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Synthesis, Characterization and Antimicrobial Activity of Homonuclear Cu(II) and Ni(II) Schiff Base Complexes

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Abstract - The current study aimed to synthesise, characterise, and investigate the antimicrobial activity of homonuclear Cu(II) and Ni(II) Schiff base complexes. Homonuclear Schiff Base Complexes chelates of Cu(II) and Ni(II) were synthesised. It appears that the complex is a potential metallo-ligand. It forms binuclear complexes when it reacts with two different metal salts, Ni and Cu. Using a Schiff base ligand made from 4-chloro-o-phenylenediamine and 3,5-dichloro-2-hydroxyacetophenone, the homo and hetero binuclear oxygen bridging Cu(II) and Ni(II) complexes were synthesized. Numerous common physicochemical methods, including elemental analysis, spectroscopic, thermal, cyclic voltammetry, and magnetic moment tests, have been used to characterise the synthesised complexes. For the mono- and binuclear compound of Cu(II) & Ni(II), spectral analysis reveals square planer shape. The antibacterial data indicates that the homo-binuclear copper complex is more active than the other mono- and binuclear complexes. Research has been done on the Schiff base and its complexes' anticancer properties.

Keywords - Schiff base, Homonuclear complexes, BSA/DNA–binding, Cytotoxicity; Metal complex Cu(II) and Ni(II).

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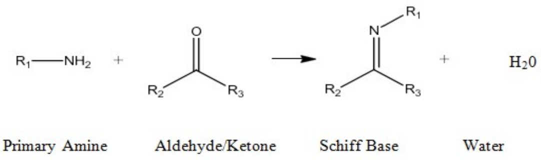
INTRODUCTION

The formation of Schiff base from ketones or aldehydes is a revocable reaction that typically occurs under base (or) acid catalysis or when heated. The formation is generally completed by separating the product, removing water, or both. According to reports, an aqueous base or acid can hydrolyze several Schiff bases back to ketones, aldehydes, and amines. Schiff bases are formed through the acid-catalyzed condensation of a primary amine (not ammonia) with an aldehyde or ketone. A SB is the nitrogen counterpart of a ketone or aldehyde, with the carbonyl group (C=O) substituted by an imine group (C=N-R), as shown in Figure 4, where R might be an alkyl or aryl group.



Schiff bases containing aryl substituents are more easily synthesized and stable than those that contain alkyl substituents, means Schiff bases of aliphatic aldehydes are readily undergo polymerisation in comparison to products from conjugation of aromatic aldehydes and are relatively unstable. [24], [25], [26] The formation of Schiff bases from ketones or aldehydes requires a protic solvent which is suitably dry in order to prevent potential hydrolysis of the newly formed imine bond. Usually, heat or acid or base catalysis is used to form SB, and the removal of water, product separation, or both can be used to control the imine formation process. The important Schiff bases, their transition metal complexes and their varied applications. It also contains a brief introduction to solvation, solute (ion)-solvent and solute (ion)-solute (ion) interactions. Purpose and usage of the present investigation as well as importance and scope of different physico-chemical properties like apparent molar volumes, partial molar volumes at infinite dilution, the viscosity B-coefficient, etc., have been mentioned. Importance of different solutes and solvents, used in the present investigation, has also been outlined.

The study's theoretical foundation works embodied in this paper has been given in detail with special reference to different physico-chemical parameters studied in solution chemistry. A brief overview of solvent effects on reactions rates and theoretical approach for the study of partial molar volumes and solvation. The experimental methods employed for the measurement of different thermodynamic and transport properties. This chapter also contains provenance and purity of the different chemicals used and describes the syntheses and physicochemical characterization of the Schiff-bases and their transition metal complexes used as solutes in the present investigation. Consequently, the interactions between ions and solvents for N, N/-ethylene-bis(salicylideneiminato)-diaquochromium(III) chloride dissolved in solutions of 1-butyl-2,3-dimethylimidazolium tetrafluoroborate and methanol at 298.15, 308.15 and 318.15 K underambient pressure. The derived measure's like evident molar volume (φV), the slope (*VS), standard partial molar volume (0φV), standard transfer volume (0ΔtφV), the viscosity B-coefficient, etc., were examined in light of the interactions between ions and solvents.

The transition state theory served as the foundation for the discussion of viscous flow thermodynamics. The densities, viscosities and refractive indices of N, N/-ethylene-bis(salicylideneiminato)-diaquochromium(III) chloride in aqueous solutions of dimethylsulfoxide were reported at 298.15, 308.15 and 318.15 K under atmospheric pressure.

The derived measure's like evident molar volume (φV), standard partial molar volume (0φV), the slope (*VS), standard isobaric partial molar expansibility (0φ E) and its temperature dependence E T P (0) 0∂φ ∂ , the viscosity B-coefficient, its temperature dependence (∂B / ∂T), solvation number (nS) and evident molar refractivity (RD), etc., were talk about on the basis of ion-ion and ion-solvent interactions. Further ionic viscosity B-coefficients (B±) and ionic solvation numbers (Sn±) were determined and discussed accordingly.

Hydrolysis – Problems in Schiff base formation: As discussed earlier mechanism of Schiff base formation is reversible in nature and formation of the imine can encounter a potential problem in which the imine double bond could be hydrolysed back to the starting materials. Heteronuclear and homonuclear complexes, particularly nickel(II) and copper(II) compounds, have sparked widespread attention in recent decades, owing to the ease of bioinorganic chemistry of nickel and copper, as well as molecular magnetism (1-2). Their interactions with metalloproteinase active sites, especially binuclear metallocentres, have received a lot of attention, as has the mimicking of such biomolecule activity. Their relationship with the active sites of metalloproteinases and metalloenzymes, which have homodinuclear and heterodinuclear metallocentres and biomolecules, has sparked significant attention (3-4). Furthermore, copper(II) and nickel(II) complexes, particularly with tetradentate oxime, replicate the chemical and physical behaviour of biological metal systems. Biological investigations of oxime ligands and metal complexes have recently grown in prominence. For the past 30 years, several investigations on the characterization and development of novel compounds modified with organic and inorganic components have been done to investigate the characteristics of DNA cleaving and combining. Nickel and copper mixtures are increasingly important in the development and design of novel magnetic materials and composites. Nickel- and copper-bridged structures are used for magnetic properties groups are especially in space and medicine industry. (E,E)-dioxime containing unsymmetrical ligands can form square pyramidal, octahedral planar complexes with cobalt(II), nickel(II), palladium(II) and copper(II) as central metal atoms. These homogeneous catalysts were based on 2,6-bis(imino)pyridyl SB ligands complexed to cobalt(II) or iron(II) ions as shown in Figure 6. From the observation of Britovsek, data shows that both Fe(II) and Co(II) had high activities, but experiment found that the activities of the iron Fe(II) are exceptionally higher. The Fe(II) complex attained highest result in ethylene polymerization when the substituents R_1, R_2, R_3 and R_4 are equal to methyl. When the *ortho*-substituent R_3 was changed to hydrogen, it has been noted that the activities had a dramatic decrease which could be explained by steric protection of the active site in controlling activities and molecularweight.

A series of novel copper (II) and nickel (II) complexes derived from chiral Schiff-base ligands [(R)/(S)-H2L(1)=(R)/(S)-2-[(1-Hydroxymethyl-propylimino)-methyl]-5-methoxy-phenol and (R)/(S)-H2L(2)=(R)/(S)-2-[(1-Hydroxymethyl-2-phenyl-ethylimino)-methyl]-5-methoxy-phenol], were synthesized and distinguish by elemental analyses, (1)H NMR spectra, FT-IR spectrum. The crystal structures of complexes 1-5 were determined through single crystal X-ray diffraction (SXRD). According to the structures, solvent molecules' oxygen atoms occupy the axial positions in Ni (II) complexes, and ligands are neutrally coordinated to the Cu/Ni (II) ion via ONO donor atoms.

METHODS

The purpose of this study is to prepare charactersie and study biological aspects of novel homodinuclear complexes of Ni (II), Cu (II) Schiff base. The pharmacological properties of the complexes obtained as Schiff base are well known for their biological and pharmacological properties. Two homodinuclear Cu(II) and Ni(II) Schiff Base Complexes will be synthesised and characterised by elemental analysis, spectroscopic methods (UV-Vis, ^{1}H NMR and IR) and single crystal X-ray crystallography. Without any additional purification, all of the reagents, starting materials, and solvents will be obtained through commercial purchases. Using appropriate and suitable methods, the melting points, infrared spectra, ultraviolet spectra, etc., will be recorded. Elemental C, H, N and S analysis will be accomplish on a Fisons EA 1108 analyzer. The condensation reaction between 2-aminobenzoic acid and 3nitrobenzaldehyde will be used to synthesise the Schiff base (HL). Metal complexes of the Schiff base with Ni(II) and Cu(II) will be synthesised and characterised by physical and spectroscopic techniques.

Experiments will be carried out with all available tools and materials, chemicals and catalysts. The result will be recorded at various stages and sequence would be drawn. Detailed data will be collected using all possible and suitable methods.

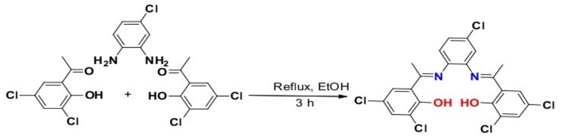
HYPOTHESIS

Two homodinuclear complexes of Ni(II) and Cu(II) were synthesised and characterised. The complexes have a good interaction with DNA and BSA and also biological property as antibacterial, antifungal anti-inflammatory, analgesic, anticonvulsant, antitubercular and antioxidant. And Human breast cancer and human prostate cancer cell lines are significantly cytotoxic to Cu complex.

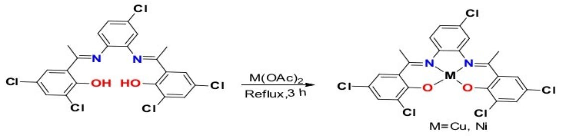
RESULTS

Mononuclear Cu(II) complex- The solution of copper(II) acetate mono hydrate (0.1997g; 1mmol) in 20 mL ethanol was added drop wise to a solution of ligand (0.5167g) in ethanol (20 mL) with constant stirring. Under reflux, the mixture was gradually heated for three hours. The resultant solution was refluxed and then allowed to slowly evaporate the solvent without being disturbed. Following a period of four days, the complex with a bluish brown color was filtered, thoroughly cleaned with ethanol, and vacuum-dried.

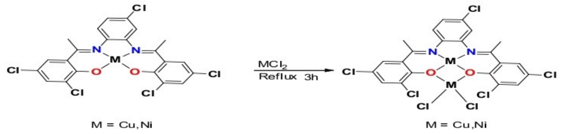
Mononuclear Ni(II) Complex- Mononuclear Ni(II) complex was prepared by addition of an ethanolic solution (20 mL) of nickel (II) acetate tetrahydrate (0.2488g; 1mmol) to a solution of ligand (0.5167g) in ethanol (20 mL) drop by drop with constant stirring. The mixture was reflux-heated for three hours and eleven minutes., which resulted in a rapid change of color from brown to greenish brown powder. The complex with a greenish brown color was filtered, thoroughly cleaned with ethanol, and vacuum-dried.



Scheme1: Synthesis of ligand



Scheme 2: Synthesis of mononuclear complexes



Scheme3: Synthesis of homo binuclear complexes

The Schiff base ligand in the stochiometric ratio 2:1 (L:M) and Schiff base ligand (L) was synthesized by simple condensation between 2-hydroxy-3-methoxybenzaldehyde with 3-aminopyridin-4-ol. The structure and formation of The established synthetic chemicals by different analytical and spectroscopic methods like, elemental analysis, UV- spectroscopy, FT-IR, Proton and Carbon NMR, mass spectrometry and Powder XRD. Further, the synthesized chelates screened for the DNA binding studies of Calf Thymus (CT)-DNA by exploiting electronic absorption spectra, relative viscosity measurements and thermal denaturation methods. The suggested DNA binding mechanism is consistent with the complexes' increased binding activity when newly synthesized ligand is present. Using gel-electrophoresis, the cleavage activities of the PUC-18 DNA were recorded both in Both in and out of of complexes. The outcomes of the cleavage experiment show that every synthesized chelate is capable of efficiently cleaving pUC-18 DNA.

It was discovered that the synthetic Schiff base ligand and its chelates were color solids, stable at room temperature, and soluble in a variety of solvents, including DMSO and DMF. The calculated values for elemental analysis data are in good accordance with experimental values. The UV–Visible spectral method is the most valuable method to know the binding studies of DNA with the chelates. The chemicals can attach to DNA through non-covalent interactions like electrostatic interactions, intercalation, or groove binding, or through covalent bonding like in complexes containing ligands that can be substituted with DNA base pairs, according to UV-visible research.

CONCLUSION

The majority of schiff bases (SBs) that have been successfully synthesised along with their mononuclear, homo, and hetero-binuclear metal complexes have nitrogen as their donor atom. However, SB ligands that have other donor atoms present can function as bi, tri, tetra, penta, or multidentate mixed donors. The primary amine or diamine and the kind of ketone or aldehyde used typically dictate the donor nature of the ligands various physio-chemical methods such as molar conductance, FT-IR, UV-Vis,1HNMR, cyclic voltammetry, thermal analysis and EPR. All the metal complexes are square planar environment which was confirmed by electronic and EPR spectral data. The findings of cyclic voltammetry confirmed that mononuclear complexes show one step one electron transfer, while quasi-reversible and two steps one electron transfer are displayed by binuclear metal complexes. Binuclear metal complexes were discovered to be more stable than mononuclear metal complexes through thermal analysis. Based on the outcomes of the antimicrobial efficaciousness test, we conclude that the hetero-binuclear Cu(II) and Ni(II) complex effectively contributes to the enhancement of bioactivity. The result for anticancer activity shows how highly cytotoxic the homo binuclear Cu(II) and Ni(II) complex is. The typical partial molar volumes have properties similar to those of metalloligands. Under ambient pressure, its reaction with various metal salts (Ni & Cu) resulted in the formation of binuclear complexes with pyridoxine hydrochloride in methanol at 298.15, 308.15, and 318.15 K. The derived measures like evident molar volume (φV), the slope (*VS), standard partial molar volume (0φV), standard transfer volume (0∆tφV), isobaric evident molar expansibility (φE), standard isobaric partial molar expansibility (0φE), the viscosity B-coefficient, its temperature derivative (∂B/∂T), solvation number (nS), etc., were discussed on the basis of specific or nonspecific solutecosolute and solute-solvent interactions. The complex and pyridoxine hydrochloride showed a 1:1 solute-cosolute interaction, according to the spectrophotometric data. Thus, it includes the final statement for the current work.

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