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An Overview of Transition Metal Complexes Used in Pharmaceuticals and Personal Care Products

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ABSTRACT

New metal-based pharmaceuticals and specific cosmetic formulations owe much to inorganic chemicals, particularly transition metals. The role of inorganic chemistry in the delivery of medications and cosmetics is briefly discussed, along with the use of these metal complexes in the pharmaceutical, microbiological, and cosmetic industries.

Keyword: Pharmaceuticals and cosmetics containing metal complexes are of interest.

INTRODUCTION

Complexes of transition metals can be cationic, neutral, or anionic species, depending on the nature of the ligands that coordinate the metal. (Cox, 2005). Many transition metal complexes have shown promise as potential medications for treating various human ailments. As a result of their multiple oxidation states, transition metals can form bonds with a wide variety of anionic compounds.

Transition metal activity has started the creation of metal-based pharmaceuticals that show promise in pharmacological applications and could provide novel treatment options (Rafique et al., 2010).

Opportunities for using metal complexes as medicinal agents have improved due to developments in inorganic chemistry. Metal complexes affect living things in a way that nonmetals do not. The range of behaviors displayed by these complexes is impressive.

A group of researchers led by Hariprasath (2010) found. New medications can be developed using the unique features of metal ions, which can be accessed through medicinal inorganic chemistry. This has resulted, for example, in the clinical use of chemotherapeutic drugs like cisplatin in cancer treatment. (Pieter et al., 2008) Transition metal complexes have emerged as increasingly critical medicinal molecules.

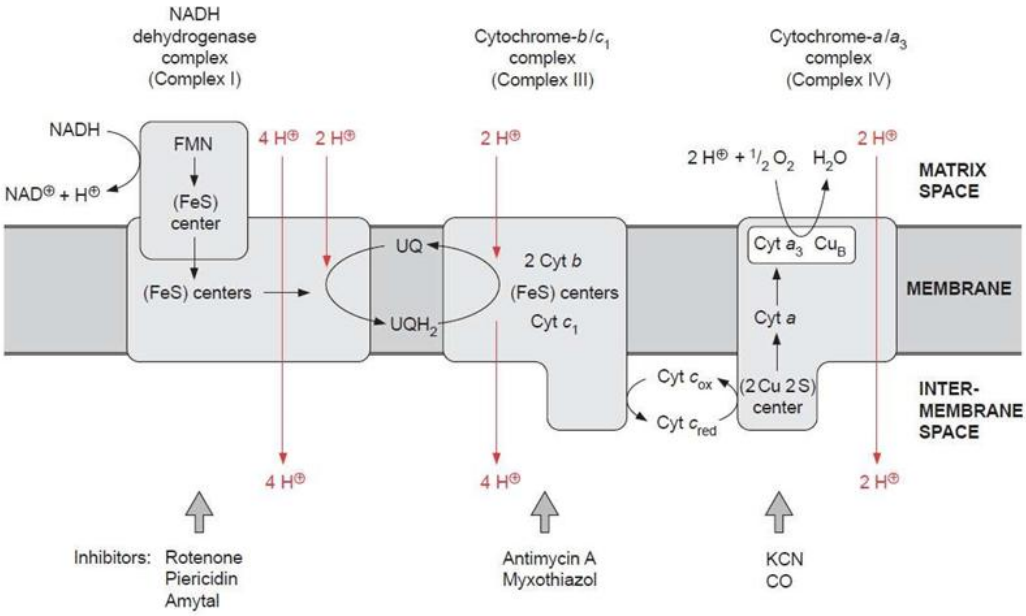
These complexes have been employed as anticancer, anti-inflammatory, anti-infectious, and anti-diabetic drugs, among other potential applications. Creating a compound of interest when using transition metal complexes as medicines take time and effort.

Despite their drawbacks, transition metal complexes dominate the chemotherapeutic market and make substantial contributions to medical treatments that were unthinkable just a few years ago. (Rafique et al., 2010). Catalysis, materials production, photochemistry, and biological systems benefit significantly from transition metal complexes.

The chemical, optical, and magnetic features they exhibit are all unique. The purpose of this article is to offer an analytical summary of the current advancement in the use of transition metal complexes in the production of pharmaceuticals and personal care products.

Antibiotics Can Prevent Metal Complexes from Forming.
Antibiotics are chemicals that prevent bacterial and fungal growth and reproduction, even at low doses. A vast range of infectious diseases can now be treated thanks to antibiotics disorders.

According to research (Koolman, 2005). Chemotherapeutic drugs are typically derived from plants, while antibiotics were first discovered in microbes. A study by Chhetri et al. (2010)



Several antibiotics, including antimycin A and myxothiazol, inhibit the electron transport by the cyt-b/c1 complex. Since the inner membrane is negatively charged, reduced cyt-c diffuses over its surface to the cyt-a/a3 complex (Fig.1), commonly known as complex IV or cytochrome oxidase. Thirteen distinct subunits make up the cyst-a/a3 complex, three of which are encoded by mitochondria.The schematic placement of complexes I, III, and IV of the mitochondrial respiratory chain is shown in Figure.1. As reported by (Heldt, 2005).

Scientists have recently determined its three-dimensional structure by analyzing the X-ray structures of cyst-a/a3 complexes isolated from beef heart mitochondria and Paracoccus denitrificans. The binding site for cyt-c is located in a broad hydrophilic area of the complex that extends into the intermembrane gap. The cyt-c oxidation process involves the transfer of electrons to a CuA cluster of copper sulfur comprising two Cu atoms. In Fig. 2, the two S-atoms of cysteine side chains connect the two Cu atoms. This copper-sulfur cluster likely accepts one electron and transfers it via cyt-a to a cyt-a3 and a Cu atom (CuB) linked to histidine at the core of a binuclear center. The Fe-atom of cyst-a3, along with CuB, forms a binuclear center that acts as a redox unit by accepting two electrons. [Fe+++.CuB++]+ 2e- → [Fe++.Cu+B]

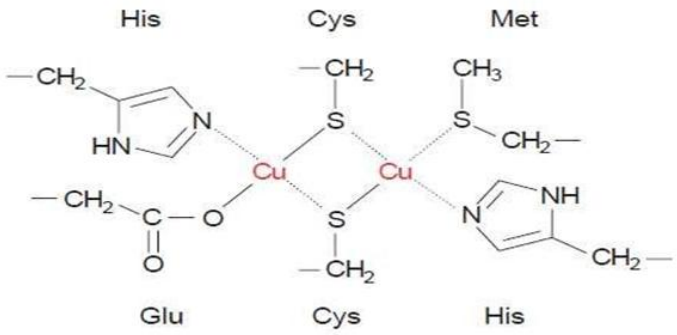


Figure 2: The cytochrome a/a3 complex copper sulfur cluster, CuA, including a Cu2+ and a Cu+ ion (Heldt and Heldt, 2005).

Pathogen Detection Test

Using broth microdilution assays, Jayaseelan et al. (2010) tested the ligand and a series of its metal complexes [Cu(II), Ni(II), Co(II), and Mn(II)] for antibacterial activity against S. aureus as a gram-positive bacteria, E. coli as a gram-negative bacteria, and the fungus A. fumigatus. Table 1 shows that the Gram-positive bacteria on all metal complexes reduce the activity of all tested bacteria at varying rates. We rank Co higher than Ni, Cu, and Mn. The same pattern holds for gram-negative bacteria; complexes are more effective against bacteria than ligands. Aspergillus fumigatus was one of the fungi that the ligand was effective against, and the metal complexes followed the pattern Cu > Co > Ni >

Mn. It is well established that chelation enhances the ligand's efficacy as a bactericidal agent. This activity enhancement during chelation may be due to electron delocalization over the entire chelating ring and the sharing of the metal's positive charge with donor atoms on the ligands. The lipid bilayers of bacterial membranes are subsequently thickened as a result.

Table 1: Ligand and Metal Complexes with Antimicrobial Activity (Jayaseelan et al., 2010)

Sample	Bacteria						Fungi		
	Gram-positive			Gram-negative					
	S.aureus			E.Coli			A.Fumigatus		
	50 µg/mL	100 µg/mL	150 µg/mL	50 µg/mL	100 µg/mL	150 µg/mL	50 µg/mL	100 µg/mL	150 µg/mL
Ligand	4	10	13	5	9	12	4	11	13
$[Cu_2(L)(NO_3)_4]$	10	13	18	11	15	17	12	15	19
$[Ni_2(L)]^{4+}4Ac^-$	9	11	16	10	14	15	12	14	17
$[Co_2(L)(NO_3)_4]$	11	13	19	13	16	19	11	14	18
$[Mn_2(L)Cl_4]$	8	10	15	9	14	15	10	15	19

Metal Compounds with Antibacterial Properties

Idemudia and Ajibade (2010) produced and studied pyrimethamine complexes with Ag(I), Co(II), and Cu(II) that are stable in the air. Ag(I) complexes have been proposed to have a linear geometry, while Co(II) and Cu(II) complexes have tetrahedral and octahedral geometries, respectively, based on their electronic spectra. At a MIC value of 0.03125 mg/ml, [Ag2(perm)2].0.7CH3OH demonstrated a more significant antibacterial potential in screening the complexes for antimicrobial activity.In a 2010 study, (Idemudia and Ajibade)

A Study of Antimicrobials

Silver complexes showed antibacterial efficacy in a selectivity test against bacterial strains, in contrast to the inactive pyrimethamine medication. All eight gram-positive and gram-negative bacterial isolates were susceptible to the antimicrobial effects of Ag(I) complexes. These results demonstrated the broad spectrum activity of the Ag(I) complexes. P. vulgaris has the minor inhibitory zone of all the bacteria tested, measuring just 7.5 mm in [Ag(perm)2 Cl]_3H2O and 12.5 mm in [Ag(perm)CH3COO]. Table 2 shows that the zone of inhibition for Staphylococcus aureus is 20.5 mm for [Ag(perm)2Cl]_3H2O and 22 mm for [Ag(perm)CH3COO. According to Table 3, the silver complexes' minimum inhibitory concentration (MIC) is 0.03125 mg/mL for all species except P. vulgaris, for which it is 0.0625 mg/mL. The MIC value for the complex [Ag(perm)CH3COO] is also 0.0625 mg/ml, effective against all species tested. According to these findings, the activity of [Ag(perm)2Cl]_3H2O is higher. To determine how much metal complex it takes to halt bacterial growth completely, scientists calculated the MBC value. For all bacteria isolates except Enterobacter cloacae and P. vulgaris, the minimum inhibitory concentration (MIC) for [Ag(perm)2Cl]_3H2O is 0.03125 mg/mL. According to Table 3, [Ag(perm)CH3COO] has an MBC of 0.0625 mg/mL against all bacterial isolates. This finding and the minimum inhibitory concentration data demonstrate that [Ag(perm)2Cl]_3H2O is more antimicrobial active. according to (Idemudia & Ajibade, 2010). Complexes demonstrate sensitive patterns of inhibitory zones against particular pathogens, as seen in Table 2.

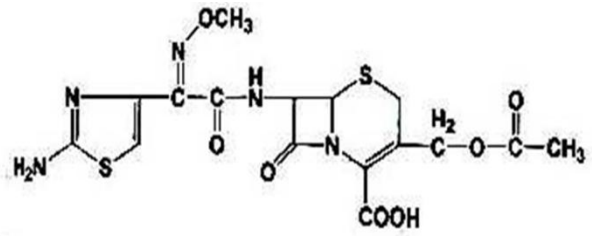
Table 3 Shows the MIC Values for Each Compound Against Each Bacterial Isolate. According To (Idemudia & Ajibade, 2010)

Microorganism	$[Ag_2(pyrm)_2Cl]\cdot 3H_2O$ mg/ml	$[Ag(pyrm)CH_3COO]$ mg/ml
Staphylococcus aureus	20.5	22.0
Streptococcus faecalis	18.5	21.5
Bacillus cereus	10.5	15.5
Bacillus pumilus	9.5	16.5
Escherichia coli	9.0	14.0
Pseudomonas aeruginosa	8.0	18.5
Enterobacter cloacae	15.5	19.5
Proteus vulgaris	7.5	12.5

Microorganism	$[Ag_2(pyrm)_2Cl]\cdot 3H_2O$ mg/ml	$[Ag(pyrm)CH_3COO]$ mg/ml
Staphylococcus aureus	0.03125	0.0625
Streptococcus faecalis	0.03125	0.0625
Bacillus cereus	0.03125	0.0625
Bacillus pumilus	0.03125	0.0625
Escherichia coli	0.03125	0.0625
Pseudomonas aeruginosa	0.03125	0.0625
Enterobacter cloacae	0.03125	0.0625
Proteus vulgaris	0.0625	0.0625

Metal Compounds of Cefotaxime Exhibit Antibiotic Action

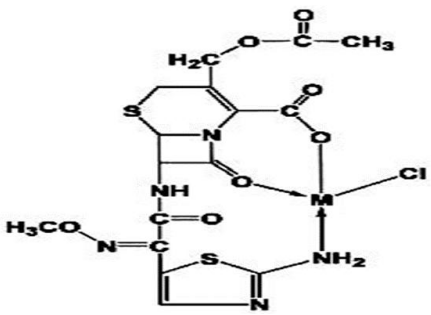
Using physicochemical and spectroscopic techniques, we were able to describe the [M(cefotaxime)Cl] complexes (M = Mn(II), Fe(III), Co(II), Ni(II), Cu(II), and Cd(II)) formed when Cefotaxime (Hcefotax) interacted with transition metal ions. They are hypothesized to have a tetrahedral shape. Cefotaxime acts as a monoanionic tridentate ligand, as shown by its IR and 1H-NMR spectra in complexes. Several strains of bacteria were used to test the complexes for antibacterial activity, and the results were compared to Cefotaxime's performance. In 2005, Anacona and Silva found that this was the case. The inability of the antibiotic to reach its sites of action, changes in the penicillin-binding proteins that are targets of the cephalosporins, or inactivation of the antibiotic by bacterial enzymes (beta-lactamases) are all possible causes of resistance to the third-generation cephalosporin antibiotic cefotaxime. However, cephalosporins vary in how susceptible they are to beta-lactamase. For instance, compared to first-generation cephalosporins, third-generation cephalosporins have more excellent resistance to hydrolysis by the beta-lactamases produced by gram-negative bacteria. Anacona and Silva (2005). As reported by Anacona and Silva (2005), Cefotaxime metal complexes were synthesized and characterized. Cefotaxime's chemical structure is depicted in Figure 3.Anacona and Silva's 2005 publication depict Cefotaxime's 3-D structure.



Cefotaxime's Proposed New Structure

According to Anacona and Silva (2005), the cefotaxime ion can accept electrons from various donor atoms. However, due to steric restrictions, the ligand can only supply a maximum of three donor atoms to any given metal center. Molecular models suggest that Cefotaxime is coordinated via carboxylate and lactic carbonyl oxygen atoms. Possible coordination geometry for the metal ions in the [M(cefotaxime)Cl] complexes (where M = Mn(II), Co(II), Ni(II), Cu(II), Cd(II)) is tetrahedral with one cefotaxime molecule and the chloride anion at the vertices. Octahedral geometries, however, are not negotiable.

On the other hand, the iron (III) complex with two chloride anions in its coordination sphere is pentacoordinate and likely has a tetragonal pyramidal or trigonal bipyramidal geometry. Binuclear structures, however, must be protected to ensure their continued existence. Despite their crystalline character, X-ray structural determination was unsuccessful for any of the products. Figure 4 depicts the proposed layout.Cefotaxime metal complexes [M(cefotaxime)Cl], (M = Mn(II), Co(II), Ni(II), Cu(II), and Cd(II)): a possible structure is shown in Fig. 4. Reference: (Anacona and Silva, 2005)



Cancer Research and Treatment using Metal Complexes

Metal complexes, particularly transition metal complexes, have been demonstrated to be quite effective in treating cancer in both older and more contemporary studies.Since the seventeenth century, metal complexes have been used to treat cancer and leukemia. It has been nearly 50 years since the discovery of the inorganic compound cisplatin, but it is still one of the most widely prescribed anticancer medications. Animal studies have revealed that metal complexes produced with other metals, such as copper, gold, gallium, germanium, tin, ruthenium, and iridium, exhibit potent anticancer action.

For example: (Hariprasath et al., 2010). Many transition metal compounds, including those based on the square planar coordination of cisplatin, have been shown to exhibit anticancer activity. Octahedral coordination numbers, however, have also been demonstrated to be functional (Thomas, 2007). It is important to note that other transition metals are also used in cancer treatment. Significant anticancer activity is also observed in titanium complexes and gold complexes. Compounds of ruthenium with arylazopyridine ligands have been shown to have cytotoxic activity in the treatment of ovarian cancer. It was found (Loo et al., 2004).

One of the most famous anticancer drugs, cis- [Pt (NH3)2Cl2], is also the only one shown to be effective against malignancies. When detected early, testicular cancer has a high success rate of curing the condition. Searches for less toxic and more broadly effective platinum-containing anticancer drugs have persisted in light of cis-[Pt(NH3)2Cl2]'s significant renal toxicity and limited application to a select number of tumor types. The second medication to enter clinical use is carboplatin ([Pt(NH3)2 (CBDCA)] (CBDCA = the cyclobutane-1,1-dicarboxylate ligand).

Cosmetics with Transition Metals

Hair chemistry makes extensive use of hair fibers in the form of cosmetics. About 85% of hair fibers comprise the complex protein keratin, while the remaining 7% is water. Besides water, 3% of the formula comprises lipids, and 2% is pigment. Melanin, a pigment synthesized from tyrosine, is the last ingredient. Aluminum (Al), calcium (Ca), and several transition metals such as iron (Fe), manganese (Mn), magnesium (Mg), copper (Cu), chromium (Cr), and zinc (Zn) are also present in hair, with the latter having a comparatively high concentration at 22 mg per 100g. This is supported by research (Butler, 2000). Nickel, a transition metal, is utilized in cosmetics because of its ability to cause skin irritation. When a drug reacts with endogenous proteins to generate a hapten-carrier conjugate, it can operate as a skin sensitizer by penetrating the stratum corneum, partitioning it into the epidermis, and eliciting an immune response.According to (Leyden and Rawlings,2002), such materials often have a low molecular weight (roughly 400 D), making them stable in various temperatures and pressures.

CONCLUSION

Coordination chemistry, which plays a significant role in enhancing the design of molecules to reduce hazardous side effects and understand their mechanisms of action, was recently used with a focus on potential metal-antibiotic medications and some cosmetics. This can be used as a beacon by chemists working on more environmentally friendly formulations of pharmaceuticals and personal care products.

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