COORDINATION COMPOUNDS FOR PHARMACEUTICALS AND DRUG DELIVERY SYSTEMS

Editor:
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Coordination Compounds for Pharmaceuticals and Drug Delivery Systems

(*Volume 1*)

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Coordination Compounds for Pharmaceuticals and Drug Delivery Systems

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FOREWORD

The book entitled "Coordination Compounds for Pharmaceuticals and Drug Delivery Systems (Volume 1)" Edited by Dr. Abhay Nanda Srivastva provides a detailed insight about the significance of coordination compounds for the treatment of many diseases. The book is a compilation of valuable chapters describing the prophylactic properties of coordination compounds in drug delivery to cure many lethal diseases. Increasing threat of diseases is momentous issue across the globe. After the Covid-19 pandemic, it has been observed that there is need to aggrandize the preparation of more efficient drugs. Coordination compounds have bolstered the drug delivery system as they leveraged the therapeutic ability of drugs. A plethora of drugs have covered the pharmaceutical industry as many class of diseases can be cured by suitable mechanism/properties viz. antibacterial, antifungal, anti-alzheimers, antidiabetic and many more provided by coordination compounds. Lethal diseases like cancer can be cured by metallic drugs. These classes of compounds possess diversity in chemical and structural against lethal microorganism. The excellent drug delivery of the cis-platin has gained credence and many metal complex based drugs are under trial. Synergistic approach of pharmaceutical chemists across the globe to develop more efficient drug have augmented the applicability of coordination compound based drugs. The book is the recapitulation of intriguing drug delivery ability of the coordination compounds. Research scholars as well as undergraduate and postgraduate students of chemistry, biochemistry, and pharmacy along with chemical and pharmaceutical industrialist will be most benefitted from this volume of book. I wish the editor, authors and publication team all the success to this book.

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PREFACE

Chemical moieties occupied with medicinal values are the most important molecules as they cure and control many diseases to make the survival of living beings easier. Medicinal chemists always try their best to produce high quality of medicinal molecules from different branches of chemistry. Coordination compounds, among the various kinds of chemicals, have their unique importance as drug like molecules. Bioactive coordination compounds possess unique mode of drug actions due to versatility of ligands and metal ions attached together in different mode of coordination. Among the commercially available frontline drugs for curing many lethal diseases, metal based pharmaceutics like Cisplatin, Carboplatin, Oxaliplatin, Salvarsan, Auranofin, Bactiracin zinc salt *etc.* also cover an enough part of global pharmaceutical industries. Diagnosis capital is also roofed with Gadobutrol and Gadodiamide, Gd(III) complexes, as the commercial MRI contrasting agent. After taking an insight of these enthralled medicinal, diagnostic and theranostic appeal of metal complexes, pharmaco-researchers are focusing on the developments of potent metallic therapeutic moiety. The first volume of the book entitled "Coordination compounds for Pharmaceuticals and Drug delivery systems" is a compilation of advancements and research findings in the area of novel metal complex designing and bioactive applications from antibacterial to anticancer. An exhaustive discussion on bioactivity of metal complexes on life style generated diseases like diabetes is also focused in a chapter of the book. The advantages of coordination compounds in different drug delivery systems have also been discussed in the chapters embedded here.

I hope this compilation will be advantageous for all the personnel belonging to drug chemistry, pharmaceutical chemistry, coordination chemistry and bio-inorganic chemistry from academia to research to industries in a very simple and comprehensive style of service as a book.

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DEDICATION

Dedicated to my respected mother *Mrs. Sandhya Srivastava* and loving kids of the family; *Shivansh, Rudransh, Divyansh, Chitransh* & *Ashutosh*

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CHAPTER 1

Advances in Coordination Compounds for the Drug Delivery System in the Human Circulatory System

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Abstract: Background: Drug delivery is a significant and evolving research area that relies on accurately quantifying drugs, particularly when developing drug delivery systems and understanding the pharmacokinetics and pharmacodynamics of actives in coordination with metals. Metals, acting as catalysts or reactants in the determination process, play a vital role in drug quantification. This study underscores the crucial role of metals in drug quantification and their coordination with actives, providing valuable insights into drug delivery and recent advances in drug applications. By emphasizing the role of metals in drug quantification, the audience can feel more informed and knowledgeable about this crucial aspect of drug delivery.

Methodology: This study utilizes Artificial Intelligence (AI) to review 1199 articles from the search engine "Advances in Coordination Compounds for the Drug Delivery System in the Human Circulatory System." The AI tools were instrumental in analyzing and synthesizing the vast data on the 'Drug Delivery System in the Human Circulatory System.' Specifically, AI was used to identify relevant articles, extract essential information, and analyze trends in the research.

Key Findings and Future Prospects: Transforming the old drug delivery system from its traditional form into a unique delivery system is a process and a journey of rejuvenation. It can significantly enhance compliance, safety, and efficacy, breathing new life into an old drug molecule. The various technological advances in unit operations, such as drying, filtration, and mixing, are crucial and the backbone of this transformation, modifying and improving drug formulations. The potential of advanced drug delivery systems utilizing lipidic, proteic, and polymeric technologies **is of immense importance**. These systems have the power to revolutionize drug delivery, offering a hopeful and exciting future for pharmaceuticals. They provide sustained drug delivery with better body distribution, protection from harsh external environments, and avoidance of drug clearance. **Hence,** a rapid drug delivery system **could be effective in case of a fast**-dissolving tablet, a sustained system could be a transdermal patch, and a highly efficient system could be a targeted drug delivery system. The

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potential of these new systems is inspiring and a call for further exploration and innovation in the field. By stressing the importance of further exploration and innovation, the **researchers** can feel optimistic about the future of pharmaceuticals.

Conclusion: Technology-based drug delivery systems play a crucial role in facilitating and storing drug molecules in suitable forms for administration. However, their scope extends beyond small molecules. The potential of cell therapies is a beacon of hope in the field, with their promise of a sustained source of complex biologics. These therapies have the potential to revolutionize drug delivery, breaking innate biological barriers and creating natural responses within the system.

Keywords: Coordination compounds, Circulatory system, Drug, Metal, Pharmaceutical.

INTRODUCTION

The recent advances in the innovation of coordination compound research have underscored the significance of drug delivery mechanisms, particularly their high selectivity, which inspires confidence in their effectiveness. The coordination compound's role in targeting various diseases, from common ailments to more complex conditions, is a testament to its medical potential. The unique and distinct structural order of drugs based on coordination compounds, a key feature, is crucial and fascinating. This unique structural order of coordination compounds is vital to the human body's biological systems. The hemoglobin (a metal complex of Fe^{2+} ions) in human blood is a key player in oxygen transport and is crucial to the functioning of the human body's metabolism [1]. It was observed that coordination compounds have been instrumental in developing novel derivatives with therapeutic potential, a field ripe with possibilities that should pique the interest and curiosity of researchers.

The medicine can be easily encapsulated in nanomaterials and used as transporters for treatment, allowing for prolonged and well-organized drug administration in the human body. In the recent past, the transformative power of nanoparticles has reshaped contemporary medicine. By enhancing bioavailability, which refers to the proportion of a drug or other substance that enters the circulation when introduced into the body and so is made available for use or excretion, improving targeting, and modulating drug release mechanisms, these innovations have opened up new possibilities. Traditional drug delivery methods, with their poor therapeutic efficacy due to rapid elimination, inadequate solubility, and systemic toxicity, are being re-imagined. Nanomaterials, with their high surface area-to-volume ratio, configurable surface properties, and controlled drug delivery applications, are leading this revolution [2].

This is one of the new innovative areas that must be explored for drug delivery at this research stage. The analysis of experimental data indicates that nanoparticles are designed for the specific targeted tissues by coupling with targeting ligands and are designed to contain numerous agents. The research suggests that the most popular drug delivery carriers are preferably based on dendrimers, liposomes, organic polymeric, and inorganic particles. These innovative methods are crucial for designing a suitable drug delivery system at the nanoscale for the coordination of polymer particles encapsulating desired components. The technique, which involves a coordination polymerization, is further followed by quick precipitation, and it offers several advantages over existing approaches. It shows its importance during application through entrapping organic dyes, quantum dots, and magnetic nanoparticles into blue fluorescent spheres created through the coordination of Zn^{2+} with 1,4-bis(imidazol-1-ylmethyl) benzene (bix) organic ligands [3]. This stretches the significance of coordination compounds in medical sciences.

This research has the potential to significantly impact drug delivery systems, offering an efficient and controlled method of drug administration. The study indicates that the unique characteristics of nanomaterials enhance the ability of medical science to entrap a wide variety of substances, which facilitates fast and efficient medical treatment. Researchers reported in their study that coordination polymer nanospheres function as better drug-encapsulating agents and can be utilized as novel functional carriers for targeted medicine delivery to specific cells. The potential impact of this research on the drug delivery systems field sparked their curiosity and eagerness to learn more about the hopeful and exciting future it presents. There are numerous sources of natural bioactive molecules, which are essential for a comprehensive understanding of their function. Several selected sources of natural bioactive molecules are available in nature, as illustrated in Fig. (**1**). These bioactive molecules possess numerous clinical applications, including anticancer, antioxidant, immunomodulatory, antidiabetic, anti-obesity, neuroprotective, and anti-inflammatory properties.

Ma and Moulton [4] have studied innovative advances in discrete coordination complexes and polymers, which facilitate upgrading their applications for drug delivery systems. They also emphasized and listed the significance of these compounds in modern research for modern drug delivery systems. Recent material science and crystal engineering research has allowed researchers to promote coordination complexes as functional materials. The most popular applications are catalysts, magnetic, non-linear optical, and porous materials [4].

CHAPTER 2

Antidiabetic Properties of Metal Complexes: Recent Advancements

Divyakshi Arya[1], Gulshan A. Khan[1], Shweta Singh[1], Anjali Upadhyay[1], M.L. Sharma[2], Ashish R. Dwivedi[3], Som S. Dubey[1] and **Sarvesh K. Pandey[1,*]**

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Abstract: The demographic count of individuals diagnosed with diabetes has risen worldwide over the past 10 years. Today, a majority of countries that are experiencing a high prevalence of diabetes are developing countries. Due to the concerning prevalence of diabetes, chemists and pharmacists are always looking for and creating novel, powerful medications to treat the condition. The metallo-drug interaction mechanism is receiving a lot of interest these days. In medicine, metals and organometallic complexes are utilized to treat a variety of illnesses. Pronounced advancements have been made in the deployment of coordination compounds of transition metals as medications to alleviate numerous human ailments. Transition metals may engage with a variety of anionic molecules and exhibit a range of oxidation states. The present status and probable upcoming ways of metal complexes of V(IV), Zn(II), Cr(III), Cu(II), and Co(II) as possible oral drug candidates against type 2 diabetes have recently reviewed. This chapter summarizes key developments in the synthesis and therapeutic assessment of metal complexes for diabetes management.

Keywords: Diabetes, Insulin mimetic property, Metal complexes, Transition metals.

INTRODUCTION

Diabetes is a chronic metabolic imbalance triggered by either inadequate insulin secretion by the pancreatic tissue or the body's reduced sensitivity to insulin, impairing glucose regulation. Insulin is a hormone responsible for modulating blood sugar levels. If not regulated and managed, diabetes gradually leads to hyperglycemia, high blood sugar, which eventually damages very sensitive and

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delicate systems in the body, notably nerves and blood vessels. There are different categories of diabetes mellitus that have been described (Fig. **1**).

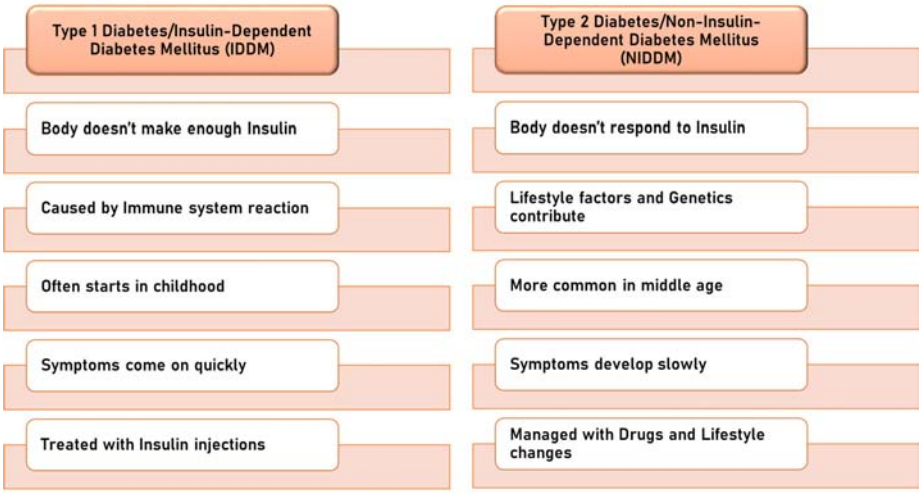

Fig. (1). Types of diabetes.

As of 2022, diabetes had impacted about 14% of adults aged 18 and older, approximately doubling since 1990. Among adults aged 30 and older with diabetes, 59% were not given any treatment to manage diabetes, and coverage for diabetes treatment was exceptionally low in low- and middle-income countries.

In 2021, diabetes was directly liable for 1.6 million deaths, roughly half of them (47%) occurring prior to the age of 70. Likewise, diabetes caused another 530,000 deaths from kidney disease and resulted in about 11% of cardiovascular deaths due to high blood glucose levels [1].

Global Prevalence

An estimated 240 million people worldwide live with unidentified diabetes, of whom approximately half of the adults affected are oblivious to having diabetes. Misdiagnosis, accompanied by the rising incidence of diabetes, places a hefty burden on the healthcare systems globally. At present, 537 million individuals, ranging in age from 20 to 79 years, with diabetes, impact nearly 10.5% of the global population. The International Diabetes Federation (IDF) determined that the healthcare expenses associated with diabetes reached $966 billion in 2021, which is anticipated to escalate to more than $1,054 billion in 2045. Consequently, the prevalence of diabetes is foreseen to escalate sharply to 643 million (11.3%) people in 2030 and 783 million (12.2%) in 2045 (Fig. **2**). This

calls for escalating global efforts to prevent, diagnose early, and manage diabetes [2].

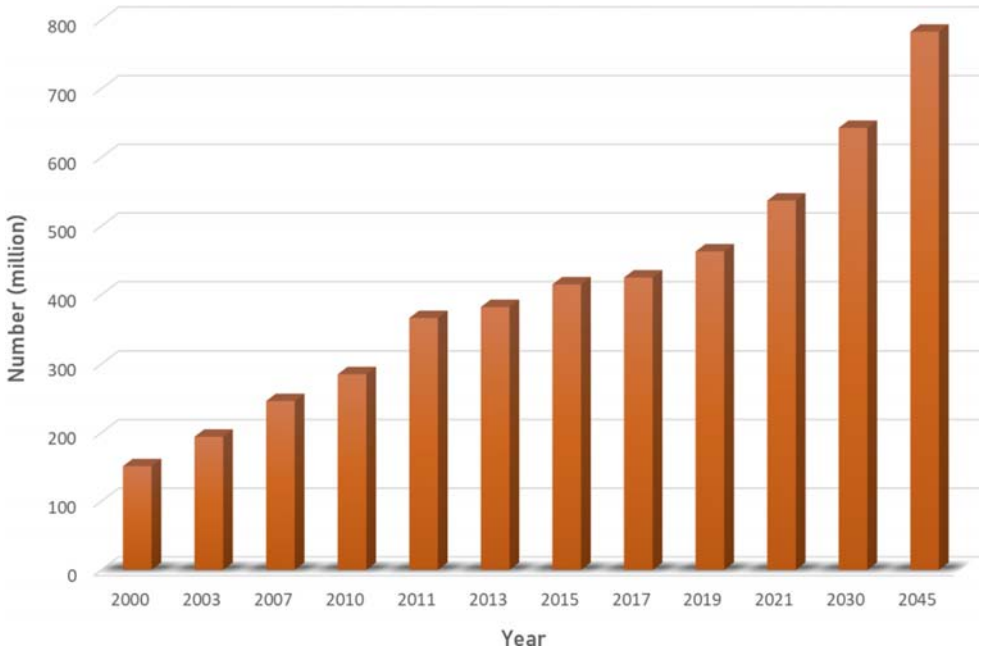

Fig. (2). The number (millions) of individuals aged 20-79 years having diabetes across the globe (envisioned numbers in case of 2030 and 2045).

The top 10 countries with the elevated incidence in the world are India, China, the USA, Pakistan, Russia, Japan, Indonesia, Bangladesh, Brazil, and Italy. The escalating health condition is now becoming a global challenge. Prevalence of diabetes consistently is amplifying four times faster in low- and middle-income nations than in the high-income nations [3]. The diabetic community is primarily found in low- or middle-income countries, and it corresponds to nearly 80% of the global dispersal, hence protruding an uneven spread of the disease [4].

Associated Risk Factors

Diabetes Mellitus (DM) is highly pervasive in populations that are swiftly undergoing transitions from a traditional to a modern lifestyle, which confers an expanded risk of the ailment. Type 2 diabetes is strongly correlated with overweight or obesity, older age, certain ethnicities, and a genetic linkage to diabetes within the family, although type 2 diabetes has an unknown etiology [5]. The evolution results due to the interaction of complex genetic (polygenic) and environmental factors [4].

CHAPTER 3

Recent Advances on Metal Dithiocarbamates and their Biological Applications

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Abstract: The growing demand for drug delivery systems and pharmaceuticals has attracted the interest of scientists worldwide, and the area of coordination/inorganic chemistry provides an enormous foundation. In this context, dithiocarbamate complexes have found many applications in biological systems. However, developing new dithiocarbamate complexes is necessary to advance cancer treatment, antiproliferative technologies, anti-leishmanial activity, and other biological activities. Recently, significant progress has been made in the development of dithiocarbamate complexes, in the consideration of the main mechanisms of action associated with these compounds, as well as in improving the main treatments for these diseases, which are being considered by the WHO (World Health Organization). Dithiocarbamate complexes are highly versatile ligands, known for their diverse structures and numerous coordination patterns that give rise to supramolecular networks. This diversity stems from the resonance structures the ligands can adopt in their complexes. A key factor driving the increasing attention in dithiocarbamate (dtc, ligand) chemistry is the ability to functionalize the different substituents on the N atom of the dtc ligand backbone. This modification can lead to intriguing crystal structures, enhanced materials, and potential biological applications. Overall, we provide a detailed review of dithiocarbamate complexes, their intriguing coordination activities, and their biological applications.

Keywords: Anti-leishmania, Anti-cancer, Biological activity, Dithiocarbamate complexes.

INTRODUCTION

The increasing interest in metal dithiocarbamate complexes arises from the ability to functionalize moieties on the dithiocarbamate (dtc) backbone, which can affect

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fsteric and electronic behavior, thereby influencing their crystal structure and biological properties. Dithiocarbamates (dtc) are monoanionic chelating ligands that are readily synthesized from secondary (2˚) amines. They form highly stable complexes with nearly all d-block and p-block elements [1 - 4]. Metal dithiocarbamate complexes have a wide range of applications across various fields, including agriculture, medicine, pharmaceuticals, manufacturing, catalysis, sensors, and materials science [5 - 12]. Numerous studies have been conducted to explore the properties of metal complexes formed with dithiocarbamate ligands. Research into the synthesis and properties of metallo-pharmaceuticals has surged since the discovery of the anticancer drug cisplatin and its analogs [13, 14]. Dithiocarbamates are easily synthesized from inexpensive and readily available secondary or primary amines by reacting with CS_2 in a basic solution, typically water, though methanol and other simple organic solvents can also be used. These ligands form stable complexes with nearly all transition metals, s-block elements, most p-block elements (excluding oxygen and the halogens), as well as the lanthanides and actinides [1 - 4]. The formation of dithiocarbamate complexes with various transition metals as well as main group metals is typically a straightforward process. It involves the addition of a water-soluble metal salt to an aqueous or methanolic solution containing a dithiocarbamate salt. This reaction leads to the formation and precipitation, which can be well collected through a simple filtration method, followed by washing and drying, resulting in a good to high yield of the dithio complexes. A key advantage of DTCs is their capacity to stabilize a large range of oxidation numbers across nearly all metals. This stabilization is ascribed to the resonance forms of dithiocarbamate (dtc) and thioureide forms (Fig. **1**). In its DTC form, classified as a soft ligand, the lone pair of electrons is localized on the sp^3 (tetrahedral) hybridized nitrogen atom, leading to a pyramidal shape of the substituents. On the other hand, the thioureide sp^2 hybridized resonance form, considered a hard ligand, adopts a planar structure, with the lone pair integrated into the C-N bond framework and extending toward the sulfur atom [15 - 17]. DTCs can coordinate with metals in various ways, with bidentate chelation being the dominant mode. This chelation significantly improves the thermodynamic stability of the compounds and increases their Coordination Number (C.N.) compared to simple monoanionic ligands.

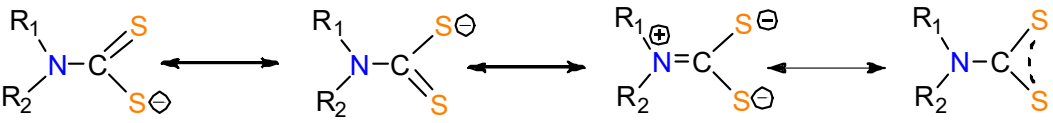

Fig. (1). Resonance form of dithiocarbamate and thiouride.

The small bite angle and the soft nature of the dithiocarbamate moiety allow these ligands to stabilize a broad range of transition metal ions and main group elements in various oxidation states [1 - 4, 18, 19]. The monodentate coordination mode is typically influenced by the absence of a vacant orbital on the metal with the appropriate symmetry to accommodate the lone pair of electrons from the second S atom. Additionally, the presence of other ligands already bonded to the metal can cause steric hindrance, preventing the coordination of the second S atom. This limitation may also occur due to the restricted vacancy left by a departing ligand, mainly in ligand exchange reactions. Dithiocarbamate ligands possess lipophilic properties and commonly coordinate with metals through various modes, with monodentate and anisobidentate being the most frequent. The electronic properties of these ligands can be adjusted by selecting different substituents [20]. Substituents on the nitrogen atom of the dithiocarbamate unit influence the overall complex structure, properties, and potential applications through secondary interactions [21]. Bulky substituents on the nitrogen atom typically hinder supramolecular aggregation by obstructing metal-sulfur interactions, while smaller substituents promote or enhance these interactions [22]. This, in turn, affects the stereo-configuration and electron density distribution, influencing the biological activity of various biomolecules, including proteins and enzymes, and potentially leading to toxic effects [23]. In this book chapter, we have summarized the synthesis of dithiocarbamate complexes and their medicinal applications such as anticancer activity, antileishmanial activity, effects on human breast cancer, anti-nematode activities, antibacterial activity, anticonvulsant properties, antianxiety activities, cytotoxic activity, DNA binding and cleavage, as well as antitumor activity.

General Synthesis of Dithiocarbamate

Dithiocarbamate (dtc) ligands, whether aliphatic or aromatic, are typically synthesized through the reaction of 1˚ or 2˚ amines with CS_2 and NaOH or KOH (Fig. **2**). In this process, nucleophiles (amines) first react directly with the electrophile (CS_2) to form a zwitterion. Subsequently, this zwitterion reacts with base (sodium or potassium hydroxide) to generate monoanionic dithiocarbamate ligands and water. The reaction is generally conducted under exothermic conditions, starting at low temperatures (0 °C or in an ice bath) and gradually increasing to room temperature [1, 11, 15, 24 - 29].

CHAPTER 4

Biological Potentials of Schiff Base Metal Complexes: A Multifaceted Approach

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Abstract: Metal-based drugs have been intensively explored in the pharmaceutical, biochemistry, agricultural, and clinical industries since the serendipitous discovery of the chemotherapeutic agent cisplatin. Coordination chemistry has been extensively studied because of its flexible bonding properties and diverse pharmacological properties. Metal complexes have exhibited a wide range of characteristics, including electrochemical, catalytic, photovoltaic, enzyme inhibitory, lipid-lowering properties, photodynamic therapy, and biological properties such as antibacterial, antitumor, antifungal, antioxidant, anticonvulsant, anti-inflammatory, antiviral, antifertility, anti-HIV, antiproliferative, and diuretic activities. Metal complexes have been shown to have higher biological activity than ligands. By introducing structural alterations to the ligands, the properties of the metal complexes will be improved. Metal complexes have distinctive characteristics, such as molecular geometries and ligand exchange, that enable them to interact with biomolecules in distinct ways and through different modes of action. Antibiotic resistance is a serious problem nowadays; thus, new drugs with a broad spectrum of action and no or minimal toxicity are needed. Metal complexes have low stability and solubility, making them difficult to introduce into clinical practice. Validation of metal-based drugs requires collaboration between chemists and biologists. In the present review, we focused on the recent development of metal complexes, including their synthesis, structure, and biological characteristics. We hope the present review will facilitate the development and introduction of more therapeutic drugs into clinical practice.

Keywords: Antimicrobial properties, Anticancer agents, Antibacterial, Antitumor, Antifungal, Antioxidant, Anticonvulsant, Bioinorganic chemistry, Coordination chemistry, Metal complexes, Schiff base.

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INTRODUCTION

Metals have A vital part in humans and may be found in many traces that are required for living things to exist. Since they are highly reactive and show a variety of coordination characteristics, transition metals can be employed to synthesize complexes, including a wide spectrum of organic ligands [1, 2]. The evolution of coordination chemistry has been significantly influenced by the characteristics and manufacture of such metal complexes. Over the past few decades, metal complexes have received much research about their possible application in the treatment of various deadly diseases [3 - 5]. Metal-based pharmaceuticals have emerged as one of the productive research fields in artificial biomedical sciences since the invention of the cisplatin pharmaceutical. In drug-derived metal complexes, through oxygen, nitrogen, and sulphur donor atoms in an ideal three-dimensional framework, the metal may coordinate ligands, allowing the molecule to detect and interact with a given biological target [6]. By introducing different groups to ligands, multiple chemical changes might increase this even further. Moreover, switching between different configurations is possible due to the enormous flexibility of coordination geometry, which is only determined by steric hindrance and ligand charge. Complexes of transition metals have demonstrated a substantial contribution to their use in the pharmaceutical sector. Metals are poisonous, non-biodegradable, and often accumulate in crucial human organs even at very high concentrations. The majority of these compounds exhibit a broad range of biologicalproperties, including antidiabetic [7, 8], anti-inflammatory [9], anticonvulsant [10], antidepressant [11], hypertensive [12], anthelmintic [13], antitubercular [14], anti-allergic [15], antifungal [16], antiviral [17], and antimicrobialproperties [18].

Schiff base complexes are furthermore well-known to show remarkable biological activity and serve as key models for physiologically significant entities, influenced by the presence of transition metal ions [19 - 21]. The -C=N-linkage in Schiff bases gives them biological and chemical significance. As a result of the nitrogen- and oxygen-giving atoms in Schiff bases, as well as their transition metal ions, the complexes they create have attracted a great deal of attention. A variety of biological effects have been reported for compounds with an aromatic ring containing one or more nitrogen atoms. It is estimated that over 75% of FDA-approved and currently available drugs contain heterocyclic nitrogen compounds [22, 23]. Numerous naturally occurring N-heterocyclic substances, which are widely dispersed, have physiological and pharmacological characteristics and are components of numerous biologically significant molecules, such as numerous antibiotics, vitamins, pharmaceuticals, dyes, agrochemicals, and nucleic acids, among many others, are among them [24].

There has been much interest in Schiff bases containing halogen groups and their metal complexes because of their antibacterial properties. Metal-based medications have grown rather important in the medical field recently and are now used to treat diseases, including diabetes, cancer, anti-inflammatory disorders, and cardiovascular diseases [25 - 27]. Many reports have been published on their application in homogeneous and heterogeneous catalysis in recent times. Many research studies have been conducted on the coordination behavior of these compounds because some metals have intrinsic chemical interests as multidentate ligands.

To give information on the present state of metal complexes and their biological profile, this review highlights literature that has been made public throughout the last few years. We hope that this study will provide a valuable opportunity to learn more about the metal complexes that are therapeutically relevant.

Biological Importance of Metal Complexes

The advancement of bioinorganic chemistry has raised interest in metal complexes, as numerous such complexes have been investigated as models for physiologically significant species. Biological molecules can bind to positively charged ions formed by metal complexes in aqueous solutions. Metal complexes may assemble into a myriad of coordination geometries, giving them distinct forms. Furthermore, a variety of unique molecular species that possess distinct coordination numbers and geometries might be provided by structurally modifying metal-based complexes. A metal complex or metal-based compound can coordinate with its ligand in a three-dimensional configuration, providing groups with the ability to be shaped to address defined molecular targets. They are distinctive for their synthetic versatility, selectivity, structure similarity, and azomethine group presence. Schiff bases are extensively studied. As a result, we've come to list a handful of their most crucial biological processes (Fig. **1**).

Antibacterial

The rise in the fatality rate of infectious illnesses is closely linked to certain bacteria that are resistant to antibiotics. The primary reason for this issue is the absence of workable solutions [28]. No doubt, an alarming situation arises for the creation of new antibacterial drugs, which have an effective mode of action. The bactericidal properties of Schiff bases are widely established. N-(salicylidene)-2-hydroxyaniline (Fig. **2**), for instance, has a MIC value of 8 I1/4mol/L and is effective against Mycobacterium TB H37Rv [29]. Tests on J774 macrophages were used to confirm compound 1's selectivity. Even at doses as high as 1000 I1/4mol/L, chemical 1 had no cytotoxic impact on J774 macrophages. Under these

CHAPTER 5

Advances in the Synthesis of Heterocyclic Schiff Base Ligands with 3d-Transition Metals as Antibacterial Agents

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Abstract: Heterocyclic Schiff Base Ligands (SBLs) and their 3d transition metal complexes have emerged as highly promising candidates in the field of antibacterial drug design. These compounds are synthesized through a condensation reaction between primary amines and aldehydes or ketones, resulting in an imine (-C=N-) functional group that serves as a versatile pharmacophore. The incorporation of heterocyclic moieties into Schiff bases further enhances their biological activity, while coordination with 3d transition metals such as Mn(II), Co(II), Cu(II), Zn(II), and Ni(II) forms metal complexes with superior stability and enhanced antibacterial activity. This chapter highlights recent advancements in the synthesis of heterocyclic SBLs with 3d transition metal complexes and examines their modes of interaction with bacterial strains. Through an analysis of both experimental and theoretical studies, we discuss the factors influencing the antibacterial activities of these metal complexes, including structural modifications, metal ion coordination, and ligand framework. The findings underscore the potential of heterocyclic Schiff base metal complexes as valuable agents in the development of novel antibacterial therapeutics.

Keywords: Antibacterial activity, Coordination chemistry, Geometry optimization, Schiff's base ligand, 3d-transition metal complex.

INTRODUCTION

Heterocyclic Schiff base ligands have become a focal point in the field of medicinal chemistry due to their versatile structural framework, ease of synthesis, and significant biological activities [1 - 3]. Schiff base ligands are typically synthesized by the condensation reaction of primary amines, aldehyde, and carbonyl compounds, resulting in compounds with an azomethine (-C=N-) group [4 - 6]. This functional group plays a crucial role in enhancing the reactivity and

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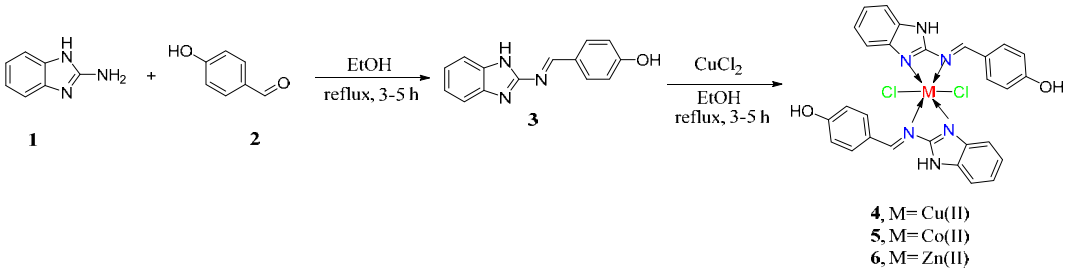
biological activity of Schiff bases, especially when coordinated with metal ions [7]. The incorporation of heterocyclic moieties into Schiff base ligands not only stabilizes these compounds but also amplifies their electronic and steric properties, making them particularly useful for antibacterial applications [8 - 10]. 3d transition metal complexes, particularly those with metals such as Mn(II), Co(II), Cu(II), Zn(II), and Ni(II), have been widely studied for their ability to enhance the pharmacological properties of Schiff bases [11 - 13] The metal ions interact with the azomethine group and other donor atoms in the Schiff base, forming stable complexes that often show superior antibacterial activity compared to the ligand alone [14 - 16]. The coordination with 3d transition metals allows these complexes to interact effectively with bacterial cell components, resulting in potential therapeutic applications against pathogenic bacteria, including both Gram-positive and Gram-negative strains [17, 18]. Advances in synthetic strategies have made it possible to develop heterocyclic Schiff base ligands with optimized structures and properties, enhancing their potential as antibacterial agents [19, 20]. Recent synthetic approaches focus on the careful selection of metal salts, ligands, and reaction conditions to achieve higher yields, better-defined structures, and antibacterial applications. The development of these Schiff base complexes offers promising avenues for new antibacterial agents that can combat infections more effectively than conventional treatments. This chapter explores recent progress in the synthesis of heterocyclic Schiff base ligands and their complexes with 3d transition metals, emphasizing the structural features that enhance their antibacterial properties. It further discusses the mechanisms by which these complexes exert their antibacterial effects, offering insights into their potential applications as therapeutic agents in the fight against bacterial infections.

Schiff's Base Approach to Antibacterial Activity

Bacteria can exist as single-celled organisms or form complex multicellular structures. Microscopic bacteria can initiate harmful processes that adversely affect human health and may develop resistance to chemical agents intended to control them [21]. Consequently, there is a pressing need to develop new antibacterial drugs.

The bidentate SBL 2-((1H-Benzoimidazole-4-ylimino)methyl)phenol **3** was synthesized through the condensation reaction between 2-aminobenzimidazole **1** and 4-hydroxybenzaldehyde **2**. Metal complexes of SBL**3** with Cu(II) **4**, Co(II) **5,** and Zn(II) **6** were also prepared (Scheme **1)** [22]. Elemental analysis and spectroscopic techniques, including Ultraviolet-Visible Spectroscopy (UV-Visible), Fourier-Transform Infrared Spectroscopy (FT-IR), CarbonNuclear Magnetic Resonance Spectroscopy (^{13}C-NMR), and Proton Nuclear Magnetic Resonance Spectroscopy (^{1}H-NMR), were synthesized to characterize compounds

3-6. The octahedral geometry of complexes **4-6** was confirmed. Cyclic voltammetry (CV) was utilized to examine the electrochemical properties of these complexes. The Antibacterialactivity of SBL **3** and theircomplexes Cu(II) **4**, Co(II) **5,** and Zn(II) **6** were evaluated against *Pseudomonas aeruginosa*(*P. aeruginosa), Escherichia coli (E. coli),* and *Staphylococcus aureus*(*S. aureus)*using the agar well diffusion method. The Cu(II) complex **4** showed the highest activity compared to other complexes.



Scheme 1. The Synthesis of SBL **3** and its complexes **4-6**.

In 2020, S. Kumaresan *et al*. synthesized aSBL, 4-nitrobenzaldehydeglycylglycine **9**, by refluxing glycylglycine (GG) **8** with 4-nitrobenzaldehyde (4-NBA) **7**. Metal complexes of SBL**9** with Co(II) **10**, Cu(II) **11**, and Zn(II) **12** were also prepared (Scheme **2**) [23]. Characterization of compounds **9-12** was carried out using various spectroscopic methods (^{1}H-NMR, ^{13}C-NMR, FT-IR, UV-Visible, and XRD analysis. The tridentate nature of the SBL **9** was confirmed, showing coordination through azomethine nitrogen, carboxylate oxygen, and deprotonated peptide nitrogen atoms. All metal complexes were water-soluble. Spectroscopic analysis confirmed that the complexes exhibit octahedral geometry. The antibacterial activity of compounds **9-12** was assessed using the disc diffusion method against *E. coli, S. aureus*, *Bacillus subtilis (B. subtilis)*, and *P. aeruginosa*. The Cu(II) complex **11** showed the highest activity among the complexes.

In 2021, Hadi Kargar and his team synthesized Cu(II) complexes **19-22**fromfour SBL**15-18** (Scheme **3**) [24]. Compounds **15-22** were characterized using molar conductivity, elemental analysis, and spectroscopic techniques like FT-IR, UV-Visible, ^{1}H, and ^{13}C-NMR, and XRD analysis. All spectroscopic studies indicated a distorted tetrahedral geometry for complexes **19-22**. The antibacterial potential of **15-22** was evaluated against *S. aureus* and *E. coli*, bacterial strains. The **19-22** showed stronger antibacterial potential compared to **15-18**.

CHAPTER 6

Ferrocene-Based Hybrids as Potent Anticancer Agents: Recent Advances and Structure-Activity Insights

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Abstract: Cancer remains a leading global health concern, second only to cardiovascular diseases. A significant challenge in managing and eliminating cancer is the continual emergence of drug-resistant strains and the limited selectivity of current anticancer therapies. This underscores the urgent need to develop novel and more effective anticancer agents. In recent years, organometallic compounds have emerged as promising candidates for anticancer therapies. Ferrocifen, a hybrid of ferrocene and phenol, has shown potential against resistant cancers and is currently in preclinical trials; thus, the ferrocene core serves as a valuable framework for developing new anticancer agents. This chapter highlights recent developments in ferrocene-based hybrids as potent anticancer agents and discusses their structure-activity relationships. This information will aid researchers in designing and developing more selective and specific novel anticancer agents to combat drug resistance.

Keywords: Amino acids, Anticancer potential, Artemisinin, Azoles, Carbohydrates, Coumarin, Drug resistance, Ferrocene, Molecular hybridization, Phenol, Pyrimidines, Puinolines, Steroid, Structure activity relationship.

INTRODUCTION

Cancer is the second leading cause of death worldwide, next to cardiovascular diseases, and continues to be a substantial health concern in the 21st century. The World Health Organization (WHO) reported around 20 million new cancer cases and 9.7 million deaths related to cancer worldwide in 2022 [1]. Furthermore, about 53.5 million individuals were living within five years of their cancer diagnosis. It is estimated that one in five people across the globe will face a cancer diagnosis in their lifetime, with one in nine men and one in twelve women

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ultimately succumbing to the disease. The global cancer burden is expected to increase by 77%, with over 35 million new cases anticipated by 2050, compared to 2022 statistics [2]. This rising burden is driven by an aging and growing population, alongside shifts in risk factors due to socioeconomic development. Key contributors include tobacco use, alcohol consumption, obesity, and environmental factors such as water and air pollution. The most prevalent cancers globally affect the breast, lungs, prostate, colorectum, liver, stomach, esophagus, and cervix.

Metal complexes have emerged as promising platforms for drug design, securing an important place in inorganic medicinal chemistry [3]. Cisplatin, the most well-known metal complex, is widely used in cancer treatment, either as a standalone therapy or in combination with other chemotherapeutic agents or radiotherapy [4, 5]. Several cisplatin derivatives, for example, oxaliplatin, carboplatin, heptaplatin, nedaplatin, and lobaplatin, have been developed and are now integral to standard cancer chemotherapy regimens. However, their use remains limited to specific cancer types, and patients often experience significant side effects, with only modest improvements in survival. Furthermore, the development of drug resistance diminishes the effectiveness of these metallodrugs, highlighting the need for more effective and less toxic alternatives in cancer treatment [6, 7]. Non-platinum metal complexes have shown promising results in preclinical and clinical studies, and some have been approved by the WHO for treating various cancers, offering hope for future therapies [8].

Iron, an essential transition metal, is vital to biological systems. It is a key component of the heme complex, which is found in cytochrome proteins that facilitate redox reactions in oxygen-transporting proteins like hemoglobin, leghemoglobin, and myoglobin. Iron's involvement in cancer cell growth makes it an important target for therapeutic development [9, 10]. Its versatile redox chemistry has led to the exploration of iron-based coordination complexes as potential cancer treatments. Bleomycin, an iron-chelating antibiotic, is a notable example, as it induces oxidative DNA damage in the presence of oxygen and H_2O_2, leading to cancer cell death [11, 12]. Similarly, iron(II) chelators have shown significant potential, particularly in overcoming drug resistance, indicating their broader application in cancer therapies [13].

Among iron-based metal complexes, ferrocene is notable for its stable, sandwich-like structure. It exhibits resistance to heat, air, and light, possesses low toxicity, is cost-effective, and demonstrates reversible redox behavior, ligand exchange capabilities, and catalytic activity [14]. These characteristics make ferrocene derivatives versatile scaffolds for drug discovery, with a broad spectrum of pharmacological activities, including antibacterial, antifungal, antimalarial,

antitubercular, antiviral, and anticancer effects [14, 15]. Ferrocifen, a hybrid of ferrocene and phenol, shows promise in treating drug-resistant cancers and is currently in preclinical trials [16], underscoring the potential of ferrocene as a framework for novel anticancer agents. Beyond its cytotoxic role, the chemistry of ferrocene also connects directly to drug-delivery applications through both coordination and redox mechanisms. The reversible Fe(II)/Fe(III) redox couple (ferrocene/ferrocenium) can act as a redox trigger: oxidation increases hydrophilicity, leading to the disassembly of hydrophobic carriers or cleavage of redox-sensitive linkers, thereby enabling controlled drug release; reduction reverses this process and stabilizes the carrier system [15, 17, 18]. Coordination chemistry further expands these applications, as ferrocenyl ligands can be incorporated into metal–organic frameworks, supramolecular cages, or polymeric assemblies to create nanostructures with tunable encapsulation and release properties, targeted delivery, and theranostic potential [17]. In addition, ferrocene has been utilized directly as a redox-activated pharmacophore, for example, *N*-alkylaminoferrocene prodrugs are selectively activated in the oxidative microenvironment of tumors, thereby improving therapeutic specificity and even allowing radiolabeling for imaging [18]. Considering this dual role of ferrocene in both therapeutic activity and delivery strategies, extensive efforts have been directed toward designing ferrocene derivatives with enhanced anticancer efficacy. This chapter provides an overview of recent advances in ferrocene-based hybrids, particularly those obtained through molecular hybridization, for the development of effective agents to overcome drug resistance.

MECHANISMS OF ANTICANCER POTENTIAL

The incorporation of ferrocene into bioactive scaffolds has attracted considerable attention due to its unique chemical and biological properties. The Fe(II)/Fe(III) redox couple confers reversible electron-transfer ability, while the sandwich structure provides remarkable chemical stability and lipophilicity [17]. These features allow ferrocene not only to serve as a structural motif but also to actively contribute to cytotoxic mechanisms when embedded in hybrid molecules. Over the past two decades, several mechanistic pathways have been proposed to explain the anticancer activity of ferrocene-based hybrids, among which three have emerged as the most prominent: generation of Reactive Oxygen Species (ROS), DNA interaction coupled with topoisomerase inhibition, and tubulin binding leading to disruption of mitotic progression [19].

Ferrocene-based compounds exhibit potent anticancer activity through these interconnected mechanisms. One primary pathway involves reversible redox cycling of the ferrocene unit within the cellular environment, interacting with endogenous reductants such as glutathione and NADPH to generate ROS,

CHAPTER 7

Fascinations in Biocoordination Chemistry involved in Metallodrugs and Herbomineral Formulations: Harnessing Indian and Global Biomedical Knowledge System

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Abstract: This chapter is an attempt to explore and integrate the world's oldest biomedical system and experiential knowledge *i.e.,* the Ayurvedic metallodrugs and herbomineral formulations, with modern evidence-based pharmaceutical/therapeutic sciences. It focuses on the application of coordination chemistry, chelation, and metal-mediated biosyntheses, bio-transport, and drug delivery systems. Key themes in this chapter include the relevance of Ayurvedic metallurgical techniques, biocompatible processing in coordination chemistry, design of bioinspired metal-ligand complexes, microbe-catalysed herbomineral preparations, and the development of metallodrugs with improved biodistribution/assimilation profiles. This substantiates the modules and models, now practiced as ADMET pathways, to address issues involved in Pharmacokinetics and Pharmacodynamics. The chapter discusses how Ayurvedic chelation, using herbal APIs as ligands, aligns with contemporary chelation approaches and highlights modern analytical methods; this validates the standardization and safety of these metallodrugs. Furthermore, it addresses the challenges in integrating various world therapies and practices, including Ayurvedic, with current regulatory standards, emphasizing the need for collaborations among chemists, pharmacologists, and traditional practitioners. Examining these intersections, this chapter establishes a foundation for developing next-generation metallodrugs inspired by Ayurvedic principles. The convergence of Ayurveda with modern pharmaceutical practices offers a holistic framework, providing safe, accessible, and effective therapeutic options. Issues relating to retro-pharmacology and re-purposed drugs shall also be discussed in principle. This interdisciplinary approach not only enhances drug efficacy and safety but also enriches global healthcare by bridging ancient wisdom with contemporary science, demonstrating the potential for Ayurveda-inspired metallodrugs to address complex health challenges in a scientifically robust and culturally sensitive manner.

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Keywords: Ayurvedic metallodrugs, Bhasma, Bioavailability, Chelation therapy, Metal-ligand complexes, Nano-scaled metal drugs nanoparticles, Traditional medicine integration.

INTRODUCTION

The integration of Indian Knowledge Systems (IKS), particularly Ayurveda, with contemporary scientific methods opens a promising avenue for holistic healthcare innovation. Ayurveda, a system of medicine practiced in India for over 5,000 years, emphasizes achieving equilibrium within the body and between individuals and their environment. A unique aspect of Ayurveda is its therapeutic applications; one of them is by using metals, *viz.* gold, silver, copper, zinc, and iron as bioactive agents and herbomineral chelates. Through highly specific metallurgical processes, including Bhasmikaran (calcination) and Shodhana (purification), these raw metals are transformed into finely processed and stable medicinal formulations known as bhasmas (assaimalable metal oxides), tested qualitatively as nano-scale particles, improved bioavailability, and controlled reactivity. These metallodrugs are essential in Ayurveda for addressing a range of ailments, from inflammation and infections to immune modulation and tissue regeneration [1]. Recent research highlights the value of IKS, suggesting that Ayurvedic metallurgical principles align well with modern pharmacological requirements for stability, selectivity, and bioavailability, supporting the continued relevance of these practices.

Biocoordination Chemistry: A Conceptual Framework

Biocoordination chemistry may be broadly defined as the study of coordination interactions between biologically relevant metal ions and organic or biomolecular ligands, leading to complexes that exhibit distinct physicochemical and biological properties. Within the Ayurvedic tradition, this concept is implicitly applied in bhasma and herbomineral formulations, where metals interact with phytoconstituents such as polyphenols, flavonoids, and organic acids to generate stable complexes (*e.g.*, copper–tannin, zinc–polyphenol, or iron–ascorbate chelates). These complexes are believed to enhance therapeutic efficacy, reduce toxicity, and improve assimilation into biological systems [1].

In contemporary medicine, the same principle governs the design of metallodrugs, where metal ions coordinate with biomolecular targets such as nucleic acids and proteins. A classic example is cisplatin, where platinum coordinates to DNA bases to inhibit replication, while more recent research explores ruthenium complexes interacting with transferrin or thiol-containing proteins [6]. These interactions exemplify how metal–ligand chemistry can be tuned to achieve selectivity, controlled reactivity, and therapeutic precision.

Thus, the Ayurvedic paradigm of metal–herb synergy and the pharmaceutical paradigm of metal–biomolecule interaction converge under the umbrella of biocoordination chemistry. This unified framework provides the necessary theoretical grounding for subsequent discussions, highlighting how ancient practices can inform modern coordination-based drug discovery and delivery.To bridge the gap between these two systems and provide a clear framework for this chapter, the following Table **1** offers a comparative analysis of the fundamental principles underlying both Ayurvedic and modern metallodrugs. This comparison highlights their shared reliance on biocoordination chemistry to achieve therapeutic outcomes.

Table 1. Comparative analysis of ayurvedic and modern metallodrugs.

System	Example(s)	Coordination Chemistry Aspect	Pharmacological Implication
Ayurvedic Metallodrugs (Bhasmas)	Yashad Bhasma (ZnO nanoparticles), Tamra Bhasma (Cu-based), Swarna Bhasma (Au-based)	Stabilized by **polyphenols, flavonoids, fulvic acid** (O-donor ligands); surface modification *via* repeated *Shodhana*/*Bhavana*; metal-oxide core with organic coating	Detoxification, immunomodulation, antioxidant, antidiabetic, wound healing
Modern Metallodrugs	Cisplatin ($Pt(NH_3)_2Cl_2$), Ruthenium(III) complexes, Platinum-based drugs, MOFs	Coordination with **N-donor ligands** (amines, DNA bases), **S-donor** (proteins, thiols), **O-donor** (carboxylates); designed chelation control	DNA crosslinking (anticancer), enzyme inhibition, targeted drug delivery, controlled release
Common Ground	—	Both rely on **metal-ligand interactions** to stabilize complexes and modulate reactivity	Highlight the role of **biocoordination chemistry** in bridging traditional and modern therapeutics

Relevance of Metallodrugs in Ayurveda

Human physiology and biochemistry have reported that alkali, alkaline earth, and transition metals (Inorganic constituents) have around 1-3 percent active presence as structural and functional elements. These inorganic elements contribute centrally by remaining involved in electrolytic balances, cellular and muscular osmosis, cardiovascular regulations, skeletal strength, neurological balances, *etc.* Hence, neither can be overlooked nor marginalized. In Ayurvedic medicine, the therapeutic use of metals is highly sophisticated, involving both biological and chemical transformations that optimize their efficacy and safety. Metals and minerals are purified and transformed through processes such as Shodhana, which removes impurities, and Bhasmikaran, which renders the metals into ash-like

CHAPTER 8

Rhenium Coordination Compounds as Promising Radiopharmaceuticals

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Abstract: Radiopharmaceuticals are compounds with radioactive isotopes that are used in nuclear medicine to diagnose and treat patients. Rhenium compounds have attracted considerable interest in bioinorganic chemistry, particularly for their potential applications in cancer therapy. Rhenium, a rare transition metal, is noted for its distinct oxidation states and diverse coordination chemistry, which enable the creation of a wide range of complexes. The theragnostic potential of rhenium coordination compounds stems from their capacity to be recognized with different isotopes, allowing for imaging and therapeutic uses. Due to their versatility, rhenium coordination compounds have been studied as radiopharmaceuticals for diagnostic and therapeutic applications. Rhenium-based imaging agents, notably those tagged with the radioactive isotope ^{188}Re, have shown promise in a variety of nuclear imaging techniques, including single-photon emission computed tomography and positron emission tomography. Rhenium(I) complexes are a promising family of anticancer medicines that have various advantages over traditional platinum-based treatments such as cisplatin. Their unique modes of action, enhanced potency in specific cancer cell lines, and ability to overcome drug resistance make them attractive candidates in cancer therapy. Furthermore, rhenium compounds may have a more favorable side effect profile and improved biodistribution, resulting in higher patient tolerance. Rhenium compounds have promise in the creation of targeted cancer medicines. Their distinct chemical features and modes of action provide substantial advantages over standard chemotherapeutics, particularly in terms of cancer cell selectivity and decreased side effects. Rhenium complexes' propensity to cause apoptosis and other forms of programmed cell death, together with their potential for combination therapy, makes them promising prospects in the fight against cancer.

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Keywords: Applications, Chemical properties, Nuclear medicine, Rhenium compounds, Radiopharmaceuticals, Radioisotopes, Scheme, Therapeutic agent, Theragnostic potential.

INTRODUCTION

Radiopharmaceuticals are radioactive isotope-containing substances used in nuclear medicine for diagnosis and treatment. These substances are delivered into the body and accumulate in certain organs or tissues, enabling the viewing and quantification of physiological processes. These compounds emit gamma rays that are detected by specialized cameras, producing images of their distribution throughout the body. In therapeutic applications, the radiation generated by the radiopharmaceutical is utilized to target and kill sick cells. Overall, radiopharmaceuticals serve an important role in nuclear medicine by allowing for non-invasive imaging and focused treatment of a variety of illnesses [1]. Of the various radionuclides examined, compounds containing rhenium have garnered significant interest due to their outstanding nuclear properties and possibilities for targeted delivery [2]. Isotopes of rhenium, including ^{186}Re and ^{188}Re, possess suitable half-lives, emission energies, and biodistribution properties, which render them attractive options for use in radiopharmaceuticals [2, 3]. Rhenium is capable of forming stable complexes with various ligands, encompassing both organometallic and coordination compounds. These complexes can be engineered to specifically target particular biological processes or receptors, thereby enhancing their selectivity and effectiveness against tumors. The adjustable chemical structures of rhenium compounds enable the creation of personalized radiopharmaceuticals that may improve treatment outcomes. A major advantage of rhenium coordination compounds is their adaptability for tailored clinical applications. By incorporating rhenium into different ligand systems, researchers can develop radiopharmaceuticals that possess improved targeting efficiency, enhanced pharmacokinetics, and reduced toxicity levels [4]. The range of rhenium coordination chemistry has led to the development of numerous rhenium-based radiopharmaceuticals, each possessing unique characteristics and uses. Rhenium-based radiopharmaceuticals provide several benefits compared to other radionuclides utilized in nuclear medicine [1]. The stability of the rhenium-ligand bond is essential for ensuring that the radiopharmaceutical stays in the body until it arrives at the target area. For instance, adjusting temperature and pH can optimize labeling yield, as seen in the synthesis of ^{186}Re-DTPA complexes, which necessitate specific conditions for effective binding. Rhenium complexes are also being explored for their potential in medicinal uses, particularly in targeted radiotherapy. The beta particles from rhenium isotopes can effectively irradiate tumors, providing a focused therapeutic option while minimizing harm to surrounding healthy tissues. The ability to focus on specific cells with rhenium-

labeled antibodies enhances the treatment's efficacy [5]. Rhenium compounds can be attached to targeting agents like antibodies or peptides, enabling them to specifically attach to cancerous cells. This customized approach facilitates direct radiation delivery to the tumor while reducing harm to surrounding healthy tissues. The use of bifunctional ligands simplifies the connection of rhenium to these targeted therapies, enhancing the specificity of the treatment [5]. Rhenium compounds can be combined with technetium to create dual-imaging probes. These probes utilize the high sensitivity of nuclear imaging techniques, like SPECT, provided by technetium, alongside the photoluminescent properties of rhenium, enhancing imaging capabilities. For instance, Re-Tc conjugates have been engineered to merge the benefits of both imaging techniques, delivering better spatial resolution and sensitivity.

By allowing focused radiation delivery straight to the tumor, ^{188}Re–HDD-lipiodol reduces the dose to surrounding healthy tissues. This focused approach can improve therapeutic efficacy while minimizing potential adverse effects [6], (Fig. **1**). ^{188}Re-HEDP (Fig. **5**), also known as ^{188}Re-mecasulfate (1-hydroxyethyliden--1,1-diphosphonic acid), is predominantly used as a radiopharmaceutical to treat bone discomfort caused by metastatic cancer (Fig. **1**) [7].

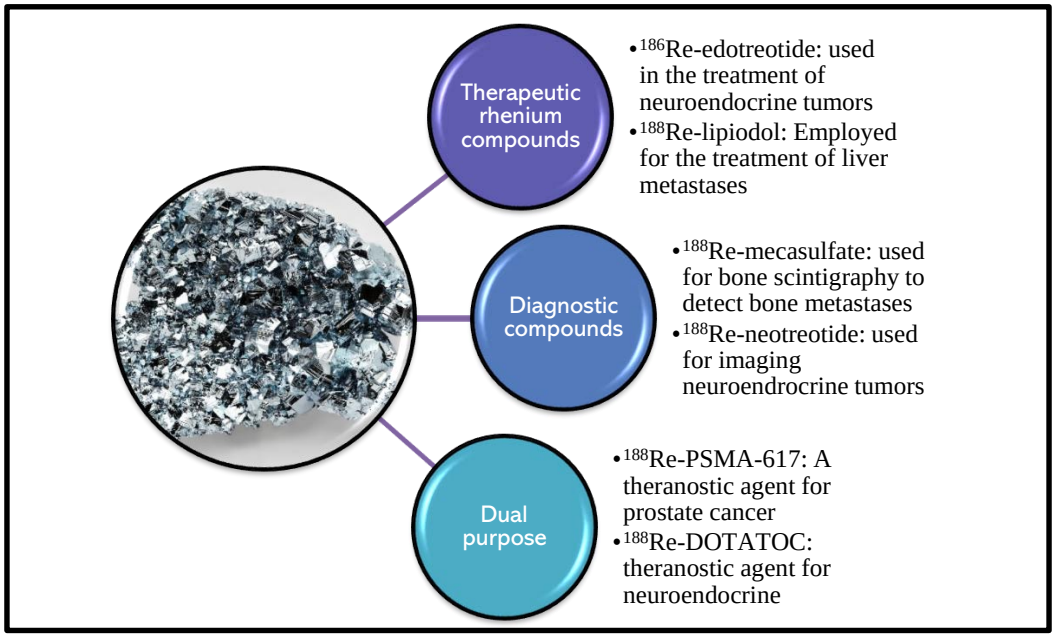

Fig. (1). Different types of rhenium compounds used in radiopharmaceutics.

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Abhay Nanda Srivastva

Dr. Abhay Nanda Srivastva has been appointed as Assistant Professor in the University Department of Chemistry at Babasaheb Bhim Rao Ambedkar Bihar University since 2017. Along with this, Dr. Srivastva has also been entrusted with additional academic and research activities as Head of the Chemistry Department at Nitishwar College (a constituent unit of B.R.A. Bihar University), Muzaffarpur, India. Before joining here, he served as Assistant Professor of Chemistry at a reputed engineering college in Delhi-NCR affiliated with Dr. A.P.J. Abdul Kalam Technical University. He obtained his Master's and Doctorate degrees in Chemistry from C.C.S. University.

His area of interest is the design of metal-based medicinal materials by adopting the approaches of coordination chemistry, nanomaterial chemistry, and green chemistry. Dr. Srivastva is supervising Ph.D. scholars in the area of his research interest. He is leading research work as the mentor of his research laboratory, 'Laboratory of Bioactive Material Synthesis (LBMS-India),' under different projects to foster budding chemists at the undergraduate and postgraduate levels. He has authored many research papers, edited books, authored books for P.G. students, and contributed chapters to publications by reputed international and national journal and book publishers. Dr. Srivastva is actively involved in academic and research activities through reviewing articles, delivering invited talks and lectures, and presenting research papers at national and international conferences, seminars, webinars, and workshops.