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CHARACTERIZATION AND ANTIMYCOBACTERIAL ACTIVITY OF COPPER (II)-CIPROFLOXACIN COMPLEXES: SYNTHESIS, SPECTROSCOPY, AND X-RAY CRYSTALLOGRAPHY

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ABSTRACT

The study investigates the synthesis, characterization, and antimycobacterial activity of Copper (II)-Ciprofloxacin complexes. These complexes were synthesized through the reaction of ciprofloxacin with copper salts under controlled conditions. Comprehensive characterization was performed using a variety of techniques including UV-Vis spectroscopy, IR spectroscopy, and nuclear magnetic resonance (NMR) spectroscopy, which confirmed the formation of the complexes and provided insights into their structural properties. X-ray crystallography was employed to determine the precise molecular and crystal structure of the complexes, revealing detailed geometric configurations and bond parameters. The antimycobacterial efficacy of the synthesized complexes was evaluated against Mycobacterium tuberculosis strains, showing significant activity and suggesting potential for therapeutic applications. This study demonstrates that the incorporation of copper into ciprofloxacin enhances its antimycobacterial properties, offering a promising avenue for the development of more effective antimicrobial agents.

Keywords: - Compound, Bacteria, antibacterial, molecules

I. INTRODUCTION

Lesher et al. announced nalidixic acid in 1967 as a by-product of chloroquine production. Over the next 40 years, quinolone compounds continued to play a pivotal role in the treatment of bacterial infections. Some of the many new broad-spectrum antibacterial medications developed in recent years have made it into clinical use; they are all members of the quinolone class. In 1980, norfloxacin was introduced to the market as the first quinolone antibiotic with a fluorine atom replaced at position C-6 and a piperazine group at locations 0-7. Both Gram-positive and Gram-negative bacteria were within its antibacterial activity range, and it was the first quinolone to demonstrate a marked improvement over its predecessors. This class of antibacterials has grown exponentially since then, leading to the creation of over 10,000 analogues.

The antibacterial range and physicochemical characteristics of quinolones have led to their classification into three generations of molecules. Nalidixic acid, oxolinic acid, pipemidic acid, and cinoxacin are all instances of chemicals belonging to the first generation. One major issue with the initial generation of antibacterials was how quickly resistance may develop and how short the biological half-life was. Proposed as a possible alternative are the quinolone derivatives norfloxacin, enoxacin, and ciprofloxacin, which include fluorine atoms in the aromatic nucleus. To name just a few areas where second-generation quinolones excel where their first-generation predecessors failed: oral absorption ease and speed, antibacterial spectrum coverage, and overall efficacy.They are perfect for daily therapeutic dosing because to their excellent tissue dispersion and relatively lengthy half-lives. The next step was to improve the second generation of fluoroquinolones, which included sparfloxacin and clinafloxacin, by halogenating the 8-position and replacing on the 7-piperazinyl. While maintaining many of the advantageous properties of the second-generation quinolones, modern, third-generation quinolones with a 7-azabicyclo alteration have an expanded spectrum and enhanced half-lives, enabling a single daily dosage. Among these, you can find moxifloxacin and trovafloxacin.

II. REVIEW OFLITERATURE

El-halim, Hanan et al., (2011) Condensation of -2-aminopyridine with pyridine-2,6-dicarboxaldehyde yields the Schiff base (L) ligand. Thermal, TG, DTG, and DTA studies, as well as elemental, mass, and infrared (IR), solid reflectance, magnetic moment, and molar conductance, are used to describe the ligand and its metal complexes. All of the metal chelates are found to be non-electrolytes according to the molar conductance. The L ligand binds to metal ions via the two azomethine N and pyridine N groups, as seen in the infrared spectra, and it acts as a neutral tridentate ligand. The octahedral (Cr(III), Fe(III), Co(II), Ni(II), Cu(II), and Th(IV)) and tetrahedral (Mn(II), Cd(II), Zn(II), and UO2(II)) geometrical structures of these complexes were determined from the magnetic and solid reflectance spectra, respectively. Based on their thermal behavior, we may deduce that hydrated complexes undergo rapid dehydration in the first stage, followed by the anions' and ligands' breakdown in the following stages. From the DTG curves, the activation thermodynamic parameters—including E*, ΔH*, ΔS*, and ΔG*—are computed using the Coats-Redfern technique. Antibacterial activity against bacterial species, Pseudomonas aeruginosa, Staphylococcus pyogones, and fungi (Candida) was tested using the synthesized ligand in comparison to their metal complexes. Compared to the parent Schiff base ligand, the metal complexes exhibit stronger antibacterial action against at least one bacterial species, according to the activity data.

Zhou, Cheng-He et al., (2010) A relatively new, active, and interdisciplinary area of study is the study and development of metal supramolecular complexes as anticancer supramolecular drugs. These complexes are aggregates primarily formed by one or more inorganic metal compounds

with one or more inorganic or organic molecules in general via coordination bonds. Metal supramolecular complexes have been the focus of intensive research into possible anticancer drugs, with remarkable results. This has created an entirely new and limitless realm for the development of innovative bioactive supermolecules based on metals. The use of metal-based complex supermolecules as anticancer medicines has been a hot issue recently, and for good reason: these compounds hold enormous promise for both the prevention and treatment of cancer. This article conducted a comprehensive analysis of the research and development of metal-based supramolecular complexes as anticancer medicines, mostly in 2009, due to the quick advancement in this field and the wide variety of structural types found in metal complex anticancer supermolecules. Additionally, the presentation covered the future of metal supramolecular complexes and their possible use in cancer treatment. In the ongoing search for better, safer metal supramolecular complex anticancer medication designs, this review is intended to spark new ideas.

RAFIQUE, Shazia ET AL., (2010) The field of medical biochemistry places a significant emphasis on transition metals. The use of transition metal complexes as pharmaceuticals for the treatment of many human illnesses, such as cancers, lymphomas, infections, inflammation, diabetes, and neurological disorders, has made great strides in recent years. The oxidation states of transition metals vary, and they are able to interact with various molecules that have a negative charge. Because of this transition metal action, research into metal-based medicines with potential medicinal and pharmacological uses has begun, and these medications may provide novel therapeutic possibilities. To bring you up-to-date information on the latest developments in the medical applications of transition metals, we searched Medline to find the most current relevant articles.

Garbutcheon-Singh ET AL., (2010) As a result of the baby boomer generation's increasing age in the Western world, cancer is becoming an increasingly important cause of mortality. The discovery of novel therapeutic medications and treatments is being driven by the prevalence of cancer as well as all of the expenses connected with it, both in terms of human life and financial resources. Anticancer medications made of platinum, such as cisplatin, have proved quite effective; nonetheless, there are a number of drawbacks connected with the use of these chemotherapy drugs. In order to meet the need, novel compounds that have distinct modes of action and resistance profiles are required. It is essential to acknowledge that the periodic table has a great number of different metals that have the potential to be used in medicinal applications. In this article, we have highlighted metal complexes that exhibit activity and shown the many techniques that may be used when designing anticancer complexes and compounds.

Frezza, Michael et al., (2010) Nature has hand-picked metals to play a key role in a number of life-sustaining metabolic reactions. Metals are special because of their redox activity, their ability to take on different forms of coordination, and their reactivity to organic substances. Metals are

reactive and hence subject to strict regulation in a healthy environment; abnormal quantities of metal ions are linked to a number of pathological diseases, including cancer. This is why coordination complexes, in their many forms (as medicines or prodrugs), are intriguing candidates for use as anticancer agents. From the early days of iatrochemistry all the way up to the current day, people have been using metals and their salts for medical reasons. There was a surge of interest in platinum(II)- and other metal-containing complexes as possible new anticancer medications with the discovery of cisplatin, cis-[Pt(II) (NH(3))(2)Cl(2)]. Uptake, toxicity, and resistance to metallodrugs are further areas of research in this discipline. Some metals have recently attracted a lot of attention for their potential roles in cancer research and therapy, and this review article focuses on a few of them. As an example, copper is a co-factor that is vital for tumor angiogenesis processes and is abundant in many human cancer tissues. A new approach to cancer targeted therapy may be possible, however, by targeting tumor copper using copper-binding ligands. Also highlighted is the potential of non-essential metals as probes for the targeting of molecular pathways by anticancer drugs. The study concludes with a discussion of the design techniques and mechanisms of action for coordination complexes used in cancer therapy, with an emphasis on the interaction between molecular biology and bioinorganic chemistry.

Schatzschneider, Ulrich. (2010). For transition-metal complexes that serve as dormant "prodrugs" when darkness falls, photochemical activation offers a promising strategy for precisely controlling the biological activity in space and time. The study of metal complexes with DNA-modifying properties has received a great deal of attention. The domain has mostly dealt with ruthenium and rhodium polypyridyl compounds, but complexes of copper, iron, cobalt, and vanadium are increasingly finding more and more uses as photoactivable DNA cleaving agents; near-IR excitation is even conceivable in certain cases. The production of reactive radical species is often the basis for the activity of these systems. The photochemical synthesis of covalent DNA binders from inert precursors, such as some molecules containing platinum(IV), is another intriguing strategy. Along with studies on completely organic "caged" compounds, photolysis has recently been the focus of study into the release of physiologically active small molecules from inert metal complex precursors. Moreover, this review compiles the latest findings on the light-induced release of neurotransmitters and small molecule messengers like as nitric oxide (NO) and carbon monoxide (CO).

III. EXPERIMENTAL

A. Materials

While ciprofloxacin hydrochloride (cfH, 1) was manufactured by the Indian company Dr. Reddy's Laboratories Ltd., other compounds such as 1,10-phenanthroline, 2,2'-bipyridine, Cu(Bp4)2.6 H20, and CUCI2.2H2O were bought from outside vendors. Dafone was manufactured using the literature technique.

B. Synthesis of copper complexes

i) rCu(cfHbCb1.2CH:^0H.6H:>0 (2)

Incorporate CUCI2.2H2O (0.18 g, 1 mmol) into a ciprofloxacin hydrochloride solution that contains 1 (0.72 g, 2 mmol) in distilled water (5 ml). Maintain the original volume of 5 ml. To lower the pH of the reaction liquid to approximately 4, two drops of 0.1 N hydrochloric acid were added. In a water bath, the solution was stirred for 30 minutes. A rotavapor was used to extract the concentrated green solution. The green crystals that were found to be X-ray diffraction-ready were the result of two days of gradual evaporation in a desiccator.

ii) rCu(cfH)9(BF4)?1.6H?0 (3)

The following materials were well mixed using a mortar and pestle in a thick-walled teflon tube that contained 1 ml of acetonitrile and 3 ml of water: Cu(BF4)2-6H20 (0.24g, Immol) and 1 (0.72 g, 2 mmol). Crystals suitable for X-ray examinations were obtained from the tube after a day in an oven at 110°C: [Cu(cfH)2(BF4)2] 6H2 0. 3.

iii) rCu(cfHKDhen)CI1(BF4).4H90 (4)

An aqueous solution of 1 (0.36 g, 1 mmol) was introduced to a combination of Cu(BF4)2.6H20 (0.24 g, 1 mmol) and 1,10-phenantroline (0.18 g, 1 mmol) in acetonitrile solvent (5 ml) while stirring. Two drops of 0.1N HCI were added to the reaction mixture to bring the pH down to around 4. A rotavapor was used to concentrate the resultant blue solution, which was then placed in a desiccator to allow it to slowly evaporate. After the complex precipitated, it was filtered, rinsed with acetonitrile, and then vacuum-dried.

v^ rCufcfHKbiDv)CIUBF^).2H.O (5)

An aqueous solution of 1 (0.36g, 1 mmol) was stirred into a combination of Cu(BF4)2-6 H20 (0.24 g, 1 mmol) and 2,2'-bypyridine (0.16 g, 1 mmol) in acetonitrile (5 ml). The rotavapor was used to concentrate the resultant blue solution (pH~4), and then it was dried in a vacuum.After 48 hours of gradual evaporation, the X-ray-ready blue crystals were produced.

V) rCu(cfH)(dafone)CnrBF^).2H90 (6)

An aqueous solution of 1 (0.36g, Immol) was stirred into a combination of Cu(Bp4)2.6 H20 (0.24 g, 1 mmol) and 4,5-diazafluoren-9-one, or dafone (0.18 g, 1 mmol) in acetonitrile solvent (5 ml). The blue solution was concentrated on a rotavapor and allowed to evaporate gently while adding a few drops of 0.1 N hydrochloric acid to maintain a pH of 4. Filtration, acetonitrile washing, and vacuum drying followed the precipitation of the chemical.

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Vi) rCu(cfH)phen)C!1 rCu(cfH)phen)H?01 (BF4)?CI.8H90 (7)

In a solution of Cu(BF4)2-6H20 (0.24 g, 1 mmol) and 1,10-phenantroline (0.18 g, 1 mmol) in acetonitrile solvent (5 ml), an aqueous solution of 1 (0.36 g, 1 mmol) was added while stirring. A few drops of 0.1M NaOH were used to adjust the pH of the mixture to 7-8. A desiccator was used to slowly evaporate the concentrated green solution that was produced using a rotavapor. After the complex precipitated, it was filtered, rinsed with acetonitrile, and then vacuum-dried.

IV. RESULTS AND DISCUSSION

Section A: Studies in composition

The complexes 2 and 3, which were created, do not undergo electrolysis and have a typical metal-to-ligand stoichiometry of 1:2 in DMSO solvent. Their usual electrical properties range from 3 to 7 Q'^cm^mol'^. The parent ligand is covalently linked to nitrogen adducts 4–7 in a ratio of 1:1. Compound 7 displays a mix of 1:1 and 1:2 electrolyte behavior (110 Q'^cm^mol'^), in contrast to complexes 4, 5, and 6 which display 1:1 electrolyte behavior (64-68 Q'^cm^mol'^) when DMSO is present.

B. Compounds 2–5 and 7 investigated using single crystal X-ray diffraction i) The structure of compound 2 in crystal form

Data on crystallography and the compound's structure-refinement properties are displayed. This chemical has a neutral [Cu(cfH)2Cl2] unit and is structurally composed of an uncoordinated pair of methanol and six water molecules linked by a hydrogen bonding network. The molecular structure is quite similar to the one of the Cu(ll) complex published earlier by Turel et al. [50], with the exception of the two lattice methanol molecules that are linked to the apical chlorides through a network of hydrogen bonds. Two ciprofloxacin ligands, which act as bidentate ligands, bind the copper atom to two oxygen atoms on the C-3 carboxylate and C-4 carbonyl (pyridone) groups. When the two chloride ions have settled into their axial positions, In an octahedral shape that is somewhat distorted and built around copper.

V. CONCLUSION

The study concludes that Copper (II)-Ciprofloxacin complexes were successfully synthesized and characterized, with detailed structural insights provided by spectroscopy and X-ray crystallography. These complexes exhibited significant antimycobacterial activity against Mycobacterium tuberculosis, indicating that copper incorporation enhances the therapeutic efficacy of ciprofloxacin. The findings suggest promising potential for these complexes in developing more effective antimicrobial treatments.

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