

Application of coordination compound in medicines biology essay



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The three series of element arising from the filling of the 3d, 4d and 5d shells, and situated in the periodic table following the alkaline earth metal, are commonly described as "transition elements", through this term is sometimes also extended to include the lanthanide and actinide (or inner transition) elements. They exhibit a number of characteristic properties which together distinguish them from other groups of elements:

(1)- they are all metals and as such are lustrous and deformable and which have high electrical and thermal conductivities. In addition, their melting and boiling points tend to be high and they are generally hard and strong.

(2)- most of them display numerous oxidation states which vary by steps of 1 rather than 2 as is usually the case with those main-group elements which exhibit more than one oxidation state.

(3)- they have an unparalleled propensity for forming coordination compounds with Lewis bases.

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Coordination compound

Transition metals readily react with halogens to form binary compounds of various colors, for example: green-black ferric chloride (FeCl_3), deep blue cobalt chloride (CoCl_2), and golden yellow nickel bromide (NiBr_2). These compounds dissolve in water to give brightly colored solutions-but of changed colors: yellow solutions (containing Fe^{3+} ions), red solutions (Co^{2+} ions), and green solutions (Ni^{2+} ions). By evaporating the solutions, crystals of these new compounds can be obtained: yellow $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$, red $\text{CoCl}_2 \cdot 6\text{H}_2\text{O}$, and green $\text{NiBr}_2 \cdot 6\text{H}_2\text{O}$. Addition of ammonia to a green nickel solution changes its color to violet, and the compound $\text{NiBr}_2 \cdot 6\text{NH}_3$ can be crystallized. In all cases these beautiful color changes occur because a new chemical species has formed, and there have been changes in the bonding of the nonmetallic substance to the metal ion. Probably the best-known

example of vivid color change is the dissolving of anhydrous white cupric sulfate (CuSO_4) in water to give a blue solution, containing $[\text{Cu}(\text{H}_2\text{O})_4]^{2+}$. Addition of ammonia yields the deep blue $[\text{Cu}(\text{NH}_3)_4]^{2+}$, which forms crystals that have the formula $[\text{Cu}(\text{NH}_3)_4]\text{SO}_4 \cdot \text{H}_2\text{O}$.

The neutral molecules NH_3 and H_2O bond directly to a metal atom by donating a lone pair of electrons to any empty orbital on the metal atom. Anions as well as neutral molecules can bond to a metal atom in this way. These neutral molecules or anions that bond to the metal are called ligands. Further examples of ligands are: Br^- , NO_2^- , CO , pyridine, $\text{P}(\text{CH}_3)_3$, and $\text{O}=\text{As}(\text{C}_2\text{H}_5)_3$. Some ligands can donate two pairs of electrons and are termed bidentate, for example, $\text{H}_2\text{N}-\text{CH}_2-\text{CH}_2-\text{NH}_2$ (ethylenediamine or en), and $\text{O}_2\text{C}-\text{CO}_2^-$ (oxalate anion or ox).

A coordination compound (or coordination complex) consists of a metal cation or neutral atom to which neutral or negatively charged ligands have bonded. The number of ligand atoms to which the metal center is directly bonded is the metal cation's coordination number (c. n.), and this number is always greater than the regular valence or oxidation number (o. n.) of the metal. The coordination complex can be negatively charged, for example, $[\text{AuCl}_4]^-$, $[\text{PtCl}_6]^{2-}$, $[\text{Co}(\text{NO}_2)_6]^{3-}$, and $[\text{Fe}(\text{CN})_6]^{3-}$; neutral, for example, $[\text{Fe}(\text{CO})_5]$, $[\text{Ni}(\text{PF}_3)_4]$, and $[\text{Rh}(\text{NH}_3)_3\text{Cl}_3]$; or positively charged, for example, $[\text{Cu}(\text{NH}_3)_4]^{2+}$, $[\text{Mn}(\text{H}_2\text{O})_6]^{2+}$, and $[\text{Pt}(\text{NH}_3)_5\text{Cl}]^{3+}$. TiCl_4 and UF_6 are neutral molecules (in which o. n. = c. n.), they are not coordination compounds; whereas $[\text{AlCl}_4]^-$ and $[\text{FeF}_6]^{3-}$ are coordination complexes in which the coordination number exceeds the oxidation number. The

chromate anion, CrO_4^{2-} , is not a coordination complex; the o. n. of the Cr atom is 6, but only four O atoms are bonded to it.

Application of coordination compounds

Coordination compounds are found in living systems and have many uses in the home, in industry, and medicine. We describe a few examples here and in the chemistry.

Coordination compounds play many roles in the animals and plants. They are essential in the storage and transport of oxygen, as electron transfer agents, as catalysts, and in photosynthesis. Here we focus on coordination compounds containing iron and magnesium.

Because of its central function as an oxygen carrier for metabolic processes, hemoglobin is probably the most studied of all the proteins. The molecule contains four folded long chains called subunits. Hemoglobin carries oxygen in the blood from the lungs to the tissues, where it delivers the oxygen molecules to myoglobin. Myoglobin, which is made up of only one subunit, stores oxygen for metabolic processes in muscle.

The porphine molecule forms an important part of the hemoglobin structure. Upon coordination to a metal, the H^+ ions that are bonded to two of the four nitrogen atoms in porphine are displaced. Complexes derived

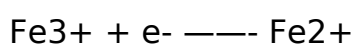
porphine

Simplified structure of the porphine molecule and the Fe^{2+} -porphyrin complex. The dashed lines represent coordinate covalent bonds.

From porphine are called porphyrins, and the iron-porphyrin combination is called the heme group. The iron in the heme group has an oxidation number +2, it is coordinated to the four nitrogen atoms in the porphine group and also to a nitrogen donor atom in a ligand that is attached to protein. The sixth ligand is a water molecule, which binds to the Fe^{2+} ion on the other side of the ring to complete the octahedral complex. This hemoglobin molecule is called deoxyhemoglobin and imparts a bluish tinge to venous blood. The water ligand can be replaced readily by molecular oxygen to form red oxyhemoglobin found in arterial blood. Each subunit contains a heme group, so each hemoglobin molecule can bind up to four O_2 molecules.

There are three possible structures for oxyhemoglobin. For a number of years, the exact arrangement of the oxygen molecule relative to the porphyrin group was not clear. Most experimental evidence suggests that the bond between O and Fe is bent relative to the heme group.

The porphyrin group is a very effective chelating agent, and not surprisingly, we find it in a number of biological systems. The iron-heme complex is present in another class of proteins, called the cytochromes. The iron forms an octahedral complex in these proteins, but because both the histidine and the methionine groups are firmly bound to the metal ion, they cannot be displaced by oxygen or other ligands, instead, the cytochromes act as electron carriers, which are essential to metabolic processes. In cytochromes, iron undergoes rapid reversible redox reaction:



Platinum Compounds in Clinical Trials

The need for new agents in cancer chemotherapy is apparent from the inability to predictably cure or induce remissions in common tumors such as breast, lung, colon, or prostate cancer. New

cytotoxic agents building on our experience and knowledge of the current armamentarium continue to play an important role in the clinical management of cancer. Approximately 28 direct structural analogs of cisplatin entered clinical trials but most have been abandoned through a combination of unacceptable toxicity profile and/or lack of improved or expanded anticancer

efficacy. 38 For new, direct structural analogs of cisplatin to find clinical use exceptional properties would need to be found. 38 Currently, there are three principal drugs ((6)-(8); Figure 7) in clinical trials-the approaches to their development represent examples of steric control of reactivity, control of oxidation state and ligand lipophilicity aimed at producing orally active agents, and manipulation of new structures to produce structurally new DNA adducts.

Nitric Oxide in Physiology and Medicine

An intriguing aspect of the role of metal complexes in medicine is the role of NO. 272, 273 The

nitroprusside ion, $[\text{Fe}(\text{NO})(\text{CN})_5]^{2-}$ is a vasodilator used in emergency situations to treat hypertensive patients in operating theaters. 274, 275 The complex is 30-100 times more potent than simple nitrites. The mechanism is

considered to be release of NO, an understanding prompted by the emergence of NO as a prominent cell signaling molecule. 273 Related to the biology of NO is production of peroxynitrite ONOO₂ through reaction of NO with O₂

_. In this regard, production of peroxynitrite may play a role in many pathological conditions. 276, 277 Water-soluble porphyrins and texaphyrins may catalytically react with ONOO₂ and may have clinical utility in peroxynitrite scavenging.

Lanthanum Carbonate

Patients with end-stage renal disease hyperphosphatemia ineffectively filter excess phosphate that enters the body in the normal diet. 278 Elevated phosphate produces the bone disorder renal

osteodystrophy. Skeletal deformity may occur, possibly associated with cardiovascular disease. Calcium deposits may further build up around the body and in blood vessels creating further

health risks. The use of lanthanum carbonate is being promoted as an alternative to aluminum-based therapies. 279, 280 Systemic absorption, and cost have produced a clinical candidate, Fosrenol (AnorMED), an intriguing use of a lanthanide compound in therapy.

Metals in medicine and in food. Synthetic coordination compounds with active drugs as ligands and innovative strategies for their delivery in the tissues

The synthesis of platinum group metal complexes with pyrimidine and purine derivatives, and non-steroidal anti-inflammatory drugs (NSAIDs) as ligands has acquired new impetus in the past decade. This fact happened because several reasons, some of which are the following. First, on the basis of pure co-ordination chemistry pyrimidines and purines, and NSAIDs are very versatile ligands and show an huge variety of ligating modes as function of the metal and the environmental conditions. Much has to be learnt on this matter even though a big amount of experimental and theoretical work has already been done [1]. The information collected from the preparative, structural and reactivity studies have high significance for several fields which span from the bio-sciences to the material sciences. Second, pyrimidines and purines, often called nucleobase derivatives (to stress their importance in the life of the cell), and NSAIDs have numerous applications as pharmaceutical agents. Third, for this type of drugs the complex formation with specific metals may improve the activity towards certain diseases and hopefully may increase the activity spectrum [1]. The combination of two or more different molecules into the same compound may bring to a multi-therapeutic agent which can be expanded by the synergic action of the metal residue (especially for platinum group metals) once the co-ordination compound dissociate inside the target tissue. Fourth, it has recently been suggested that photo-activation of DNA thiobases, may offer a novel approach for the treatment of nonmalignant diseases like psoriasis or of superficial tumours that are accessible via phototherapy

[2]. Rhodium- and Ruthenium-complexes with thiobases and NSAIDs are not much investigated by the community of inorganic and co-ordination chemists, at least as it is revealed by the small number of structures deposited at the Cambridge Structural Database (CSD) (Release November 2005, ca. twenty structures). On continuing our project on co-ordination chemistry of platinum group metal complexes with active drugs as ligands, we recently performed the synthesis and characterization of some new compounds. The highlights of this research together with a brief analysis of the works by other will be presented to the Emory students.

Coordination Compounds for Medicine and Biology

The interaction of transition metal ions with biological molecules provides one of the most fascinating areas of coordination chemistry. The application of this field to biomedical uses is dealt with in 5 chapters. Chapter 18 by N. Farrell, deals with the use of metal complexes as drugs and chemotherapeutic agents. Farrell concentrates on Pt anticancer drugs and, in particular, the differing interactions of mono-, di- and trinuclear complexes with DNA and the differing antitumour effects this may produce. Chapter 19, by É. Tóth, L. Helm and A. E. Merbach, describes the application of transition metal ions and in particular and in medicinal and biomedical applications. It is an informative read and the individual chapters offer good introductions to the various areas.

Chelating Ligands

A very special application of coordination compounds occurs in what is called the chelate effect. Chelation takes place when ligands “bite” or “bee sting”

the metal in more than one place at a time. Using dental “biting”
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terminology, if a ligand has two “teeth” to bite a transition metal, it is called a bidentate (two teeth) ligand. One example of this is called ethylenediamine, $\text{NH}_2\text{CH}_2\text{CH}_2\text{NH}_2$. Figure 5 shows simultaneous donation of two electrons each from the two nitrogen atoms of ethylenediamine. A five membered ring is produced involving the metal, two nitrogen atoms, and two carbon atoms.

A hexadentate ligand such as ethylenediamine tetraacetic acid, EDTA, bites a metal cation in six places simultaneously by wrapping itself around the cation (Figure 6). This produces an extremely strong chelated compound. Using EDTA, such ions as calcium, Ca^{2+} , can be extracted from and tested in drinking water.

Chelated transition metal ions are also found in a wide variety of biochemical situations. A basic structural unit called metalloporphyrin is shown in Figure 7. It can be thought of as several ethylenediamine-like units fused and blended together into a single tetradentate (4 teeth) chelating ligand. Changing the central metal, M, changes the biochemical activity of the chelated coordination compound.

Bioinorganic Systems

Coordination compounds play important roles in nature. Chlorophyll, which is involved in photosynthesis in plants, is a coordination complex of magnesium. Hemoglobin, the oxygen transporter in the human body, is a coordination complex of iron. Vitamin B₁₂, necessary for the prevention and cure of pernicious anemia, is a coordination complex of cobalt. In all three compounds, the metal ion is in an approximately octahedral environment, its

coordination number is 6, and bonded to it are the four nitrogen atoms of a planar porphyrin-like ring. The basic planar ring structure is closely related to that of the extremely stable blue pigment, Cu(II)phthalocyanine.

All metals will form coordination compounds. The stability of a coordination compound depends on the nature of the ligands and the atomic number and oxidation state of the metal.

Metal-Containing Proteins, Macrocycles, and Coordination Complexes in Therapeutic Applications and Disease

Treatment of diseases with natural and synthetic materials has been an aspiration of mankind since the dawn of human development. From the use of willow-bark to the marketing of aspirin, a steady move from folk remedies to the use of chemistry and biology to develop new therapies has been observed. In terms of metal-containing drugs, the platinum-containing drug cisplatin has long been the most effective metal-containing anticancer drug on the market.

However, severe side effects of conventional drugs are associated with the inability to distinguish between healthy and cancer cells. Hence, a concerted world-wide effort is in progress to discover and characterise new drugs that may distinguish between healthy and cancer or other diseased cells. New techniques of drug delivery are sought and the use of natural products, proteins, antibodies, and synthetic polymers as drug delivery devices capable of targeting a diseased site is being investigated.

These issues are nicely illustrated by macrocycles such as porphyrins, phthalocyanines, and related systems. Some of these compounds exhibit <https://assignbuster.com/application-of-coordination-compound-in-medicines-biology-essay/>

selective absorption by cancer cells and have the ability to photosensitize formation of singlet oxygen. These attributes have led to the development of alternative cancer treatments known as photodynamic therapy. Sadly, many potentially good new therapeutic agents often never leave the designers' laboratory due to some pharmacological problems associated with its in vivo use. The use of drug delivering devices, including water-soluble synthetic polymeric drug delivery systems, may help overcome many pharmacological drug-related problems, including those of solubility, specificity, and biocompatibility, factors that currently prevent many potentially good therapeutic agents from reaching clinics.

The focus of this special issue is the synthesis, characterisation, physical studies, and application of synthetic metal-containing complexes and natural occurring proteins in serious human diseases such as cancer, diabetes, arthritis, viral disease, malaria, and tuberculosis with special focus on the following:

porphyrins, phthalocyanines, and related complexes in photodynamic cancer therapy;

proteins, enzymes, and synthetic polymeric drug delivery systems in the treatment of cancer and other diseases;

coordination and organometallic compounds in cancer, arthritis, malaria, and viral disease.

Towards these goals, L. Josefsen and R. Boyle describe in their review article the development and application of metal-based photosensitisers, including

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porphyrins and phthalocyanines, in photodynamic therapy. Four other publications highlight different aspects of porphyrin-based macrocyclic photosensitisers. S. Lee et al. focus on the cellular uptake and toxicity of thiotetra (ethylene glycol) monomethyl ether-functionalized porphyrazines. J.-Y. Liu et al. focus on in vitro photodynamic activity of novel amphiphilic zinc(II) phthalocyanines bearing oxyethylene-rich substituents. E. Antunes and T. Nyokong highlight the syntheses and photophysical properties of tetraazatetrabenzcorrole photosensitizers. Sakamoto et al. present a fundamental study of zinc bis(1, 4-didecylbenzo)-bis(2, 3-pyrido)porphyrine for application in photodynamic therapy of cancer.

Considering polymeric drug delivery systems, South African E. Neuse's excellent review describes the use of synthetic polymers as metal-containing drug delivery vehicles in medicine. M. David Maree et al. provided a fine treatise on why biocompatible synthetic polymeric drug delivery systems are becoming increasingly popular as drug delivering devices. They also demonstrate the principles behind these systems in a practical study utilising ferrocene and phthalocyanine derivatives anchored on a water-soluble polymeric drug carrier derived from lysine and aspartic acid. Italians Longo and Vasapollo demonstrated the use of phthalocyanine-based molecularly imprinted polymers as nucleoside receptors. X. Sun et al. report on the identification of proteins related to nickel homeostasis in *Helicobacter pylori* by immobilized metal affinity chromatography and two-dimensional gel electrophoresis. P. Nagababu reported DNA-binding and photocleavage studies of cobalt (III) ethylenediamine pyridine complexes.

Metal based drugs

Metal-Based Drugs publishes research on all aspects concerning the interaction of metals with diseases such as cancer, infection, inflammation, and with cardiovascular, CNS and metabolic diseases. The journal accepts papers on the synthesis and characterization, on preclinical activity, from the fate in living organisms to their mechanisms of action including the physiological effects and toxicity, and on clinical therapeutics of chemical structures based on metals and useful for the therapy or for the diagnosis of human diseases. Metal-Based Drugs is a multidisciplinary and authoritative reference on the role and on the use of metals in medicine. Metal-Based Drugs puts emphasis on all the metals and on metal compounds characterized and synthesized to fit with the modern aspects of molecular diagnosis and disease control, particularly on nanotechnologies and on the control of genes and of gene expressions. Metal-Based Drugs will also stimulate structure-activity relationships studies of cellular and molecular targeting of metal compounds.

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