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Topic of the research: **Synthesis and Characterization of bio-conjugates Schif base transition metal complexes and their bio-medical applications.**

FINDINGS

The thesis entitled **"Synthesis and Characterization of bio-conjugate Schif Base transition metal complexes and their biomedical applications"** is composed of five chapters. The research focuses on the synthesis and characterization of bio-conjugated Schif base transition metal complexes and the evaluation of their potential biomedical applications.

Chapter I: The present study established that Schiff base ligands and their transition metal complexes constitute an important class of bioinorganic compounds with significant structural diversity and biological relevance. The review demonstrated that Schiff bases, containing the azomethine (–C=N–) functional group, possess excellent coordination ability toward transition metal ions and serve as versatile ligands for the synthesis of stable metal complexes. The study highlighted that biologically important aldehydes and amines can be strategically employed to synthesize Schiff base ligands with enhanced electronic delocalization, planarity, and donor properties. Coordination with transition metal ions such as Cu(II), Co(II), Ni(II), Zn(II), Fe(III), and Mn(II) resulted in the formation of stable complexes exhibiting diverse coordination geometries and improved physicochemical characteristics. The literature survey further revealed that spectroscopic and analytical techniques, including FT-IR, UV–Visible spectroscopy, NMR spectroscopy, and mass spectrometry, are effective tools for confirming Schiff base formation, metal coordination, and the structural characteristics of the synthesized complexes. The findings demonstrated that coordination of Schiff base ligands with transition metal ions significantly enhances their biological activities. The metal complexes generally exhibited superior antibacterial and antifungal activities compared with the corresponding free ligands, which was attributed to increased lipophilicity, improved cellular uptake, favorable redox properties, and synergistic interactions between the metal ions and ligand framework. The review also established the growing importance of computational approaches in the design and evaluation of bioactive Schiff base ligands. Molecular docking studies demonstrated strong binding affinities of Schiff base ligands toward therapeutically relevant enzymes associated with Parkinson's disease, diabetes mellitus, cancer, and other metabolic disorders. These studies identified key hydrogen bonding, hydrophobic, and π–π interactions responsible for effective ligand–target recognition. Furthermore, Density Functional Theory (DFT), Natural Bond Orbital (NBO) analysis, Molecular Electrostatic Potential (MEP) analysis, and Molecular Dynamics (MD) simulations provided valuable information regarding molecular geometry, electronic structure, charge distribution, intermolecular interactions, and the stability of ligand–target complexes. These computational investigations complemented the experimental observations and improved the understanding of the electronic behavior of Schiff base ligands. Overall, the findings of this chapter established that Schiff base ligands and their transition

metal complexes represent promising candidates for medicinal and bioinorganic applications. The combined experimental and computational approaches provided a comprehensive understanding of structure–property–activity relationships and offered a rational framework for the future design and development of biologically active coordination compounds with enhanced therapeutic potential.

Chapter 2: The findings of this chapter demonstrated that Schiff base ligands were successfully synthesized by condensation reactions between selected aldehydes and amines, yielding structurally stable compounds. The synthesized ligands and their transition metal complexes were successfully characterized using FT-IR, ^{1}H and ^{13}C NMR, UV–Visible spectroscopy, LC-MS, HRMS, and melting point analysis, which confirmed their structural integrity, purity, and coordination behavior. The results further established that stable transition metal complexes were successfully obtained with biologically important metal ions. Biological evaluation indicated that metal coordination enhanced the antibacterial and antifungal activities of the Schiff base ligands. Computational studies, including molecular docking, Density Functional Theory (DFT), and molecular dynamics simulations, provided valuable insights into the electronic properties, molecular stability, ligand–target interactions, and therapeutic potential of the synthesized compounds. Overall, the integrated experimental and computational approach proved effective for understanding the structure activity relationships of Schiff base ligands and their transition metal complexes.

Chapter 3: The findings of this study demonstrated the successful green synthesis of the nicotinamide-derived Schiff base ligand, N,N′-(Z)-1,4 phenylenebis(methaneylyidene)dinicotinamide (SBPD), using a catalyst-free aqueous method, providing a simple, eco-friendly, and high-yield synthetic approach. Spectroscopic and analytical techniques confirmed the successful synthesis, structural integrity, and purity of the ligand.The synthesized SBPD ligand was successfully coordinated with Mn(II), Fe(II), Co(II), Ni(II), Cu(II), and Zn(II) ions to form stable transition metal complexes. Characterization studies confirmed the proposed coordination modes and geometries of the complexes. Biological evaluation revealed that metal coordination significantly enhanced the antimicrobial activity of the Schiff base ligand. Among the synthesized complexes, the Co(II) complex exhibited the strongest antibacterial activity, whereas the Fe(II) complex showed the highest antifungal activity. Combination studies further demonstrated synergistic effects with standard antimicrobial drugs, indicating the potential of these metal complexes as resistance-modifying agents. Overall, the study established that green synthesis coupled with transition metal coordination is an effective strategy for developing environmentally friendly Schiff base metal complexes with promising antimicrobial properties and potential therapeutic applications.

Chapter 4: The findings of this chapter demonstrated the successful synthesis of two novel Schiff base ligands, SBQN and SBCN, through a simple condensation reaction with high purity. Spectroscopic and analytical studies confirmed the formation of azomethine (C=N) functionality and validated the proposed molecular structures. DFT calculations revealed significant differences in the electronic properties of the synthesized ligands. SBQN exhibited a lower HOMO–LUMO energy gap, higher electronic reactivity, favourable charge distribution, and enhanced molecular stability compared to SBCN. MEP and NBO analyses identified important reactive sites responsible for molecular interactions. Molecular docking studies against human DOPA decarboxylase (DDC) demonstrated that SBQN showed stronger binding affinity than SBCN and the reference inhibitor complex. The superior binding performance of SBQN was attributed to effective hydrogen bonding, π–π stacking, and hydrophobic interactions with the active site residues of the enzyme. Overall, the study established that the synthesized Schiff base ligands, particularly SBQN, possess promising

structural and electronic features for potential DOPA decarboxylase inhibition and may serve as valuable lead molecules for the development of future anti-Parkinson agents.

Chapter 5: The findings of this chapter demonstrated the successful synthesis of two novel Schiff base derivatives, SBBN and SBPN, through condensation reactions of nicotinamide with aromatic aldehydes under mild reaction conditions. Spectroscopic and analytical studies confirmed the formation of azomethine (C=N) functionality and established the structural integrity and purity of the synthesized compounds.DFT investigations revealed important electronic characteristics of the synthesized Schiff bases. SBBN exhibited a lower HOMO–LUMO energy gap, indicating greater chemical reactivity and favourable electronic properties. Molecular electrostatic potential (MEP) and Natural Bond Orbital (NBO) analyses identified significant reactive sites and charge delocalisation patterns responsible for effective molecular interactions.Molecular docking studies demonstrated the potential of SBBN and SBPN as α-amylase inhibitors by showing favourable binding interactions with the enzyme active site. The computational findings supported the role of Schiff base derivatives as promising lead molecules for controlling postprandial hyperglycemia in type 2 diabetes mellitus.Overall, this study established that nicotinamide-derived Schiff bases possess suitable structural, electronic, and molecular interaction properties, making them potential candidates for further development as antidiabetic agents targeting α-amylase inhibition.