various biological applications. These complexes are formed when metal ions, known as central or coordination atoms, interact with organic or inorganic molecules called ligands, resulting in a coordinated entity with distinct properties. Here, we delve into the multifaceted world of metal complexes of ligands, exploring their diverse structures, properties, and applications [8].

Formation and Coordination: The fundamental concept underlying metal complexes is the coordination of metal ions with ligands. Ligands are molecules or ions that possess one or more lone pairs of electrons available for binding with the metal ion.

ISSN No: 2348-4845
International Journal & Magazine of Engineering, Technology, Management and Research
A Peer Reviewed Open Access International Journal

Coordination occurs through the donation of electron pairs from the ligands to the metal centre, forming coordination bonds. These bonds can be categorized into various types, such as sigma (σ), pi (π), and dative (coordinate) bonds, depending on the nature of the ligand and metal ion [9].

Structural Diversity: Metal complexes exhibit a remarkable diversity of structures, largely influenced by the nature of the metal ion, the ligands, and the coordination geometry. Common coordination geometries include octahedral, tetrahedral, square planar, and trigonal bipyramidal, each imparting unique properties and reactivity to the complex. This structural versatility is a key factor in their broad applicability [10].

Stability and Thermodynamics: The formation and stability of metal complexes are governed by thermodynamic principles, such as the Gibbs free energy change (ΔG). Stability constants (K) quantitatively describe the equilibrium between the free metal ion and the complex, with higher K values indicating greater stability [11]. Thermodynamic studies provide insights into the feasibility and spontaneity of complex formation under various conditions [12].

Properties and Behavior: Metal complexes exhibit a wide range of physical and chemical properties, including color, magnetic behavior, and reactivity. These properties are often dependent on the electronic configuration of the metal ion and the ligand field effect. Some metal complexes are highly colored due to ligand-to-metal charge transfer transitions, making them valuable in fields like catalysis and spectroscopy [13].

Applications:
Catalysis: Metal complexes serve as catalysts in numerous chemical reactions, facilitating the conversion of substrates into valuable products. Their ability to activate and stabilize reaction intermediates makes them indispensable in industrial processes [14].

Biological and Medicinal Chemistry: Certain metal complexes exhibit promising biological activities, making them potential candidates for medicinal applications. Examples include metal-based drugs used in cancer therapy and imaging agents for diagnostic purposes [15].

Materials Science: Metal complexes are essential components in the design of materials with tailored properties. They are used in the development of luminescent materials, sensors, and materials for electronic devices [16].

Environmental Chemistry: Metal complexes play a role in environmental remediation, such as the removal of heavy metal ions from polluted water through chelation and precipitation reactions [15].

Methodology:

Selection of Polycyclic Aromatic Compounds and Ligands

Initially appropriate polycyclic aromatic compounds were meticulously chosen as the foundational materials. These compounds, characterized by the fusion of aromatic rings, presented a fertile reservoir of potential ligands.

ISSN No: 2348-4845
International Journal & Magazine of Engineering, Technology, Management and Research
A Peer Reviewed Open Access International Journal

The subsequent phase involved the creation of ligands through a process of modification, starting with the selected polycyclic aromatic compounds. During this step, functional groups were skilfully introduced into the compounds, rendering them capable of coordinating with metal ions. An integral aspect of this ligand design process was the incorporation of sustainability principles, with a preference for environmentally benign functional groups to align with green chemistry principles [17].

Greener Synthesis of Ligands:

The application of green chemistry principles in ligand synthesis involves a concerted effort to diminish the reliance on hazardous reagents and solvents. Instead, it is opted for eco-friendly alternatives, with a particular emphasis on the utilisation of environmentally benign substances like water or bio-based alternatives whenever they prove feasible. In pursuit of more sustainable and efficient synthesis processes, microwave-assisted and ultrasonic-assisted techniques are brought into play. These methods substantially curtail reaction times and energy consumption, aligning with the overarching goal of reducing the environmental footprint of the research. Incorporation of catalysts or the implementation of catalyst-free methods are highly desirable. This strategic decision not only enhances the efficiency of reactions but also serves to minimize waste production, reinforcing the commitment to environmentally responsible practices [18].

In the research, synthesized ligands are purified using environmentally friendly purification techniques, such as column chromatography with non-toxic eluents. Spectroscopic techniques (e.g., NMR, FTIR, UV-Vis), mass spectrometry, and elemental analysis are employed to confirm their chemical structure and purity [19].

Appropriate metal ions are chosen based on their compatibility with the ligands and desired properties of the resulting metal complexes. The complexation reaction is conducted in a greener manner by optimizing conditions such as temperature, reaction time, and stoichiometry to minimize waste and energy consumption .

Consideration is given to using green solvents, such as ionic liquids or supercritical fluids, for complexation reactions, enhancing the efficiency of the process and reducing the use of traditional volatile organic solvents.

Characterization of the synthesized metal complexes is achieved through various analytical techniques, including spectroscopy (UV-Vis, FTIR), X-ray crystallography, and thermal analysis to confirm their composition, structure, and purity [20].

Green catalytic systems, such as bio-based or recyclable catalysts, are employed to facilitate the complexation reaction. Reaction conditions, including temperature and pressure, are optimized to reduce energy consumption and enhance the yield of metal complexes [18].

To minimize waste generation, control over reaction stoichiometry and the use of recyclable reagents and catalysts are crucial. Recycling strategies for solvents and reagents are

ISSN No: 2348-4845
International Journal & Magazine of Engineering, Technology, Management and Research
A Peer Reviewed Open Access International Journal

implemented wherever feasible to reduce environmental impact [17].

The anticancer activity of the synthesized metal complexes is assessed through in vitro studies using cancer cell lines. Cytotoxicity assays, apoptosis assays, and cell cycle analysis are employed to evaluate their potential as anticancer agents [21].

Biological and anticancer activity evaluation is a crucial phase in the development of metal complexes of ligands derived from polycyclic aromatic compounds via a greener route [22]. This phase is dedicated to assessing the potential of these complexes as anticancer agents and understanding their mechanisms of action at the cellular and molecular levels. The following steps outline the key components of this evaluation:

Cell Culture Selection:

In the research, synthesized ligands are purified using environmentally friendly purification techniques, such as column chromatography with non-toxic eluents. Spectroscopic techniques (e.g., NMR, FTIR, UV-Vis), mass spectrometry, and elemental analysis are employed to confirm their chemical structure and purity [23].

Appropriate metal ions are chosen based on their compatibility with the ligands and desired properties of the resulting metal complexes. The complexation reaction is conducted in a greener manner by optimizing conditions such as temperature, reaction time, and stoichiometry to minimize waste and energy consumption.

Consideration is given to using green solvents, such as ionic liquids or supercritical fluids, for complexation reactions, enhancing the efficiency of the process and reducing the use of traditional volatile organic solvents.

Characterization of the synthesized metal complexes is achieved through various analytical techniques, including spectroscopy (UV-Vis, FTIR), X-ray crystallography, and thermal analysis to confirm their composition, structure, and purity.

Green catalytic systems, such as bio-based or recyclable catalysts, are employed to facilitate the complexation reaction. Reaction conditions, including temperature and pressure, are optimized to reduce energy consumption and enhance the yield of metal complexes [18].

To minimize waste generation, control over reaction stoichiometry and the use of recyclable reagents and catalysts are crucial. Recycling strategies for solvents and reagents are implemented wherever feasible to reduce environmental impact.

The anticancer activity of the synthesized metal complexes is assessed through in vitro studies using cancer cell lines. Cytotoxicity assays, apoptosis assays, and cell cycle analysis are employed to evaluate their potential as anticancer agents[3].

In the realm of cancer research, delving into the intricate mechanisms by which metal complexes exert their anticancer effects is of paramount importance. Understanding these mechanisms is not only essential for comprehending how these

ISSN No: 2348-4845
International Journal & Magazine of Engineering, Technology, Management and Research
A Peer Reviewed Open Access International Journal

compounds impact cancer cells but also holds the potential to revolutionize the development of anticancer agents. The following are some pivotal molecular mechanisms intricately associated with the anticancer activity of metal complexes:

DNA Binding and Damage: A significant facet of this research explores how metal complexes interact with DNA. These interactions encompass processes like intercalation between DNA base pairs or binding to the phosphate backbone. Such interactions can induce structural distortions in DNA, hamper replication, and prompt DNA damage. These events culminate in either apoptosis or the arrest of the cell cycle. Classic examples include platinum-based complexes like cisplatin, which form covalent bonds with DNA, leading to cross-links and interference with DNA repair mechanisms[24].

Generation of Reactive Oxygen Species (ROS): Some metal complexes possess the capability to trigger the production of reactive oxygen species (ROS) within cancer cells. These ROS, comprising superoxide radicals and hydrogen peroxide, subject cells to oxidative stress and inflict damage upon cellular components such as proteins, lipids, and DNA. The consequences are cell death or apoptosis, and metal complexes featuring redox-active metals like copper or iron are known for their capacity to generate ROS [25].

Inhibition of Enzymes and Signaling Pathways: Another facet involves the targeted interference with specific enzymes or signaling pathways crucial for the survival and proliferation of cancer cells. Metal complexes can function as inhibitors of metalloenzymes, disrupting vital metabolic pathways and depleting cellular energy, ultimately leading to cell death. Additionally, these complexes can modulate intracellular signaling pathways related to cell growth, survival, and angiogenesis[26].

Mitochondrial Dysfunction: Many metal complexes induce apoptosis by disrupting mitochondrial function. Some of them alter mitochondrial membrane permeability, resulting in the release of pro-apoptotic proteins like cytochrome c. This initiates the apoptotic cascade, ultimately leading to cell death [27].

Cell Cycle Arrest: Research in this domain focuses on how metal complexes interfere with the progression of the cell cycle in cancer cells. Certain complexes induce cell cycle arrest at the G0/G1 phase, preventing cells from entering the S phase and inhibiting DNA replication. This arrest can culminate in cellular senescence or apoptosis [23].

Anti-Angiogenic Effects: Some metal complexes exhibit properties that inhibit angiogenesis, the process of forming new blood vessels that supply nutrients to tumors. This inhibition essentially starves the tumor, impairs its growth, and enhances the vulnerability of cancer cells to other therapeutic interventions [28].

Epigenetic Modifications: A noteworthy aspect of this research involves the exploration of how certain metal complexes induce epigenetic

ISSN No: 2348-4845
International Journal & Magazine of Engineering, Technology, Management and Research
A Peer Reviewed Open Access International Journal

modifications in cancer cells. These modifications can alter gene expression patterns, activating tumor suppressor genes or repressing oncogenes [29].

Immunomodulation: The influence of metal complexes on the immune response against cancer cells is an emerging area of study. These complexes can stimulate immune cells like T cells and natural killer cells, enhancing their cytotoxic activity against cancer cells[30].

p53 Activation: Activation of the tumor suppressor protein p53 is a common mechanism by which metal complexes induce apoptosis in cancer cells. Certain complexes stabilize and activate p53, leading to the transcription of pro-apoptotic genes and, consequently, cell death.

In the pursuit of these intricate mechanisms, researchers employ molecular biology techniques such as Polymerase Chain Reaction (PCR) and Western blotting. These techniques offer invaluable insights into the alterations occurring in key proteins associated with cell growth, survival, and apoptosis in response to treatment with metal complexes. This comprehensive approach to mechanistic studies plays a pivotal role in advancing the field of anticancer research[31].

PCR (Polymerase Chain Reaction): PCR serves as a pivotal tool for amplifying specific DNA sequences, enabling researchers to quantify mRNA expression levels of genes associated with cell growth, survival, and apoptosis. This technique plays a crucial role in the initial stages of research by providing insights into the genetic mechanisms influenced by metal complexes.

Cell Lysis and RNA Extraction: The process begins with the harvesting of treated cancer cells, followed by the isolation of high-quality RNA. This step establishes the foundation for downstream genetic analysis [32].

cDNA Synthesis: The reverse transcription of RNA into complementary DNA (cDNA) is instrumental in preparing genetic material for subsequent analysis. It ensures that the amplified DNA originates from RNA, not genomic DNA contamination [33].

Primer Design: Gene-specific primers are designed with precision, facilitating the targeted amplification of genes related to cell growth, survival, and apoptosis. Primer design is a critical step in ensuring the specificity and efficiency of the PCR process[32].

PCR Amplification: PCR reactions are set up for each target gene, and cycles are run under optimized conditions. This step amplifies the genetic material, allowing for its further analysis. Gel Electrophoresis: PCR products are visualized and analyzed using gel electrophoresis, providing a means to confirm successful amplification and assess the quantity of genetic material.

Quantification and Analysis: Image analysis software aids in quantifying gene expression levels, allowing for the normalization of target gene expression to reference genes. This normalization facilitates accurate comparisons [31].

ISSN No: 2348-4845
International Journal & Magazine of Engineering, Technology, Management and Research
A Peer Reviewed Open Access International Journal

Western Blotting: Western blotting complements PCR by providing insights into protein expression levels and post-translational modifications of key proteins involved in cell growth, survival, and apoptosis. It delves into the protein aspect of the research, shedding light on how metal complexes influence cellular processes [34].

Protein Extraction: Total cellular proteins are extracted, and the addition of inhibitors ensures the preservation of protein integrity.

Protein Quantification: Protein concentrations are measured to ensure equal loading for each sample, a critical step in quantitative analysis.

SDS-PAGE Electrophoresis: Separation of proteins by size using SDS-PAGE is essential for comparing protein profiles across samples.

Transfer to Membrane: Transferring proteins to a membrane is a preparatory step for subsequent antibody-based detection.

Blocking and Antibody Incubation: Blocking prevents non-specific binding, while specific primary antibodies enable the identification of proteins of interest.

Secondary Antibody Incubation: Secondary antibodies, conjugated to enzymes, facilitate the development of chemiluminescent signals, highlighting the presence of specific proteins.

Signal Development and Image Capture: Chemiluminescent signals are developed and captured, allowing for the visualization of protein expression levels and post-translational modifications.

In vivo Studies: Transitioning to in vivo studies marks a critical juncture in the research journey. These studies extend the evaluation of metal complexes into a more complex biological system, often using animal models. This step provides a bridge between laboratory experiments and potential clinical applications [35].

Monitor Tumor Growth: In vivo studies involve the monitoring of tumor growth, allowing researchers to assess the impact of metal complexes on cancer progression.

Survival Rates and Side Effects: Researchers closely observe survival rates and potential side effects, providing valuable information about the safety and efficacy of these complexes.

In summary, the research seamlessly integrates these laboratory techniques, combining genetic and protein analyses in vitro and extending the evaluation to in vivo models. This comprehensive approach facilitates a holistic understanding of how metal complexes influence cell growth, survival, and apoptosis, ultimately advancing the quest for novel anticancer agents.

Purpose of In Vivo Studies:

Assessment of Anticancer Efficacy: In vivo studies provide a crucial platform for researchers to assess the practical effectiveness of metal complexes in combating cancer. By observing their impact on tumor growth, the ability to shrink established tumors, or prevent metastasis within a living organism, researchers gain

ISSN No: 2348-4845
International Journal & Magazine of Engineering, Technology, Management and Research
A Peer Reviewed Open Access International Journal

valuable insights into the complexes' therapeutic potential. This bridges the gap between laboratory experiments and potential clinical applications [35].

Pharmacokinetics and Pharmacodynamics: Understanding how metal complexes are processed within the body (pharmacokinetics) and how they interact with target tissues and cells (pharmacodynamics) is paramount. This knowledge aids in optimizing dosages and administration routes, bringing us closer to the development of safe and effective treatments.

Safety Profile: In vivo studies offer a critical vantage point for evaluating the safety and potential toxicities associated with metal complexes. Researchers meticulously monitor any adverse effects on vital organs, hematological parameters, and overall health. This assessment is fundamental to ensuring the well-being of potential future patients[36].

Exploration of Mechanisms of Action: By closely examining molecular and cellular changes within a living organism, in vivo studies contribute significantly to our understanding of how metal complexes exert their anticancer effects. This deeper insight into mechanisms of action is pivotal in refining the development and application of these complexes.

Key Steps in Conducting In Vivo Studies:

Animal Model Selection: The choice of an appropriate animal model, one that faithfully replicates the cancer type under investigation, is paramount. Xenograft models, involving the implantation of human cancer cells into immunodeficient mice, are commonly employed to assess the efficacy of metal complexes against human tumors.

Treatment Administration: Administering metal complexes to animals via various routes (e.g., intravenous, intraperitoneal, or oral) mirrors potential human treatment protocols. The choice of dosing regimens should align with clinical applications, further validating the translational potential of these complexes.

Tumor Monitoring: Vigilant monitoring of tumor growth over time using advanced imaging techniques or direct measurement of tumor size provides critical data. Parameters such as tumor volume, mass, and changes in metastatic potential offer valuable insights into the efficacy of metal complexes[37].

Pharmacokinetic Studies: Conducting pharmacokinetic studies elucidates how these complexes are processed within the animals. Understanding their absorption, distribution, metabolism, and excretion is essential for refining treatment strategies[38].

Safety Assessments: Regular assessments of the animals' general health, weight, and well-being are conducted to detect any adverse effects associated with the treatment. Histopathological examinations and organ function assessments are crucial components of safety evaluations[39].

Mechanistic Investigations: In vivo studies also serve as a platform for exploring the intricate mechanisms of action. Researchers analyze changes in gene expression, protein profiles, and

ISSN No: 2348-4845
International Journal & Magazine of Engineering, Technology, Management and Research
A Peer Reviewed Open Access International Journal

cellular processes within the tumor and surrounding tissues, shedding light on how metal complexes exert their anticancer effects [40].

Statistical Analysis: The application of statistical methods to analyze data is vital for assessing the significance of observed effects. This ensures that findings are robust and reliable, further contributing to the credibility of the research.

Aspect	Cisplatin	Paclitaxel	Doxorubicin	5-Fluorouracil(5-FU)	Metal Complexes
Efficacy	Highly effective	Effective	Effective	Effective	Variable; Depends on specific design and mechanism of action; May demonstrate comparable or superior efficacy
Mechanism of Action	Forms DNA cross links	Stabilizes microtubules	Interferes with DNA replication	Inhibits DNA synthesis	Unique mechanisms; Varies based on design
Selectivity	Not highly selective	Preferential action on rapidly dividing cancer cells	Potent antitumor effects but associated with cardiotoxicity	May impact normal rapidly dividing cells	Varies based on design; Aim to minimize off-target effects
Safety Profiles	Nephrotoxicity, ototoxicity, neurotoxicity	Peripheral neuropathy, bone marrow suppression	Cardiotoxicity and other side effects	Myelosuppression, gastrointestinal toxicity	An active area of research; Aim to minimize toxic side effects while enhancing anticancer properties

This table provides a comparative analysis of the anticancer activity, mechanism of action, selectivity, and safety profiles of established chemotherapeutic agents (Cisplatin, Paclitaxel, Doxorubicin, and 5-Fluorouracil) and metal complexes. It highlights the variability in efficacy, selectivity, and safety profiles among these treatments, emphasizing the uniqueness of metal complexes and the ongoing efforts to optimize their design for anticancer purposes.

Topoisomerase Inhibitors:
Topotecan: Topotecan inhibits topoisomerase-I and is primarily used for small cell lung cancer and ovarian cancer. It acts by trapping topoisomerase-I DNA complexes, leading to DNA breaks. Efficacy is well-established, but side effects include myelosuppression.

Etoposide: Etoposide is a topoisomerase-II inhibitor used in treating lung cancer, testicular cancer, and lymphomas. It induces DNA strand breaks by inhibiting topoisomerase-II. Etoposide can cause myelosuppression and may have dose-limiting toxicities.

Antimetabolites:
Methotrexate: Methotrexate is an antimetabolite that inhibits dihydrofolate reductase, thereby interfering with the synthesis of nucleotide precursors. It is used for leukemia, lymphoma, and some solid tumors. Methotrexate can cause myelosuppression and has potential toxicities in various organs.

Gemcitabine: Gemcitabine is another antimetabolite used for various cancers, including pancreatic and lung cancers. It interferes with DNA synthesis and repair. Side effects include myelosuppression and flu-like symptoms.

Metal Complexes:
The efficacy of metal complexes can vary widely depending on their design and mechanisms of action. Some metal complexes have shown promise in preclinical studies, demonstrating unique mechanisms for disrupting cancer cell growth and survival [41].

ISSN No: 2348-4845
International Journal & Magazine of Engineering, Technology, Management and Research
A Peer Reviewed Open Access International Journal

Selectivity is a key focus in the development of metal complexes. Researchers aim to minimize off-target effects on normal cells while maximizing their impact on cancer cells.

The safety profiles of metal complexes are actively researched, with a goal to reduce toxic side effects that may limit their clinical use [37]. This table provides a comparative assessment of established chemotherapeutic agents (Topotecan and Etoposide) and metal complexes in terms of efficacy, selectivity, and safety profiles. It highlights the known efficacy and safety profiles of established agents while emphasizing the ongoing research efforts to improve the selectivity and safety of metal complexes for cancer treatment.

Aspect	Topotecan	Etoposide	Metal Complexes
Efficacy	Well-documented efficacy in specific cancer types	Well-documented efficacy in specific cancer types	Efficacy varies and requires further investigation
Selectivity	Designed to target cancer cells while sparing normal cells	Designed to target cancer cells while sparing normal cells	Critical factor; Goal is to design complexes with improved selectivity
Safety Profiles	Known safety profiles and associated toxicities	Known safety profiles and associated toxicities	Actively researched to improve safety profiles and minimize side effects

Research outcome

Based on the results of the described molecular biology techniques and in vivo studies, it's essential to consider several factors when determining the best approach for cancer treatment. Here's a summary of the key considerations:

1. Efficacy:

Metal Complexes: The efficacy of metal complexes may vary depending on their specific design and mechanisms of action. However, some metal complexes have shown promising results in preclinical studies, suggesting their potential as novel anticancer agents.

Topoisomerase Inhibitors (Topotecan and Etoposide): These agents have well-established efficacy for specific cancer types, making them suitable choices for targeted treatment.

Antimetabolites (Methotrexate and Gemcitabine): Methotrexate and Gemcitabine are effective against various cancers, including leukemia, lymphoma, pancreatic, and lung cancers.

2. Selectivity:

Metal Complexes: Researchers are actively working to optimize the selectivity of metal complexes, aiming to minimize off-target effects on normal cells while maximizing their impact on cancer cells. This selectivity is a key focus in the development of metal-based anticancer agents.

Topoisomerase Inhibitors: Topotecan and Etoposide have well-established mechanisms of action that primarily target rapidly dividing cancer cells. However, they may still affect normal cells to some extent.

Antimetabolites: Methotrexate and Gemcitabine can impact normal rapidly dividing cells, which can lead to side effects like myelosuppression.

ISSN No: 2348-4845
International Journal & Magazine of Engineering, Technology, Management and Research
A Peer Reviewed Open Access International Journal

3. Safety Profiles:

Metal Complexes: The safety profiles of metal complexes are an active area of research. Scientists are working to reduce toxic side effects that may limit their clinical use. Safety is a critical consideration in the development of metal complexes.

Topoisomerase Inhibitors: These agents may have known side effects, including myelosuppression.

Antimetabolites: Methotrexate and Gemcitabine can cause myelosuppression and other toxicities.

4. Personalized Treatment: The choice of treatment should be personalized based on the specific cancer type, patient characteristics, and available therapeutic options. Consideration should also be given to potential drug interactions and patient tolerability.

5. Combination Therapy: In some cases, combining different treatment modalities or agents may be more effective in combating cancer. Combining metal complexes with established chemotherapeutic agents or other targeted therapies may be explored for enhanced efficacy.

Conclusion

In conclusion, the research into the anticancer activity of novel metal complexes derived from polycyclic aromatic compounds has revealed a promising avenue for the development of potential anticancer agents. These complexes have been designed and synthesized using greener and more sustainable methods, aligning with the principles of green chemistry. The comprehensive methodology for their synthesis, characterization, and evaluation has shed light on their potential therapeutic value.

Synthesis and characterization techniques, such as spectroscopy and X-ray crystallography, have confirmed the chemical structure and purity of these metal complexes. In vitro studies using cancer cell lines have provided valuable insights into their cytotoxicity and mechanisms of action, including apoptosis and cell cycle arrest. In vivo studies using animal models have allowed for a more comprehensive assessment of their efficacy and safety profiles.

Comparative analyses with established chemotherapeutic agents have highlighted the unique potential of these metal complexes, although further research is needed to optimize their selectivity and safety. The field of metal complexes of ligands derived from polycyclic aromatic compounds represents a promising area of research with the potential to expand the arsenal of anticancer treatments available to patients.

As research in this area continues to evolve, it is essential to consider factors such as efficacy, selectivity, and safety when determining the best approach for cancer treatment. Personalized treatment strategies and the exploration of combination therapies may further enhance the effectiveness of these novel metal complexes in the fight against cancer.

ISSN No: 2348-4845
International Journal & Magazine of Engineering, Technology, Management and Research
A Peer Reviewed Open Access International Journal

References

[1] H. O. M. Al-Dahmoshi, "Anticancer Activity of Some Medicinal Plants: Minireview," Research Review, May 2023, doi: 10.52845/JMRHS/2023-6-5-1.

[2] Y. A. Gaikwad et al., "Novel Mixed Ligand Transition Metal Complexes: Synthesis, Characterization, and Biological Evaluation," SSRN Electronic Journal, Aug. 2022, doi: 10.2139/SSRN.4169450.

[3] A. Adan, Y. Kiraz, and Y. Baran, "Cell Proliferation and Cytotoxicity Assays," Curr Pharm Biotechnol, vol. 17, no. 14, pp. 1213–1221, Aug. 2016, doi: 10.2174/1389201017666160808160513.

[4] G. G. Chen and P. B. S. Lai, "Apoptosis in carcinogenesis and chemotherapy : apoptosis in cancer," 2009, Accessed: Sep. 17, 2023. [Online]. Available: https://www.researchgate.net/publication/341979944_Apoptosis_A_Programmed_cell_death-A_Review

[5] A. Malhi, T. Kampik, H. Pannu, M. Madhikermi, and K. Framling, "Explaining Machine Learning-Based Classifications of In-Vivo Gastral Images," 2019 Digital Image Computing: Techniques and Applications, DICTA 2019, pp. 1–7, 2019, doi: 10.1109/DICTA47822.2019.8945986.

[6] "(PDF) Structure Activity Relationship." https://www.researchgate.net/publication/318987614_Structure_Activity_Relationship (accessed Sep. 17, 2023).

[7] G. Ioele et al., "Anticancer Drugs: Recent Strategies to Improve Stability Profile, Pharmacokinetic and Pharmacodynamic Properties," Molecules, vol. 27, no. 17, Sep. 2022, doi: 10.3390/MOLECULES27175436.

[8] R. A. Ward, S. Fawell, N. Floc'H, V. Flemington, D. McKerrecher, and P. D. Smith, "Challenges and Opportunities in Cancer Drug Resistance," Chem Rev, vol. 121, no. 6, pp. 3297–3351, Mar. 2021, doi: 10.1021/ACS.CHEMREV.0C00383.

[9] R. K. Sodhi, "Metal Complexes in Medicine: An Overview and Update from Drug Design Perspective," Cancer Ther Oncol Int J, vol. 14, no. 2, Jun. 2019, doi: 10.19080/CTOIJ.2019.14.555883.

[10] D. T. Weiss et al., "Structural diversity of late transition metal complexes with flexible tetra-NHC ligands," Dalton Transactions, vol. 44, no. 42, pp. 18329–18339, 2015, doi: 10.1039/C5DT02386F.

[11] S. Muthaiah, A. Bhatia, and M. Kannan, "Stability of Metal Complexes," Stability and Applications of Coordination Compounds, Jul. 2020, doi: 10.5772/INTECHOPEN.90894.

[12] R. Uzal-Varela et al., "Thermodynamic Stability of Mn(II) Complexes with Aminocarboxylate Ligands Analyzed Using Structural Descriptors," Inorg Chem, vol. 61, no. 35, pp. 14173–14186, Sep. 2022, doi: 10.1021/ACS.INORGCHEM.2C02364.

[13] E. B. Tarabukina, E. I. Fatullaev, A. P. Filippov, and K. A. Abzaeva, "Behavior of metal complexes of polyacrylic acid in solutions," International Journal of Polymer Analysis and Characterization, vol. 24, no. 1, pp. 10–17, Jan. 2019, doi: 10.1080/1023666X.2018.1514691.

[14] I. V. Yentekakis, D. P. Gournis, and M. A. Karakassides, "Nanomaterials in

ISSN No: 2348-4845
International Journal & Magazine of Engineering, Technology, Management and Research
A Peer Reviewed Open Access International Journal

Catalysis Applications," Catalysts, vol. 13, no. 3, Mar. 2023, doi: 10.3390/CATAL13030627.

[15] C. G. L. Veale, T. O. Olomola, P. Chellan, and A. L. Edkins, "Biological and Medicinal Chemistry in Africa," ChemBioChem, vol. 24, no. 8, Apr. 2023, doi: 10.1002/CBIC.202300060.

[16] V. K. Jain and R. S. Chauhan, "Metal–Chalcogenolates: Synthesis and Applications in Material Chemistry," Chalcogen Chemistry: Fundamentals and Applications, pp. 58–82, Feb. 2023, doi: 10.1039/BK9781839167386-00058.

[17] Y.-L. Lai et al., "Selective separation of pyrene from mixed polycyclic aromatic hydrocarbons by a hexahedral metal-organic cage," Chinese Chemical Letters, p. 108326, Mar. 2023, doi: 10.1016/J.CCLET.2023.108326.

[18] "(PDF) Green Synthesis, Spectral Characterization and Biological Activities of Cu(II) Complex with Nitrogen Donor Ligands." https://www.researchgate.net/publication/370299763_Green_Synthesis_Spectral_Characterization_and_Biological_Activities_of_CuII_Complex_with_Nitrogen_Donor_Ligands (accessed Sep. 17, 2023).

[19] P. Noriega, G. Gortaire, and E. Osorio, "Mass Spectrometry and Its Importance for the Analysis and Discovery of Active Molecules in Natural Products," Natural Drugs from Plants, May 2022, doi: 10.5772/INTECHOPEN.97733.

[20] "(PDF) Synthesis and Characterization new metal complexes of heterocyclic units and study antibacterial and antifungal." https://www.researchgate.net/publication/333405454_Synthesis_and_Characterization_new_metal_complexes_of_heterocyclic_units_and_study_antibacterial_and_antifungal (accessed Sep. 17, 2023).

[21] M. Kumbar, S. A. Patil, S. S. Toragalmath, S. M. Kinnal, A. Shettar, and J. H. Hosakeri, "Anticancer activity studies of novel metal complexes of ligands derived from polycyclic aromatic compound via greener route," J Organomet Chem, vol. 914, May 2020, doi: 10.1016/J.JORGANCHEM.2020.121219.

[22] M. Kumbar, S. A. Patil, S. S. Toragalmath, S. M. Kinnal, A. Shettar, and J. H. Hosakeri, "Anticancer activity studies of novel metal complexes of ligands derived from polycyclic aromatic compound via greener route," J Organomet Chem, vol. 914, May 2020, doi: 10.1016/J.JORGANCHEM.2020.121219.

[23] J. H. Abdulameer and M. F. Alias, "Heavy Metal Complexes of 1, 2, 3-Triazole derivative: Synthesis, Characterization, and Cytotoxicity Appraisal Against Breast Cancer Cell Lines (MDA-MB-231)," Baghdad Science Journal, vol. 19, no. 6, pp. 1410–1422, 2022, doi: 10.21123/BSJ.2022.7178.

[24] B. J. Pages, D. L. Ang, E. P. Wright, and J. R. Aldrich-Wright, "Metal complex interactions with DNA," Dalton Transactions, vol. 44, no. 8, pp. 3505–3526, Feb. 2015, doi: 10.1039/C4DT02700K.

[25] F. J. Corpas, D. K. Gupta, and J. M. Palma, "Production sites of reactive oxygen species (ROS) in organelles from plant cells," Reactive Oxygen Species and Oxidative Damage in Plants Under Stress, pp. 1–22, Sep. 2015, doi: 10.1007/978-3-319-20421-5_1.

[26] N. Patadiya, N. Panchal, and V. Vaghela, "A REVIEW ON ENZYME

ISSN No: 2348-4845
International Journal & Magazine of Engineering, Technology, Management and Research
A Peer Reviewed Open Access International Journal

INHIBITORS," International Research Journal Of Pharmacy, vol. 12, no. 6, pp. 60–66, Jun. 2021, doi: 10.7897/2230-8407.1206145.

[27] H. Cheng et al., "Mechanisms of metal-induced mitochondrial dysfunction in neurological disorders," Toxics, vol. 9, no. 6, Jun. 2021, doi: 10.3390/TOXICS9060142.

[28] M. Zec et al., "Anti-metastatic and Anti-angiogenic Properties of Potential New Anti-cancer Drugs Based on Metal Complexes of Selenosemicarbazones," Anticancer Agents Med Chem, vol. 12, no. 9, pp. 1071–1080, Oct. 2012, doi: 10.2174/187152012803529682.

[29] C. H. Leung, L. J. Liu, K. H. Leung, and D. L. Ma, "Epigenetic modulation by inorganic metal complexes," Coord Chem Rev, vol. 319, pp. 25–34, Jul. 2016, doi: 10.1016/J.CCR.2016.03.014.

[30] R. Liu et al., "Immunomodulation-Based Strategy for Improving Soft Tissue and Metal Implant Integration and Its Implications in the Development of Metal Soft Tissue Materials," Adv Funct Mater, vol. 30, no. 21, May 2020, doi: 10.1002/ADFM.201910672.

[31] S. M. Alfadul, E. M. Matnurov, A. E. Varakutin, and M. V. Babak, "Metal-Based Anticancer Complexes and p53: How Much Do We Know?," Cancers (Basel), vol. 15, no. 10, May 2023, doi: 10.3390/CANCERS15102834.

[32] I. Stoikov, I. N. Ivanov, D. Donchev, E. Dobreva, R. Hristova, and S. Sabtcheva, "High quality RNA extraction from Pseudomonas aeruginosa and other bacteria with a novel rapid and cost-effective method," Biotechnology and Biotechnological Equipment, vol. 37, no. 1, 2023, doi: 10.1080/13102818.2023.2234502.

[33] M. Kumbar, S. A. Patil, S. S. Toragalmath, S. S. Jawoor, and A. Shettar, "Synthesis of novel metal (II) complexes tailored from 9-oxo-9H-fluorene-1-carboxylic acid via green protocol: DNA cleavage and anticancer studies," Inorganica Chim Acta, vol. 500, Jan. 2020, doi: 10.1016/J.ICA.2019.119210.

[34] B. T. Kurien and R. Hal Scofield, "Western blotting: An introduction," Western Blotting: Methods and Protocols, pp. 17–30, Jun. 2015, doi: 10.1007/978-1-4939-2694-7_5.

[35] N. M. Nasar, M. Samuel, P. Jayaraman, F. S. Sheela, and N. Raman, "Virtual and in vitro, in vivo Screening of Transition Metal Complexes of N,N-Chelating Ligand: Experimental and Theoretical Investigations," Asian Journal of Chemistry, vol. 35, no. 3, pp. 639–648, Mar. 2023, doi: 10.14233/AJCHEM.2023.27565.

[36] M. O'Shaughnessy et al., "In Vivo Activity ofMetal Complexes Containing 1,10-Phenanthroline and 3,6,9-Trioxaundecanedioate Ligands against Pseudomonas aeruginosa Infection in Galleria mellonella Larvae," Biomedicines, vol. 10, no. 2, Feb. 2022, doi: 10.3390/BIOMEDICINES10020222/S1.

[37] R. Meena, P. Meena, A. Kumari, N. Sharma, and N. Fahmi, "Schiff Bases and Their Metal Complexes: Synthesis, Structural Characteristics and Applications," Schiff Base in Organic, Inorganic and Physical Chemistry, Mar. 2023, doi: 10.5772/INTECHOPEN.108396.

[38] T. Jurca, E. Marian, L. G. Vicaş, M. E. Mureşan, and L. Fritea, "Metal Complexes of Pharmaceutical Substances," Spectroscopic Analyses - Developments and Applications, Dec. 2017, doi: 10.5772/65390.

ISSN No: 2348-4845
International Journal & Magazine of Engineering, Technology, Management and Research
A Peer Reviewed Open Access International Journal

[39] S. Wanninger, V. Lorenz, A. Subhan, and F. T. Edelmann, "Metal complexes of curcumin - synthetic strategies, structures and medicinal applications," Chem Soc Rev, vol. 44, no. 15, pp. 4986–5002, Aug. 2015, doi: 10.1039/C5CS00088B.

[40] J. P. Coelho, J. Matern, R. Q. Albuquerque, and G. Fernández, "Mechanistic Insights into Statistical Co-Assembly of Metal Complexes," Chemistry – A European Journal, vol. 25, no. 38, pp. 8960–8964, Jul. 2019, doi: 10.1002/CHEM.201900604).

[41] J. P. Coelho, J. Matern, R. Q. Albuquerque, and G. Fernández, "Front Cover: Mechanistic Insights into Statistical Co-Assembly of Metal Complexes (Chem. Eur. J. 38/2019)," Chemistry – A European Journal, vol. 25, no. 38, pp. 8911–8911, Jul. 2019, doi: 10.1002/CHEM.201902071.