Mixed ligand based copper(II) complex and its antimicrobial activity

R. Suhasini\textsuperscript{a}, Poonam R. Inamdar\textsuperscript{b} and A. Sheela*\textsuperscript{b}

\textsuperscript{a}Department of Chemistry, Auxilium College, Vellore-632 006, Tamilnadu, India
\textsuperscript{b}Materials Chemistry Division, School of Advanced Sciences, VIT University, Vellore-632 014, Tamilnadu, India

E-mail: asheela@vit.ac.in

Abstract: Transition metal complexes of mixed ligand systems have played a pivotal role in the development of inorganic chemistry. Metal chelates have been preferred for therapeutic applications over inorganic salts due to their tunable coordination geometries and their efficiency to bring about desirable effect at minimum dosage levels\textsuperscript{1}. Mixed ligand complexes of curcumin with bipyridine, phenanthroline and other ancillary ligands have been proved as efficient anticancer agents\textsuperscript{3}. In the current study, the synthesis of Cu\textsuperscript{II} complex of mixed ligands of diethylmalonate and salicylaldehyde, possessing similar binding modes as curcumin and salicylaldehyde is described. The synthesized complex [Cu(sal)(dem)].2H\textsubscript{2}O is characterized by UV-Visible, FT-IR and mass spectral techniques to ascertain the structure of complex. These types of complexes are expected to possess potential antimicrobial and anticancer applications.

Keywords: Mixed ligand complexes, \textbeta{}-diketones, antibacterial activity.

Introduction

Metal complexes of mixed ligands have a greater significance in the history of development of coordination chemistry. \textbeta{}-Diketones have been used as an ideal ligand system for almost 120 years as their derivatives are known since 1887. The nature of bonding and chelation modes is elucidated by Werner and Morgan\textsuperscript{4}. The ligand shows facile keto-enol tautomerism and binds to metal ions as a bidentate ligand. From the existing literature survey, it appears that diketones and their related complexes have been extensively studied towards various biological applications such as antioxidant, antitumor, antibacterial etc., and are also used as analytical reagents\textsuperscript{3}. These are considered as one of the important compounds in organic chemistry for their antioxidant, antitumor and antibacterial potentials. It also acts as a key intermediate for the preparation of various heterocyclic compounds of medicinal importance. It is also an important pharmacophore of HIV-1 integrase inhibitors in keto-enol form\textsuperscript{5}. Physiological regulation is effective with some metal complexes due to the interaction of negatively charged biomolecules with positively charged metal centre. Metal complexes of drug moieties are found to improve the activity of the drugs by decreasing the toxicity. In view of the above, in our current study, we have reported synthesis and characterization of Cu\textsuperscript{II} complex using salicylaldehyde and diethylmalonate (DEM).

Bacterial resistance is a major concerned health problem with drug resistant pathogenic species. \textit{Methicillin resistant}, \textit{Staphylococcus aureus} (MRSA), \textit{Pseudomonas aeruginosa}, \textit{Acinetobacter baumannii}, \textit{Escherichia coli} and \textit{Vancomycin resistant}, \textit{Enterococci} are a few examples of multiple class of antibacterial agents that have developed greater resistance to different drugs. There is a need to explore effective antibacterial agents to overcome the limited choice of drugs for therapeutic treatment\textsuperscript{6} and in this regard metal complexes have continuously been in focus.

It has also been reported that copper metal complexes exhibit an effective inhibitory activity better than that of the corresponding free ligands against all Gram-positive bacteria and fungi\textsuperscript{7}. Thus, based on the literature survey, above synthesized, novel complex has been subjected to antimicrobial study especially against highly pathogenic Gram-positive bacterial and fungal strain, so as to study its biological potential which has not been reported so far.
Experimental

Materials and methods:

All the chemicals used are of analytical reagent grades and metal salts are also of standard quality. Salicylaldehyde and diethyl malonate (Sigma-Aldrich), copper sulphate (Thomas Baker) are procured and used without purification. All solvents are of standard spectroscopic grade. UV and Visible spectra are recorded in JASCO Company made in Japan with a scan speed 400/min. FTIR spectrophotometry are recorded in Shimadzu resolution of 4 cm⁻¹ of model IR Affinity 1.

Synthesis of mixed ligand Cu II complex:

Ethanolic solution of diethyl malonate (3.4 mmole; 0.50 ml) and salicylaldehyde (3.4 mmole; 0.345 ml) are prepared. The two ligands are added dropwise simultaneously to the hot ethanolic solution of copper sulphate (3.4 mmole, 0.8466 g) and refluxed for half an hour. 5% aqueous NaOH is added till pH reaches 5-6 and stirred for 3 h. The obtained precipitate are dried at room temperature.

Antibacterial and antifungal activity of [Cu(sal)(dem)].2H₂O:

Synthesized [Cu(sal)(dem)].2H₂O is studied for antibacterial and antifungal activities by well diffusion method. Potato dextrose agar was prepared and complex solution in DMSO was treated against bacterial strains such as Klebsiella pneumonia, Staphylococcus aureus (Gram +ve) and Escherichia coli (Gram -ve) and fungal strains such as Candida albicans, Aspergillus niger and Aspergillus fumigatus. The stock solution (1 mg mL⁻¹) of the test chemical is prepared by dissolving 2 mg of the test compound in 5 mL of DMSO solvent. Blank DMSO is kept as control to compare the results with the sample. The bacteria were subcultured in agar medium and for fungi, it is done in potato dextrose agar medium and are incubated for 24 h at 37 °C. Standard antibacterial drug, ciprofloxacin and standard antifungal drug, ketoconazole are used for comparison. The petri discs are incubated for 48 h at 37 °C.

Results and discussion:

[Cu(sal)(dem)].2H₂O:

Bluish green solid; yield (65%), melting point (183 °C). The FTIR spectra show strong and medium bands appearing at 1610.56 cm⁻¹, 1691.57 cm⁻¹ corresponding to diketo group υ(C=O). 1595.13 cm⁻¹ assigned to υ(C=O aldehyde) and 549.71 cm⁻¹ assigned to υ(Cu-O). UV spectra show λ max value as 209 nm.

The complexes are synthesized in good yields and recrystallized. The absorption spectra of these complexes have shown intense UV bands which are assignable to intraligand π-π* transitions at 209 nm. The absorption bands observed in visible region as broad peak at 900 nm for complex are due to d-d transitions. FTIR studies support the formation of complexes as we have observed the shifts in stretching frequencies corresponding to the functional groups of the ligands. In the ligand DEM, ketenol groups was observed at 3425.58 cm⁻¹ which is disappeared in complex. Two -C=O stretch in diethyl malonate are observed at 1751.36 and 1735.93 cm⁻¹ which is shifted to lower wave number at 1691.57 and 1610.56 cm⁻¹ in the complex. Similarly, -OH stretch in salicylaldehyde at 3414.10 cm⁻¹ disappeared in the complex. -C=O stretch in salicylaldehyde observed at 1645.28 cm⁻¹ shifted to lower wave number at 1595.13 cm⁻¹ in complex. The typical Cu-O bond stretching frequency for the complex occurring at 549.71 cm⁻¹ is not observed in the ligand IR spectra. The mass spectrum of complex [Cu(sal)(dem)].2H₂O shows a molecular ion peak (M⁺) at m/z 297 that is equivalent to its molecular weight having the formula CuCl₁₄H₂₅O₈. The mass spectrum shows a base peak with m/z 167.33 corresponding to the molecular weight of diethylmalonate [C₇H₁₂O₂]. The fragment peaks observed at m/z 122, 237, 211 are due to the fragment ions [C₇H₈O₂]⁺⁺, [C₁₄H₂₃O₇]⁺⁺, [C₁₄H₂₁O₆]⁺⁺ respectively.
In vitro antibacterial and antifungal assays:

The complex \([\text{Cu(sal)(dem)}] \cdot 2\text{H}_2\text{O}\) shows maximum zone of inhibition 13 mm against \textit{Staphylococcus aureus}, whereas, standard antibacterial drug ciprofloxacin shows 25 mm against the same shown in Fig. 2. Similarly complex shows maximum zone of inhibition 11 mm against \textit{Escherichia coli} and 5 mm against \textit{Klebsiella pneumonia}, whereas, standard antibacterial drug shows 20 mm and 25 mm against the same.

Considering the antifungal activity complex \([\text{Cu(sal)(dem)}] \cdot 2\text{H}_2\text{O}\) shows maximum zone of inhibition 9 mm against \textit{Candida albicans}, whereas, standard antifungal drug ketoconazole shows 13 mm against the same shown in Fig. 2. Similarly complex shows maximum zone of inhibition 7 mm against \textit{Aspergillus niger} and 5 mm against \textit{Aspergillus fumigatus} whereas standard antifungal drug shows 10 mm and 18 mm against the same.

Conclusion

\(\text{Cu}^{II}\) complex of mixed ligands of diethylmalonate and salicylaldehyde is synthesized and characterized. Antibacterial and antifungal activities against \textit{Staphylococcus aureus} and \textit{Candida albicans} shows maximum zone of inhibition by \([\text{Cu(sal)(dem)}] \cdot 2\text{H}_2\text{O}\) complex thereby acting as an efficient antibacterial and antifungal agent.

References