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METAL COMPLEXES IN DRUG DESIGN

Mr.Kale D.V.
Dept. of Chemistry,
Shrimant Babasaheb Deshmukh
Mahavidyalay, Atpadi, Sangli (MS)

Dr. Rathod S. D.
Dept. of Chemistry
Milind College of Science,
Aurangabad (MS)

ABSTRACT

A significant growing interest in the design of metallic compounds as drugs and diagnostic agents is currently observed in a field of scientific investigation, appropriately referred to as medicinal inorganic chemistry. Investigations in this area have mostly focused on the speciation of metal species in biological media based on the possible interactions of these metal ions with various biomolecules, in an effort to contribute to the future development of new therapeutic or diagnostic agents. Metallopharmaceuticals used as anticancer agents, metal-mediated antibiotics, antibacterial, antiviral, antiparasitics, antiarthritics, antidiabetic and radio-sensitizing agents appear in therapeutic medicinal inorganic chemistry. Medicinal uses and applications of metals and metal complexes are of increasing clinical and commercial importance.

INTRODUCTION

Many metallic elements play important roles in living systems. One characteristic of metals is that they readily lose electrons to form positively charged ions that are soluble in biological fluids. Metals in this cationic form play their part in biology. Metal ions are electron deficient, whereas most biological molecules such as proteins and DNA are electron rich. The attraction of these opposing charges leads to a general tendency for metal ions to associate and interact with organic molecules. This same principle applies to the affinity of metal ions for many small molecules and ions vital to life, such as oxygen. Given this wide scope for the interactions of metals in biology, it is not surprising that natural evolution has led to the induction of many metals into essential biological functions.

Metals perform a variety of functions such as carrying oxygen throughout the body and locking electrons. Hemoglobin, an iron-rich protein that binds to oxygen, carries this important molecule to the body's tissues. Metal ions such as Zn 2 provide the structural framework for the regulation of gene function in the cell's nucleus. Similarly, calcium-rich minerals are the basis of bones, the structural framework of the human body. Zinc is a natural component of insulin, a substance important for the regulation of sugar metabolism. Metals such as copper,

zinc, iron and manganese are incorporated into catalytic proteins, metalloenzymes, which facilitate a multitude of chemical reactions necessary for life. Metal complexes are already in clinical use, and encourage further study for new metallodrugs such as metal-mediated antibiotics, antibacterials, antivirals, antiparasitics, radio-sensitizing agents and anticancer compounds. However, their mechanisms of action are often unknown. Recently, more than a thousand potential anticancer metal compounds from the National Cancer Institute (NCI) tumor-screening database were analyzed based on putative mechanisms of action and classified into four broad classes, those with sulfhydryl groups. According to their preference, to force was chelation. , generation of reactive oxygen species and production of lipophilic ions. Several potential antitumor agents have been investigated based on their anti-angiogenesis or pro-apoptotic behavior. These studies include both designed and natural products in association with essential metal ions such as copper, or iron. Because metal ions play such a broad role in biological systems, the following questions arise: Can metal ions be incorporated into drugs? Are coordination compounds potential pharmacological agents? Would metal coordinates be useful?

THE METAL COMPLEX – AN EMERGING TOOL IN DRUG DISCOVERY

Transition metals play an important role in medicinal biochemistry. Research has shown significant advances in the use of transition metal complexes as drugs to treat many human diseases such as carcinomas, lymphoma, infection control, diabetes, anti-inflammatory and neurological disorders. Transition metals exhibit different oxidation states and can interact with many negatively charged molecules. This activity of transition metals has triggered the development of metal-based drugs with promising pharmacological application and may provide unique therapeutic opportunities. To provide an update on recent advances in the medicinal use of transition metals, a Medline search was performed to identify recent relevant literature. Transition metals represent the 'd' block elements, which are included in Groups III - XII of the periodic table. Their 'D' shells are in the process of filling. This property of transition metals is the foundation of coordination complexes. A metal complex or a coordination compound consists of a central metal atom, which is bound to a surrounding array of molecules or ions. Sophus Jorgensen in Denmark synthesized metal compounds for the first time in the mid-1870s. In 1893, a major breakthrough in this area came when Alfred Werner investigated a range of compounds, including cobalt, chlorine, and ammonia. For his work he was awarded the Nobel Prize in 1913.

METAL COMPLEXES IN CANCER THERAPY

As cancer remains a major killer in the developed world, a broad spectrum of novel and exciting approaches are being developed and tested. The importance of metal compounds in medicine is undeniable, as can be judged by the use of many metal-based compounds in the treatment of various diseases. In terms of anti-tumor activity, a wide range of compounds of both transition metal and main group elements have been investigated for efficacy. The existence of a connection between cancer and metals has been widely accepted by researchers. Therefore, "Metal-containing drugs and novel coordination complexes in therapeutic anticancer applications of anti-cancer agents in medicinal chemistry" aims to present an updated overview of this topic and to cover recent developments in the field. of metal-based anticancer agents. Significant progress has been achieved in metal-based agents. Nevertheless, there is an urgent need for new drugs to treat cancer or to develop drugs with new mechanisms of action. It appears that metal complexes provide a rich platform for the design of new anti-cancer drugs. The metal, its oxidation state, the number and type of coordinate ligands, and the coordination geometry of the complexes can confer a variety of properties. On the other hand, ligands not only control metal reactivity but also play an important role in determining the nature of interactions involved in the recognition of biological target sites such as DNA, enzymes and protein receptors. These variables offer immense potential diversity for the design of metallodrugs. They also introduce several challenges in the synthesis of such derivatives. Changes in the structure of the heterocycle are likely to be accompanied by changes in the associated biological activity. Therefore, it is important to identify the nature of the metal complex, which is present in the biological medium and is undergoing biological testing, and ideally the species that reach the target site.

The compounds described in Figure 1 are used to treat tumor metastasis and hepato-cellular and nasopharyngeal carcinoma. For thousands of years, metal complexes have played important and diverse roles in medicine. From the antiseptic properties of copper complexes, to the long-term use of gold complexes in Chinese and Arabic medicine, the metals' unique and useful therapeutic benefits have long been recognized and used. The therapeutic application of metal complexes in modern medicine arguably began with the discovery of the anticancer properties of cisplatin. In addition to the continued clinical use of cisplatin against specific types of cancer, this discovery also inspired a new generation of effective, and in some cases selective, metal-based cancer therapeutics, thereby providing alternatives to the classical drug. demonstrated the potential of metal complexes as Molecular inhibitors of human disease.

METAL COMPLEXES IN DIABETES MEDICINE

Diabetes mellitus (DM), which develops a number of secondary complications such as atherosclerosis, microangiopathy, renal dysfunction and failure, cardiac abnormalities, diabetic retinopathy and ocular disorders, can be classified as insulin-dependent type 1 or non-insulin-dependent type 2 classified as WHO. Although a variety of insulin preparations for type 1 DM and synthetic drugs for type 2 DM have been developed and used clinically, they have several problems such as physical and medical problems due to defects associated with daily insulin injections and side effects. Mental pain. In the 21st century, a new class of pharmaceuticals must be introduced as many drugs are going out of patent. For this reason, metallopharmaceuticals containing vanadium and zinc ions are expected to treat both types of DM, making effective use of the unique characteristics of the metals. The current status of the development of insulin-mimetic vanadium and zinc complexes with different coordination modes is reviewed, with a focus on the preparation and structures of the complex and in vitro and in vivo evaluation as well as possible mechanisms. For this reason, many vanadium compounds are being developed for pharmaceutical use to treat or improve both types of DM. In addition to the therapeutic effect of vanadium ion (VA) and vanadium complexes, these vanadium compounds have a preventive effect on the onset of streptozocin STZ-induced diabetes in the context of nitric oxide released from macrophages. Thus, vanadium is expected not only to treat DM but also to prevent DM. In addition to vanadium complexes, zinc complexes have been proposed to be new candidates in the treatment of type 2 DM. Designing new vanadium complexes requires stereochemical considerations for how to bind complexes with receptors such as the glucose transporter and other enzymes, as well as consideration of vanadium's redox properties. Designing new zinc complexes, on the other hand, requires attention to stability and structural properties under physiological conditions. Designing new zinc complexes, on the other hand, requires attention to stability and structural properties under physiological conditions. Zinc and vanadium metal ions were tested for their anti-diabetic activity.

METAL COMPLEXES IN ANTIBIOTICS

Although most antibiotics do not require metal ions for their biological activities, there are many antibiotics such as bleomycin (BLM), streptonegrin (SN) and bacitracin that require metal ions to function properly. The metal ions coordinated in these antibiotics play an important role in maintaining the proper structure and/or function of these antibiotics. Removal of metal ions from these antibiotics may alter the structure and/or function of these antibiotics.

Similar to the case of metalloproteinases, these antibiotics are called "metalloantibiotics". Metalloantibiotics can interact with many different types of biomolecules, including DNA, RNA, proteins, receptors, and lipids that give them unique and distinct bioactivity. In addition to microbial-derived metalloantibiotics, many metalloantibiotic derivatives and metal complexes of synthetic ligands also show antibacterial, antiviral, and antineoplastic activities, which are also briefly discussed to provide a comprehensive understanding of the term "metalloantibiotics".

EXAMPLES OF METALLOANTIBOITICS

1) Bleomycin

Bleomycin (BLM, also known as blenoxane) was first isolated as a Cu-containing glycooligopeptide antibiotic from the culture medium of Streptomyces verticulus and later found to be an antiviral agent as well. It was soon discovered as an anticancer agent and has since become one of the most widely used anticancer drugs, most commonly used to treat testicular cancer, lymphoma, and head and neck cancer, as well. Used in the treatment of AIDS-related Kaposi's sarcoma. In combination with cisplatin and adriamycin.

2) Antibacterial study of cephradine metal complexes

Cephradine showed antimicrobial activity against various human pathogens. However cephradine had much more potent activity and created larger areas for Escherichia coli, Corynebacterium hoffmannii, Streptococcus faecalis, Corynebacterium diphtheria and Proteus vulgaris than for Salmonella typhi. Like the above complexes, the cephradine zinc complex also reduced the activity of microorganisms. Corynebacterium diptheriae, Streptococcus faecalis, Proteus vulgaris and Klebsiella pneumoniae were mildly susceptible. Moderately susceptible were Salmonella typhi, Streptococcus pyogenes, Staphylococcus aureus and Escherichia coli. Klebsiella pneumoniae, Escherichia coli, Corynebacterium hoffmannii and Staphylococcus aureus showed smaller sphere sizes than in the case of the Cephradine cadmium complex. Salmonella typhi, Corynebacterium diphtheriae, Streptococcus pyogenes, Proteus vulgaris and Streptococcus faecalis showed moderate sensitivity.

METAL COMPLEXES IN GENE THERAPY

An experiment on 'Biodegradable Polymer-Metal Complexes for Gene and Drug Delivery' has introduced some of the recent developments in the enhancement of non-viral gene expression. It is anticipated that this field will continue to grow and expand to address issues related to non-viral methods of gene delivery. While improvements in transfection efficiency have been made and research is geared toward understanding the underlying mechanisms of many gene

delivery vehicles, issues of toxicity, transfection efficiency and host response still remain problems for some gene delivery applications. There are a number of issues that still need to be resolved regarding the application of non-viral gene delivery vehicles for human treatment. However, the polymer-metal complex efficacy in increasing the in vitro and in vivo levels of gene expression suggests that it is a promising method. Further research on gene expression using metal-bound polymeric materials would certainly seem worthwhile.

TRANSITION METAL COMPLEXES AS ANTI-INFLAMMATORY AGENTS AND FREE RADICAL QUENCHERS

Transition metals have also been used as anti-inflammatory and anti-arthritic agents. Several injectable Transition Gold complexes such as sodium orothiomalt, orothioglucose, and sodium orothiopropanol are used clinically in the treatment of severe cases of rheumatoid arthritis. Gold and silver nanoparticles conjugated with a heparin derivative have antiangiogenesis properties. Silver nanoparticles are used in the development of an antimicrobial gel formulation for topical use. Gold has been used in the treatment of peripheral psoriatic arthropathy. As a product of oxygen metabolism, superoxide anion can trigger oxidative injury to tissues. This activity has been suggested to be associated with riper fusion and inflammatory diseases, as well as neurological disorders such as Parkinson's disease and Alzheimer's disease.

CONCLUSION

With advances in medicinal chemistry, the role of transition metal complexes as therapeutic compounds is becoming increasingly important. Recent advances in medicinal chemistry have made it possible to form a number of transition metal complexes with organic ligands of interest, which can be used as therapeutic agents. Significant progress has been made in the synthesis of platinum-based anticancer drugs such as cisplatin. These drugs have proven to be highly effective chemotherapeutic agents for the treatment of various types of cancer. The use of transition metal complexes as therapeutic compounds has become more and more evident. These complexes offer a great variety in their action; Not only do they have anti-cancer properties, but they are also used as anti-inflammatory, anti-infection and anti-diabetic compounds. The development of transition metal complexes as drugs is not an easy task; Getting compound interest requires a lot of effort. In addition to all these limitations and side effects, transition metal complexes are still the most widely used chemotherapeutic agents and make a major contribution to pharmacological therapeutics in a way that was unimaginable a few decades ago.

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