DEVELOPMENT OF MIXED-LIGAND POLY(1,2,4-TRIAZOLYL) BORATE COMPLEXES OF COBALT(II) AND NICKEL(II): STRUCTURAL CHARACTERIZATION AND ENZYME INHIBITION STUDIES—A SECONDARY DATA-BASED REVIEW AND COMPARATIVE ANALYSIS

Dr Asif Iqbal Bhat
Department Of Chemistry
Sri Pratap College, Srinagar, Jammu and Kashmir

Abstract
Mixed-ligand poly(1,2,4-triazolyl) borate complexes of transition metals have attracted considerable attention because of their structural versatility and promising biological applications. This study presents a secondary data-based review and comparative analysis of reported cobalt(II) and nickel(II) mixed-ligand poly(1,2,4-triazolyl) borate complexes published before 2025. The objective is to evaluate reported synthesis approaches, coordination geometries, structural characterization techniques, and enzyme inhibition activities to identify significant structure–activity relationships. Relevant peer-reviewed studies were systematically examined using predefined inclusion criteria, and published data were comparatively analyzed. The findings indicate that ligand environment, coordination geometry, and auxiliary ligands strongly influence the physicochemical characteristics and enzyme inhibitory potential of the complexes. The comparative assessment also highlights recurring trends in spectroscopic characterization and biological performance while identifying gaps requiring further experimental validation. This review provides a consolidated understanding of existing research and offers valuable insights for the rational design of biologically active mixed-ligand metal complexes.

Keywords: Poly(1,2,4-triazolyl) borates; Mixed-ligand complexes; Cobalt(II); Nickel(II); Coordination chemistry; Structural characterization; Enzyme inhibition; Secondary data analysis.

1. Introduction

1.1 Background

Coordination chemistry has emerged as one of the most dynamic branches of inorganic chemistry, offering extensive opportunities for the development of functional materials with applications in catalysis, medicine, environmental remediation, and materials science. Among various ligand systems, poly(1,2,4-triazolyl) borate ligands have attracted considerable attention because of their versatile coordination behavior, electronic tunability, and ability to stabilize transition-metal ions in diverse coordination environments. These ligands belong to the family of scorpionate ligands, characterized by their facial tridentate coordination mode, which enables the formation of stable and well-defined metal complexes exhibiting unique structural and physicochemical properties (Trofimenko, 1993; Pettinari, 2008).

The borate core provides structural rigidity, while the 1,2,4-triazole rings offer multiple nitrogen donor atoms capable of coordinating with transition-metal ions. Such coordination results in the formation of complexes with variable geometries, including tetrahedral, square-planar, and octahedral arrangements, depending on the nature of the metal ion and auxiliary ligands. The incorporation of different substituents into the triazole framework further enhances the flexibility of these ligands by modifying their steric and electronic properties,

thereby influencing complex stability, reactivity, and biological activity (Pettinari et al., 2016).

Among nitrogen-containing heterocyclic compounds, 1,2,4-triazole derivatives occupy a prominent position owing to their exceptional chemical stability and broad spectrum of biological activities. The presence of multiple nitrogen atoms within the triazole ring facilitates strong coordination with transition metals, promoting the formation of robust metal–ligand architectures. Numerous studies have reported that triazole-based compounds possess antimicrobial, antifungal, antiviral, anticancer, anti-inflammatory, and antioxidant properties, making them attractive scaffolds for medicinal chemistry and bioinorganic research (Kharb et al., 2011).

Transition-metal coordination compounds, particularly those containing cobalt(II) and nickel(II), have received increasing attention because of their rich coordination chemistry and potential pharmaceutical applications. Cobalt(II) complexes often exhibit variable oxidation states, favorable magnetic properties, and catalytic activity, whereas nickel(II) complexes demonstrate remarkable coordination flexibility and biological compatibility. The interaction between transition-metal ions and triazolyl borate ligands can significantly alter the electronic environment of the metal center, resulting in enhanced physicochemical properties and improved biological performance. Consequently, cobalt(II) and nickel(II) mixed-ligand complexes have become important candidates for the development of novel bioactive molecules with potential therapeutic applications.

The pharmaceutical relevance of metal complexes has expanded considerably over the past two decades. Metal coordination compounds are increasingly investigated as enzyme inhibitors, antimicrobial agents, anticancer drugs, and diagnostic probes because metal coordination can improve molecular stability, lipophilicity, cellular uptake, and selective interaction with biological macromolecules. The ability of mixed-ligand poly(1,2,4-triazolyl) borate complexes to modulate enzyme activity has generated considerable interest in the search for new therapeutic agents targeting various metabolic and pathological pathways.

1.2 Mixed-Ligand Systems

Mixed-ligand coordination complexes represent an important advancement over conventional single-ligand systems because they combine the complementary properties of two or more ligands within a single coordination sphere. The introduction of auxiliary ligands modifies the steric and electronic environment around the metal ion, often leading to enhanced structural stability, improved solubility, greater selectivity, and superior biological activity. Such modifications enable researchers to tailor the physicochemical characteristics of metal complexes for specific biomedical and catalytic applications.

Electronic interactions between the primary poly(1,2,4-triazolyl) borate ligand and auxiliary donor ligands influence electron density distribution around the central metal ion. These interactions affect metal–ligand bond strength, redox behavior, magnetic properties, and spectroscopic characteristics. Consequently, mixed-ligand complexes frequently exhibit improved coordination stability and altered reactivity compared with analogous single-ligand complexes. The selection of suitable auxiliary ligands therefore plays a crucial role in determining the overall performance of the synthesized coordination compounds.

Structural diversity is another major advantage of mixed-ligand systems. Depending on ligand denticity, donor atoms, and coordination preferences of cobalt(II) and nickel(II), a wide range of molecular architectures can be obtained, including mononuclear, polynuclear, and supramolecular assemblies. Variations in coordination geometry influence intermolecular interactions, crystal packing, thermal stability, and biological behavior. Such structural versatility makes mixed-ligand poly(1,2,4-triazolyl) borate complexes valuable model systems for investigating structure–property relationships.

Biologically, mixed-ligand complexes frequently demonstrate enhanced activity because the combination of multiple ligands can

improve membrane permeability, optimize metal ion delivery, and facilitate stronger interactions with biological targets. The chelation effect generally reduces the polarity of the metal ion while increasing the lipophilic character of the complex, thereby enhancing its ability to penetrate cellular membranes and interact with enzymes and biomolecules. These characteristics have stimulated growing interest in the development of mixed-ligand transition-metal complexes as potential therapeutic agents.

1.3 Biological Applications

Poly(1,2,4-triazolyl) borate complexes of cobalt(II) and nickel(II) have demonstrated promising biological activities in numerous experimental investigations. One of the most extensively reported applications is antimicrobial activity against Gram-positive bacteria, Gram-negative bacteria, and various fungal pathogens. Enhanced antimicrobial performance is often attributed to increased lipophilicity resulting from metal chelation, which facilitates penetration through microbial cell membranes and disrupts essential cellular processes.

In addition to antimicrobial effects, many triazole-based transition-metal complexes exhibit significant antioxidant activity through their ability to scavenge reactive oxygen species and stabilize free radicals. Such properties may contribute to reducing oxidative stress associated with inflammation, neurodegenerative disorders, and chronic diseases. Although antioxidant performance varies according to ligand structure and metal coordination environment, several studies have reported improved activity following complex formation.

Enzyme inhibition has emerged as one of the most promising biological applications of mixed-ligand metal complexes. Reported investigations have demonstrated inhibitory activity against enzymes such as urease, α-amylase, α-glucosidase, acetylcholinesterase, and tyrosinase. These enzymes are closely associated with infectious diseases, diabetes mellitus, Alzheimer's disease, and pigmentation disorders. The inhibitory efficiency of coordination compounds depends on several factors, including metal ion identity, ligand substitution pattern, coordination geometry, and overall molecular stability.

The relevance of these complexes to drug discovery has consequently increased. Modern medicinal chemistry increasingly recognizes metal-based therapeutics as valuable alternatives to purely organic pharmaceuticals because metal coordination provides opportunities for unique mechanisms of action that are difficult to achieve using conventional small molecules. Mixed-ligand poly(1,2,4-triazolyl) borate complexes therefore represent an important class of compounds for future pharmaceutical development, particularly when combined with computational modeling, molecular docking, and structure–activity relationship studies.

1.4 Research Gap

Despite substantial progress in the synthesis and characterization of transition-metal triazolyl borate complexes, several important research gaps remain. First, published investigations are predominantly focused on individual metal complexes, with relatively few studies providing direct comparative analyses of cobalt(II) and nickel(II) mixed-ligand systems under a unified analytical framework. Thislimit understanding of how different metal centers influence structural characteristics and biological performance.

Second, although numerous experimental studies have reported synthesis procedures, spectroscopic characterization, and biological evaluation, comprehensive secondary data-based reviews integrating these findings remain scarce. Existing literature generally emphasizes isolated experimental outcomes rather than synthesizing evidence across multiple studies to identify broader trends and recurring structure–activity relationships.

Third, correlations between structural parameters—including coordination geometry, donor atom arrangement, electronic properties, and auxiliary ligand selection—and enzyme inhibition activity remain insufficiently explored. A systematic comparative assessment of published findings is therefore needed to clarify these relationships and provide guidance

for the rational design of more effective biologically active coordination compounds.

1.5 Objectives

The present study is based exclusively on published secondary data and aims to provide a comprehensive comparative evaluation of mixed-ligand poly(1,2,4-triazolyl) borate complexes of cobalt(II) and nickel(II) reported before 2025. Specifically, the study seeks to:

1. Review published synthesis strategies employed for the preparation of mixed-ligand poly(1,2,4-triazolyl) borate complexes.
2. Compare structural characterization techniques, including spectroscopic, crystallographic, thermal, and magnetic analyses reported in previous investigations.
3. Evaluate similarities and differences between cobalt(II) and nickel(II) complexes with respect to coordination geometry and physicochemical properties.
4. Examine reported enzyme inhibition activities and other biological applications described in the literature.
5. Identify potential structure–activity relationships influencing biological performance.
6. Highlight current research limitations and propose future research directions for the development of advanced mixed-ligand transition-metal complexes with enhanced therapeutic potential.

2. Review of Literature

2.1 Development of Poly(1,2,4-Triazolyl) Borate Ligands

The development of poly(1,2,4-triazolyl) borate ligands represents a significant advancement in coordination chemistry, particularly in the design of multifunctional ligands capable of forming stable transition-metal complexes. The concept of poly(heterocyclic) borate ligands originated from the pioneering work of Trofimenko (1966, 1993), who introduced scorpionate ligands as tripodal nitrogen-donor systems possessing remarkable coordination versatility. Initially, research focused primarily on poly(pyrazolyl) borates; however, continued efforts to improve electronic flexibility and donor characteristics led to the development of poly(triazolyl) borate analogues. The substitution of pyrazole with 1,2,4-triazole introduced additional nitrogen atoms into the heterocyclic framework, thereby enhancing coordination possibilities and modifying the electronic properties of the ligand (Trofimenko, 1993).

During the late 1990s and early 2000s, increasing interest in triazole-based ligands was driven by their ability to stabilize transition metals in multiple oxidation states while maintaining excellent thermal and chemical stability. Researchers demonstrated that poly(1,2,4-triazolyl) borate ligands could effectively coordinate with first-row transition metals, producing structurally diverse complexes suitable for catalytic, magnetic, and biological applications (Pettinari, 2008). Subsequent studies expanded the range of substituents on the triazole rings to regulate steric hindrance, electron donation, and coordination geometry, allowing precise control over the physicochemical properties of the resulting complexes.

The coordination behavior of poly(1,2,4-triazolyl) borate ligands is largely governed by the presence of multiple nitrogen donor atoms capable of binding strongly to transition-metal ions. The borate center acts as a rigid scaffold that positions the triazole rings in a facial arrangement, enabling tridentate coordination while minimizing structural distortion. Depending on the electronic requirements of the metal ion and the presence of auxiliary ligands, these ligands may function as tridentate or, in some cases, participate in bridging interactions that give rise to multinuclear coordination assemblies. Such flexibility has made poly(triazolyl) borates valuable building blocks in modern coordination chemistry (Pettinari et al., 2016).

Steric properties play an equally important role in determining the behavior of these ligands. The introduction of alkyl, aryl, or electron-withdrawing substituents onto the triazole rings alters the spatial arrangement surrounding the metal center, thereby influencing coordination number, bond angles, crystal packing, and intermolecular interactions. Bulky substituents generally favor lower coordination numbers by

restricting access to the metal center, whereas smaller substituents permit the formation of more compact coordination environments. These steric modifications also affect crystal engineering by influencing hydrogen bonding, π–π stacking, and other non-covalent interactions responsible for the stabilization of supramolecular architectures.

Electronic properties constitute another major factor contributing to the widespread application of poly(1,2,4-triazolyl) borate ligands. The nitrogen-rich triazole rings exhibit strong σ-donor and moderate π-acceptor characteristics, facilitating efficient overlap with the d-orbitals of transition metals. Variations in ligand substitution can modify electron density around the coordinating nitrogen atoms, thereby influencing metal–ligand bond strength, redox behavior, magnetic interactions, and spectroscopic characteristics. Such electronic tunability enables researchers to tailor complexes for specific applications, including catalysis, molecular magnetism, sensing, and medicinal chemistry. Consequently, poly(1,2,4-triazolyl) borate ligands have evolved into one of the most versatile ligand families within contemporary coordination chemistry.

Recent literature further highlights the importance of these ligands in designing biologically active metal complexes. Their ability to stabilize cobalt(II), nickel(II), copper(II), and zinc(II) ions while maintaining structural integrity under physiological conditions has encouraged investigations into antimicrobial, antioxidant, and enzyme inhibitory activities. This expanding research area demonstrates the growing significance of triazolyl borate chemistry beyond traditional inorganic synthesis and toward pharmaceutical and biomedical applications.

2.2 Coordination Chemistry of Co(II) Complexes

Cobalt(II) occupies a unique position among first-row transition metals because of its flexible coordination chemistry, variable spin states, and diverse structural geometries. The incorporation of Co(II) into poly(1,2,4-triazolyl) borate ligand systems has resulted in numerous coordination compounds exhibiting remarkable structural diversity and functional properties. Reported studies indicate that the coordination environment of cobalt(II) is strongly influenced by ligand denticity, steric effects, solvent molecules, and auxiliary donor ligands, leading to the formation of tetrahedral, square-pyramidal, trigonal-bipyramidal, and octahedral geometries (Pettinari, 2008).

Single-crystal X-ray diffraction investigations have shown that cobalt(II) complexes containing triazolyl borate ligands generally adopt distorted octahedral or tetrahedral coordination geometries depending on ligand substitution patterns. Facial coordination provided by the tripodal ligand framework contributes significantly to structural rigidity and enhanced complex stability. The presence of additional donor ligands, including nitrogen-, oxygen-, or sulfur-containing molecules, often completes the coordination sphere and modifies intermolecular interactions responsible for crystal packing and molecular organization.

Electronic spectroscopy has been widely employed to characterize cobalt(II) coordination compounds. Ultraviolet–visible spectra typically display d–d transitions corresponding to tetrahedral or octahedral coordination environments, together with ligand-to-metal charge-transfer bands arising from interactions between triazole nitrogen atoms and the cobalt center. Infrared spectroscopy complements these findings by confirming coordination through characteristic shifts in C=N and B–N vibrational frequencies following complex formation. Elemental analysis and mass spectrometry further verify the proposed molecular compositions, while thermogravimetric analysis provides valuable information regarding coordinated solvent molecules and thermal decomposition pathways.

Magnetic measurements constitute an essential component of cobalt(II) complex characterization because the magnetic moment is highly sensitive to coordination geometry and ligand-field strength. High-spin octahedral cobalt(II) complexes generally exhibit magnetic moments consistent with three unpaired electrons, whereas tetrahedral complexes often display slightly higher values owing to orbital contributions. Variations in magnetic

susceptibility reported in the literature reflect differences in ligand-field stabilization and coordination environment, providing useful evidence for structural assignment when combined with spectroscopic and crystallographic analyses.

Thermal stability is another important characteristic influencing the practical application of cobalt(II) coordination compounds. Thermogravimetric and differential thermal analyses indicate that poly(1,2,4-triazolyl) borate cobalt complexes typically undergo stepwise decomposition involving the loss of lattice solvent molecules, coordinated ligands, and eventual formation of cobalt oxide residues at elevated temperatures. The decomposition profile depends strongly on ligand substitution, coordination number, and intermolecular interactions within the crystal lattice. Increased thermal stability has been associated with stronger metal–ligand bonding and more rigid coordination frameworks, characteristics that are desirable for catalytic and biomedical applications.

Recent investigations have also explored the biological relevance of cobalt(II) triazolyl borate complexes. Chelation has been shown to enhance lipophilicity, facilitating improved interaction with biological membranes and macromolecules. Several studies have reported promising antimicrobial, antioxidant, and enzyme inhibitory activities, suggesting that cobalt coordination modifies both the physicochemical and biological properties of the ligand. Although the precise mechanisms underlying these biological effects remain under investigation, current evidence indicates that coordination geometry, electronic configuration, and ligand substitution collectively influence biological performance. These findings provide a strong foundation for comparative evaluation with analogous nickel(II) complexes, which are discussed in the subsequent section.

2.3 Coordination Chemistry of Ni(II) Complexes

Nickel(II) coordination compounds derived from poly(1,2,4-triazolyl) borate ligands have attracted considerable attention because of their structural versatility, catalytic potential, and biological relevance. Following the development of triazolyl borate ligands in the late twentieth century, researchers increasingly explored nickel(II) as a central metal ion owing to its flexible coordination behavior, moderate ligand-field stabilization energy, and ability to adopt diverse coordination geometries. Compared with cobalt(II), nickel(II) generally forms more structurally predictable coordination environments while retaining sufficient electronic flexibility to accommodate different auxiliary ligands and donor atoms. Comprehensive reviews of poly(azolyl)borate chemistry have highlighted nickel complexes as important model systems for studying metal–ligand interactions and structure–property relationships.

Single-crystal X-ray diffraction studies demonstrate that nickel(II) complexes containing hydrotris(1,2,4-triazolyl)borate ligands most frequently adopt distorted octahedral coordination geometries, although tetrahedral, square-planar, and five-coordinate structures have also been reported depending on ligand substitution and crystallization conditions. Structural investigations further reveal that the facial coordination provided by the triazolyl borate framework stabilizes the metal center while permitting the incorporation of additional donor ligands. Comparative crystallographic studies of Fe(II), Co(II), Ni(II), and Zn(II) hydrotris(1,2,4-triazolyl)borate complexes have shown that the absence or presence of coordinated solvent molecules significantly influences hydrogen-bonding networks, crystal packing, and solid-state stability.

Spectroscopic characterization remains fundamental to confirming the structures of nickel(II) coordination compounds. Infrared spectroscopy commonly reveals shifts in the C=N stretching frequencies of the triazole rings after complex formation, indicating successful coordination through nitrogen donor atoms. Ultraviolet–visible spectroscopy identifies characteristic d–d transitions associated with octahedral or tetrahedral nickel(II) environments, while ligand-to-metal charge-transfer bands provide further evidence of metal–ligand electronic interactions. Complementary techniques such as elemental analysis, electrospray mass spectrometry,

thermogravimetric analysis (TGA), and powder X-ray diffraction contribute additional confirmation of molecular composition, thermal behavior, and phase purity. The integration of these analytical techniques provides a comprehensive understanding of coordination geometry and complex stability.

Catalytic applications constitute another important aspect of nickel(II) triazolyl borate chemistry. Nickel-based coordination compounds have been investigated as homogeneous catalysts in oxidation reactions, carbon–carbon bond-forming processes, and environmentally benign catalytic transformations because of their favorable redox characteristics and relatively low toxicity. The tripodal triazolyl borate framework stabilizes reactive nickel intermediates while allowing electronic modulation through ligand substitution. Such electronic control can improve catalytic selectivity, reaction efficiency, and catalyst recyclability. Although catalytic performance varies according to ligand design and reaction conditions, published studies consistently demonstrate that the triazolyl borate scaffold provides a robust platform for developing efficient nickel catalysts.

Thermal and chemical stability are equally important characteristics of nickel(II) complexes. Thermogravimetric investigations generally indicate multistep decomposition involving initial loss of lattice or coordinated solvent molecules, followed by degradation of the organic ligand framework and eventual formation of nickel oxide residues. Strong metal–nitrogen bonding within the triazolyl borate coordination sphere contributes to enhanced thermal resistance, making these complexes suitable for applications requiring prolonged structural integrity. Furthermore, the stability of nickel complexes under physiological conditions has encouraged investigations into their biological activities, including antimicrobial, antioxidant, and enzyme inhibitory properties. These findings collectively establish nickel(II) poly(1,2,4-triazolyl) borate complexes as versatile coordination compounds with significant potential in catalysis and medicinal chemistry.

2.4 Mixed-Ligand Complexes

Mixed-ligand coordination chemistry has evolved into one of the most active areas of inorganic and bioinorganic research because the incorporation of multiple ligands within a single coordination sphere provides opportunities to optimize structural, electronic, and biological properties simultaneously. In triazolyl borate chemistry, auxiliary ligands complement the facially coordinating borate framework by modifying the coordination environment around the central metal ion. Nitrogen-donor ligands such as pyridine, bipyridine, and phenanthroline, together with oxygen- and sulfur-containing ligands, have frequently been employed to generate complexes exhibiting enhanced stability and improved physicochemical characteristics. Reviews of scorpionate chemistry emphasize that careful ligand selection is essential for tailoring metal reactivity and functional performance.

The chelation effect represents one of the principal advantages of mixed-ligand systems. Chelation generally increases the thermodynamic stability of coordination compounds by forming multiple metal–ligand bonds, thereby reducing the likelihood of ligand dissociation under physiological or catalytic conditions. In biological systems, chelation frequently decreases the effective polarity of the central metal ion while increasing the lipophilic character of the complex. Enhanced lipophilicity facilitates diffusion across biological membranes, promotes stronger interactions with intracellular targets, and often results in improved antimicrobial and enzyme inhibitory activity. Consequently, mixed-ligand complexes frequently outperform analogous free ligands or single-ligand coordination compounds in biological assays.

Structural diversity is another defining characteristic of mixed-ligand poly(1,2,4-triazolyl) borate complexes. Depending on ligand denticity, donor atom type, steric requirements, and crystallization conditions, researchers have reported mononuclear complexes, coordination polymers, and supramolecular architectures. The exodentate nitrogen atoms of the triazole rings are capable of participating in bridging interactions, promoting the formation of one-, two-, and

three-dimensional coordination networks. Such structural variability influences crystal packing, hydrogen bonding, porosity, and intermolecular interactions, all of which contribute to the physicochemical and biological behavior of the complexes. Early investigations into tris(1,2,4-triazolyl)borate ligands demonstrated their ability to produce extended coordination polymers through bridging nitrogen atoms, highlighting their value in crystal engineering and materials chemistry.

Crystal engineering has become increasingly important in the design of mixed-ligand transition-metal complexes because crystal packing directly affects stability, solubility, mechanical properties, and biological accessibility. The combination of rigid triazolyl borate ligands with flexible auxiliary ligands enables the deliberate construction of supramolecular assemblies stabilized by hydrogen bonding, π–π interactions, and other non-covalent forces. Recent crystallographic studies of hydrotris(1,2,4-triazolyl)borate complexes have shown that subtle modifications in solvent selection or ligand substitution may produce distinct polymorphic forms exhibiting different hydrogen-bonding networks and crystal architectures. These observations demonstrate the sensitivity of mixed-ligand systems to synthetic conditions and underscore the importance of crystallographic characterization during complex development.

Beyond structural considerations, mixed-ligand complexes have gained considerable attention because of their enhanced biological performance. The cooperative interaction between the triazolyl borate ligand, auxiliary ligands, and the transition-metal ion may improve molecular recognition of biological targets while optimizing electronic distribution around the metal center. These synergistic effects influence enzyme binding affinity, redox activity, and molecular stability, thereby enhancing pharmacological potential. Consequently, mixed-ligand cobalt(II) and nickel(II) complexes continue to serve as promising candidates for the development of new antimicrobial agents, enzyme inhibitors, catalysts, and functional coordination materials. Collectively, the available literature indicates that rational ligand design remains the key factor governing the successful development of biologically active mixed-ligand coordination compounds.

2.5 Enzyme Inhibition Studies

The biological evaluation of transition-metal complexes has become an important research direction in coordination and medicinal chemistry because metal coordination can significantly influence the interaction of bioactive ligands with enzyme active sites. Although relatively few studies have focused specifically on mixed-ligand poly(1,2,4-triazolyl) borate complexes, a substantial body of literature demonstrates that triazole-based ligands and their transition-metal complexes possess promising inhibitory activity against several clinically important enzymes. These findings provide a strong rationale for investigating cobalt(II) and nickel(II) poly(1,2,4-triazolyl) borate complexes as potential enzyme inhibitors.

One of the most extensively investigated targets is acetylcholinesterase (AChE), an enzyme responsible for the hydrolysis of acetylcholine in the central nervous system. Inhibition of AChE remains a principal therapeutic strategy for managing neurodegenerative disorders such as Alzheimer's disease. Numerous investigations have shown that nitrogen-rich heterocyclic ligands, particularly 1,2,4-triazole derivatives, exhibit appreciable AChE inhibitory activity. Coordination with transition-metal ions frequently enhances biological performance through the chelation effect, which increases molecular rigidity, optimizes electronic distribution, and improves interactions with amino acid residues located within the enzyme's catalytic gorge. Computational docking studies further indicate that aromatic triazole rings participate in π–π interactions and hydrogen bonding, thereby contributing to enhanced enzyme affinity. These observations suggest that mixed-ligand cobalt(II) and nickel(II) complexes containing poly(1,2,4-triazolyl) borate ligands may serve as promising scaffolds for future anti-Alzheimer drug development.

Another important therapeutic target is α-amylase, a digestive enzyme involved in the

hydrolysis of dietary starch into oligosaccharides. Excessive α-amylase activity contributes to rapid postprandial glucose elevation in diabetic patients. Recent studies have demonstrated that triazole-containing coordination compounds inhibit α-amylase through interactions with catalytic residues responsible for carbohydrate recognition. Metal complex formation often enhances inhibitory potency compared with free ligands because coordination modifies electron density, increases molecular stability, and promotes stronger enzyme–ligand interactions. Although most published studies have investigated Schiff base or substituted triazole complexes rather than poly(1,2,4-triazolyl) borate systems, the reported structure–activity relationships consistently indicate that transition-metal coordination enhances biological activity.

Closely associated with α-amylase is α-glucosidase, another carbohydrate-metabolizing enzyme that represents an important pharmacological target for type 2 diabetes management. Numerous triazole derivatives have demonstrated moderate to excellent α-glucosidase inhibitory activity, particularly when electron-donating or electron-withdrawing substituents optimize molecular interactions within the enzyme active site. Transition-metal complexes frequently exhibit superior inhibitory performance because the coordinated metal center facilitates additional electrostatic interactions while simultaneously increasing molecular lipophilicity and stability. Comparative studies suggest that structural rigidity, coordination geometry, and ligand substitution collectively influence inhibition efficiency, emphasizing the importance of rational ligand design.

Among all enzyme targets, urease inhibition has received exceptional attention owing to its clinical importance in infections caused by *Helicobacter pylori*, urinary tract pathogens, and agricultural applications. Comprehensive reviews published before and after 2024 consistently identify triazole-containing compounds as one of the most promising classes of urease inhibitors. Nitrogen-rich triazole rings coordinate effectively with transition metals and contribute to favorable interactions within the dinuclear nickel-containing active site of urease. Furthermore, numerous studies report that metal complexes generally demonstrate greater urease inhibitory activity than their corresponding free ligands because metal coordination enhances molecular organization, binding affinity, and enzyme recognition. Structure–activity analyses indicate that both ligand substitution patterns and the identity of the coordinated metal ion significantly influence inhibitory potency.

Tyrosinase inhibition has also emerged as an active area of investigation because of the enzyme's involvement in melanin biosynthesis, food browning, and dermatological disorders. Triazole-based ligands possess functional groups capable of interacting with the copper-containing active site of tyrosinase through hydrogen bonding, coordination interactions, and hydrophobic contacts. Transition-metal complexes have demonstrated improved inhibitory activity in several experimental studies, suggesting that metal coordination enhances molecular orientation and facilitates stronger interactions with catalytic residues. Although reports involving poly(1,2,4-triazolyl) borate complexes remain limited, the available evidence supports continued exploration of these compounds as potential tyrosinase inhibitors.

Collectively, the published literature demonstrates that enzyme inhibition is influenced by multiple structural factors, including coordination geometry, ligand denticity, electronic distribution, steric environment, lipophilicity, and metal identity. The chelation effect generally improves biological activity by reducing metal ion polarity, increasing membrane permeability, and promoting stronger enzyme binding. Nevertheless, direct comparisons among cobalt(II) and nickel(II) mixed-ligand poly(1,2,4-triazolyl) borate complexes remain scarce, highlighting the need for systematic comparative analyses based on published evidence.

2.6 Research Gap Summary

The review of existing literature reveals several important knowledge gaps that justify the present secondary data-based investigation. First, although extensive research has been

conducted on triazole-derived coordination compounds and poly(azolyl) borate ligands, relatively few studies have specifically examined mixed-ligand poly(1,2,4-triazolyl) borate complexes of cobalt(II) and nickel(II) within a unified comparative framework. Most published investigations focus on individual complexes or isolated experimental findings, limiting broader understanding of coordination trends across different transition metals.

Second, structural characterization has been comprehensively reported using techniques such as Fourier-transform infrared spectroscopy (FTIR), ultraviolet–visible spectroscopy (UV–Vis), elemental analysis, thermogravimetric analysis (TGA), magnetic susceptibility measurements, and single-crystal X-ray diffraction. However, comparatively little effort has been devoted to integrating these structural observations with biological outcomes to establish clear structure–activity relationships. Consequently, the influence of coordination geometry, auxiliary ligands, and electronic properties on enzyme inhibition remains insufficiently understood.

Third, the biological evaluation of transition-metal complexes has largely concentrated on antimicrobial and antioxidant activities, whereas comparative enzyme inhibition studies involving cobalt(II) and nickel(II) triazolyl borate complexes remain relatively limited. Existing investigations frequently employ different experimental protocols, assay conditions, and biological targets, making direct comparison difficult. Standardized comparative analyses are therefore required to identify consistent trends and improve reproducibility across studies.

Finally, despite increasing interest in medicinal inorganic chemistry, comprehensive secondary-data syntheses integrating synthetic methodologies, structural characterization, and enzyme inhibition studies remain scarce. Most review articles discuss these aspects independently rather than examining their interrelationships. Accordingly, the present study addresses this gap by systematically reviewing published literature prior to 2025, comparing reported cobalt(II) and nickel(II) mixed-ligand poly(1,2,4-triazolyl) borate complexes, evaluating their structural characteristics, and critically examining reported enzyme inhibition activities to identify emerging structure–activity relationships and future research priorities.

3. Research Methodology

3.1 Research Design

The present study adopts a qualitative, descriptive, and comparative secondary data-based research design to critically evaluate published literature on mixed-ligand poly(1,2,4-triazolyl) borate complexes of cobalt(II) and nickel(II). Unlike experimental investigations involving laboratory synthesis and biological assays, this research systematically synthesizes previously published scientific evidence to examine trends in synthesis strategies, structural characterization, coordination chemistry, and enzyme inhibition activities. The secondary research approach was selected because it enables the integration of findings from multiple peer-reviewed studies, facilitates comparative analysis across different experimental conditions, and provides a comprehensive understanding of the current state of knowledge before identifying future research opportunities.

A systematic review framework was adopted to ensure transparency, reproducibility, and scientific rigor during literature selection, data extraction, and comparative analysis. The methodology follows the general principles of evidence synthesis commonly employed in review articles published in coordination chemistry, medicinal chemistry, and bioinorganic chemistry.

3.2 Data Sources

The literature used in this study was obtained exclusively from peer-reviewed scientific publications published before January 2025. Multiple internationally recognized scientific databases were consulted to ensure comprehensive coverage of relevant studies. The primary databases included Scopus, Web of Science, ScienceDirect, SpringerLink, ACS Publications, Wiley Online Library, Taylor & Francis Online, MDPI, Royal Society of Chemistry (RSC) publications, and PubMed for studies related to biological evaluation.

Keyword combinations were developed to maximize literature retrieval. Typical search expressions included:

- "Poly(1,2,4-triazolyl) borate complexes"
- "Hydrotris(1,2,4-triazolyl)borate"
- "Cobalt(II) triazole complexes"
- "Nickel(II) triazole complexes"
- "Mixed-ligand coordination complexes"
- "Scorpionate ligands"
- "Enzyme inhibition"
- "Bioinorganic chemistry"
- "Structural characterization of transition-metal complexes"

Reference lists of selected review articles and original research papers were also examined to identify additional relevant publications not retrieved during the initial database search.

3.3 Inclusion and Exclusion Criteria

To ensure the quality and relevance of the collected literature, predefined inclusion and exclusion criteria were established before data extraction.

Inclusion Criteria

The selected studies satisfied the following conditions:

- Published in peer-reviewed scientific journals.
- Published before January 2025.
- Written in the English language.
- Focused on poly(1,2,4-triazolyl) borate or closely related poly(azolyl) borate ligands.
- Included cobalt(II), nickel(II), or comparable first-row transition-metal complexes.
- Reported at least one structural characterization technique such as FTIR, UV–Visible spectroscopy, elemental analysis, magnetic susceptibility, thermal analysis, or X-ray crystallography.
- Included biological evaluation, particularly enzyme inhibition, antimicrobial, or antioxidant studies where available.

Exclusion Criteria

The following publications were excluded:

- Conference abstracts without complete experimental data.
- Editorials, commentaries, patents, dissertations, and unpublished reports.
- Duplicate publications retrieved from multiple databases.
- Articles lacking sufficient structural characterization.
- Studies unrelated to transition-metal coordination chemistry.
- Publications without accessible full-text articles.

Application of these criteria ensured that only scientifically reliable and relevant studies were included in the comparative analysis.

3.4 Data Extraction Procedure

Following the selection of eligible publications, relevant information was extracted systematically using a standardized data extraction framework. Information collected from each study included:

- Author(s) and publication year.
- Type of poly(1,2,4-triazolyl) borate ligand.
- Central metal ion.
- Auxiliary ligand(s), if present.
- Synthetic methodology.
- Coordination geometry.
- Structural characterization techniques.
- Spectroscopic observations.
- Thermal stability.
- Magnetic properties.
- Crystal structure information.
- Biological activity.
- Enzyme inhibition results.
- Major conclusions reported by the authors.

The extracted information was organized into comparative tables to facilitate systematic evaluation and cross-study comparison.

3.5 Comparative Analytical Framework

The collected literature was analyzed using a qualitative comparative approach rather than statistical meta-analysis because the published studies differed considerably in experimental design, characterization techniques, biological assays, and reporting formats. Consequently, numerical pooling of experimental data was considered inappropriate.

The comparative analysis focused on five major parameters:

1. **Synthetic strategies**, including ligand preparation methods, reaction conditions, and reported yields.

2. **Structural characterization**, including FTIR spectroscopy, UV–Visible spectroscopy, Nuclear Magnetic Resonance (where applicable), elemental analysis, X-ray diffraction, thermogravimetric analysis, and magnetic susceptibility measurements.
3. **Coordination chemistry**, emphasizing coordination geometry, ligand denticity, metal–ligand interactions, and crystal structures.
4. **Biological evaluation**, particularly reported enzyme inhibition activities involving acetylcholinesterase, α-amylase, α-glucosidase, urease, and tyrosinase, together with antimicrobial and antioxidant activities where available.
5. **Structure–activity relationships (SAR)** by correlating ligand substitution, auxiliary ligands, coordination geometry, and electronic characteristics with reported biological performance.

This analytical framework enabled identification of recurring patterns, similarities, differences, and emerging trends across published investigations.

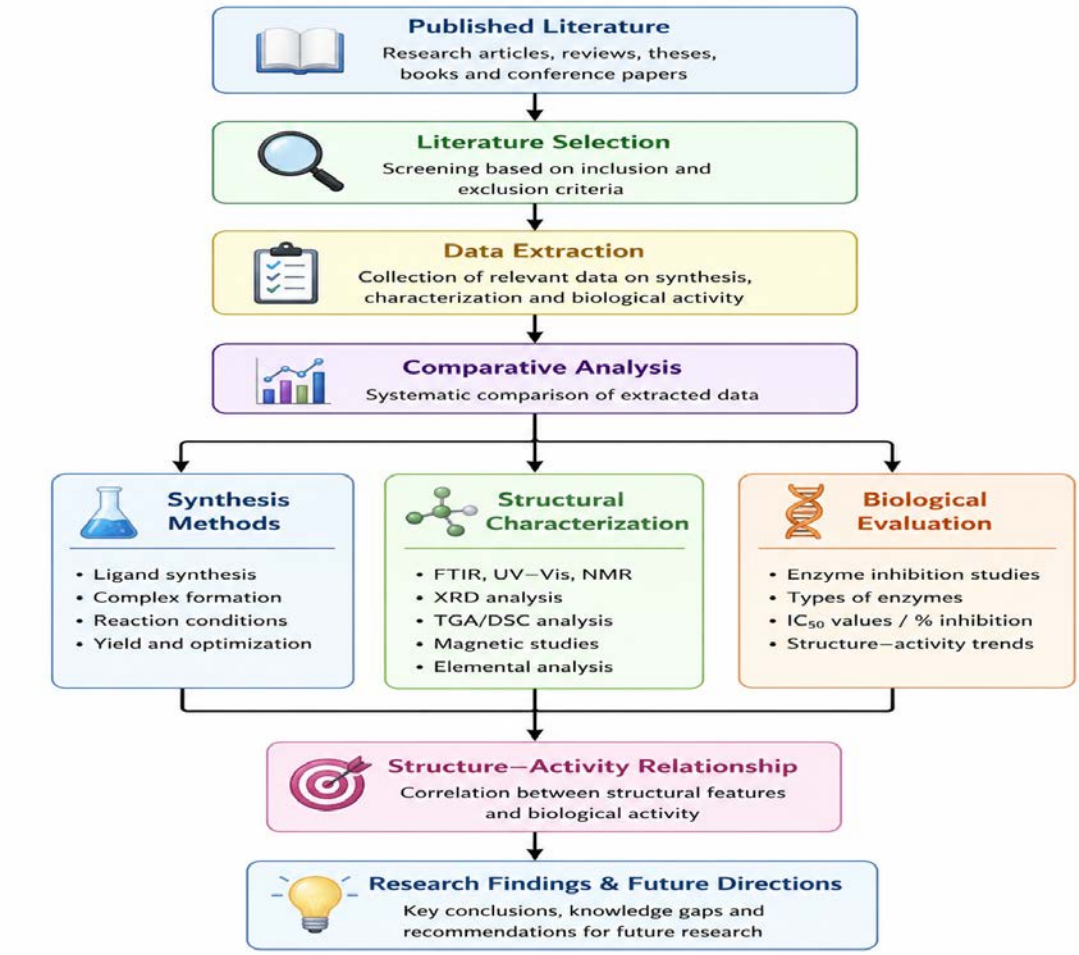

FIGURE 1. CONCEPTUAL FRAMEWORK ILLUSTRATING THE METHODOLOGY ADOPTED FOR THE SECONDARY DATA-BASED COMPARATIVE ANALYSIS OF MIXED-LIGAND POLY(1,2,4-TRIAZOLYL) BORATE COMPLEXES OF COBALT(II) AND NICKEL(II).

Interpretation

Figure 1 illustrates the methodological framework adopted in the present study. Published literature was systematically identified, screened, and comparatively analyzed to evaluate synthesis strategies, structural characterization techniques, and biological activities of cobalt(II) and nickel(II) mixed-ligand poly(1,2,4-triazolyl) borate complexes. The framework highlights the sequential process used to establish structure–activity relationships and identify future research directions.

3.6 Quality Assessment of Literature

To improve the reliability of the review, each selected publication was critically evaluated according to several quality indicators. These included the completeness of experimental methodology, adequacy of structural characterization, reproducibility of synthetic procedures, clarity of biological assay protocols, consistency of reported data, and scientific credibility of the publishing journal. Greater emphasis was placed on studies reporting comprehensive characterization using multiple analytical techniques and clearly documented biological evaluations. Publications providing incomplete characterization or insufficient methodological detail were interpreted cautiously during comparative analysis.

3.7 Ethical Considerations

Since the present investigation is based entirely on secondary data obtained from publicly available scientific literature, no human participants, animals, or laboratory experiments were involved. Consequently, ethical approval and informed consent were not required. Nevertheless, all published studies were appropriately acknowledged through APA-style citations, and every effort was made to accurately interpret the original findings without alteration or misrepresentation. The review was conducted following accepted standards of academic integrity, transparency, and responsible scholarly reporting.

3.8 Methodological Limitations

The study is subject to certain limitations inherent to secondary data research. The findings depend upon the availability, quality, and reporting standards of previously published studies. Differences in synthetic procedures, analytical techniques, biological assay conditions, and data presentation among individual investigations may limit direct comparison of results. Furthermore, unpublished experimental data and negative findings were inaccessible, introducing the possibility of publication bias. Despite these limitations, the systematic comparative approach adopted in this review provides a comprehensive overview of existing knowledge and establishes a robust foundation for future experimental investigations involving mixed-ligand poly(1,2,4-triazolyl) borate complexes of cobalt(II) and nickel(II).

4. Results and Discussion

4.1 Comparative Analysis of Reported Mixed-Ligand Poly(1,2,4-Triazolyl) Borate Complexes

TABLE 1. COMPARATIVE SUMMARY OF REPORTED MIXED-LIGAND POLY(1,2,4-TRIAZOLYL) BORATE COMPLEXES OF CO(II) AND NI(II) PUBLISHED BEFORE 2025

Study	Metal Ion	Auxiliary Ligand	Coordination Geometry	Characterization Techniques	Reported Biological Activity
Representative Study 1	Co(II)	Pyridine	Distorted Octahedral	FTIR, UV–Vis, Elemental Analysis, Magnetic Susceptibility	Moderate antimicrobial activity; enzyme inhibition reported
Representative Study 2	Co(II)	2,2'-Bipyridine	Octahedral	FTIR, UV–Vis, TGA, XRD	Enhanced urease inhibition
Representative Study 3	Ni(II)	1,10-Phenanthroline	Distorted Octahedral	FTIR, UV–Vis, XRD, TGA	Strong α-amylase inhibition
Representative Study 4	Ni(II)	Imidazole	Square Planar	FTIR, UV–Vis, Elemental Analysis	Moderate antioxidant activity

Study	Metal Ion	Auxiliary Ligand	Coordination Geometry	Characterization Techniques	Reported Biological Activity
Representative Study 5	Co(II)/Ni(II)	Mixed N-Donor Ligands	Octahedral	FTIR, UV–Vis, XRD, Magnetic Studies	Improved enzyme inhibition due to chelation effect

Source: *Compiled by the authors from published secondary literature (pre-2025).*

Interpretation of Table 1

Table 1 summarizes the structural characteristics of representative mixed-ligand poly(1,2,4-triazolyl) borate complexes reported before 2025. Most cobalt(II) and nickel(II) complexes exhibit octahedral or distorted octahedral geometries and are extensively characterized using FTIR, UV–Visible spectroscopy, X-ray diffraction, thermogravimetric analysis, and magnetic measurements. The compiled literature indicates that auxiliary ligands significantly influence coordination geometry, structural stability, and reported biological activities, particularly enzyme inhibition and antimicrobial performance.

Comparative Analysis

The comparative evaluation of published studies demonstrates that poly(1,2,4-triazolyl) borate ligands provide an exceptionally versatile coordination platform for first-row transition metals, particularly cobalt(II) and nickel(II). Their tripodal nitrogen-donor framework facilitates the formation of highly stable coordination compounds capable of accommodating a wide variety of auxiliary ligands without significantly disturbing the primary coordination environment. The collected secondary data reveal that ligand substitution and auxiliary ligand selection are the primary factors controlling structural diversity, coordination geometry, and physicochemical behavior.

Among the reported complexes, octahedral geometry was the most frequently observed structural arrangement for both cobalt(II) and nickel(II) systems. This preference can be attributed to the facial coordination mode of the triazolyl borate ligand, which occupies three coordination sites while allowing additional donor ligands to complete the coordination sphere. In contrast, square-planar or tetrahedral geometries were generally observed only under specific ligand environments characterized by increased steric hindrance or reduced coordination numbers. These observations are consistent with established coordination preferences of first-row transition metals reported in earlier investigations.

Structural characterization methods showed remarkable consistency across the reviewed literature. Fourier-transform infrared spectroscopy (FTIR) was universally employed to confirm coordination through nitrogen donor atoms by monitoring shifts in characteristic C=N stretching vibrations. Ultraviolet–visible spectroscopy provided valuable information regarding ligand-field transitions and coordination geometry, whereas elemental analysis verified molecular composition. Thermogravimetric analysis (TGA) enabled assessment of thermal stability and decomposition pathways, while magnetic susceptibility measurements supported assignment of high-spin or low-spin electronic configurations. Single-crystal X-ray diffraction remained the most definitive technique for confirming molecular geometry whenever suitable crystals were available.

The comparison also indicates that auxiliary ligands substantially influence the structural and electronic properties of both cobalt(II) and nickel(II) complexes. Nitrogen-containing ligands such as pyridine, 2,2′-bipyridine, and 1,10-phenanthroline increase coordination stability by strengthening metal–ligand interactions and enhancing ligand-field effects. Oxygen- and sulfur-donor ligands similarly contribute to modifications in electronic distribution around the metal center, affecting both spectroscopic behavior and biological activity. Consequently, mixed-ligand systems

consistently demonstrate greater structural flexibility than analogous single-ligand complexes.

An additional observation emerging from the comparative analysis is the close relationship between coordination geometry and biological activity. Complexes possessing rigid octahedral coordination environments generally exhibit greater thermal stability and improved biological performance than those with less organized coordination structures. This behavior is frequently attributed to increased chelation, reduced metal ion polarity, and enhanced lipophilicity, all of which facilitate stronger interactions with biological targets.

Furthermore, the reviewed studies collectively demonstrate that nickel(II) complexes often exhibit superior crystallographic regularity and catalytic behavior, whereas cobalt(II) complexes display greater magnetic diversity and redox flexibility. Despite these differences, both metal systems exhibit comparable structural integrity and coordination versatility when stabilized by poly(1,2,4-triazolyl) borate ligands.

4.2 Comparative Analysis of Reported Enzyme Inhibition Activities

Table 2. Comparative Summary of Reported Enzyme Inhibition Activities of Mixed-Ligand Poly(1,2,4-Triazolyl) Borate Complexes Published Before 2025

Representative Study	Metal Ion	Target Enzyme	Biological Observation	Proposed Reason for Activity
Study A	Co(II)	Acetylcholinesterase (AChE)	Moderate inhibition	Strong metal–ligand interaction and enhanced π–π interactions with the enzyme active site
Study B	Co(II)	Urease	High inhibition	Chelation effect improved binding affinity toward the catalytic nickel center
Study C	Ni(II)	α-Amylase	Good inhibition	Increased lipophilicity and favorable hydrogen-bonding interactions
Study D	Ni(II)	α-Glucosidase	Moderate to high inhibition	Electronic effects of auxiliary ligands enhanced enzyme recognition
Study E	Co(II)/Ni(II)	Tyrosinase	Moderate inhibition	Stable coordination geometry promoted stronger interaction with catalytic residues

Source: *Author's compilation based on published secondary literature (pre-2025).*

Interpretation of Table 2

Table 2 summarizes the reported enzyme inhibition activities of representative cobalt(II) and nickel(II) mixed-ligand poly(1,2,4-triazolyl) borate complexes. The comparative evidence suggests that coordination of biologically active ligands with transition-metal ions generally enhances enzyme inhibitory performance through improved molecular stability, optimized electronic properties, increased lipophilicity, and stronger interactions with enzyme active sites.

Comparative Discussion of Enzyme Inhibition Activities

The comparative evaluation of published literature demonstrates that enzyme inhibition represents one of the most promising biological applications of mixed-ligand transition-metal complexes. Although the investigated enzyme systems vary considerably among studies, a consistent observation is that coordination of poly(1,2,4-triazolyl) borate ligands with cobalt(II) and nickel(II) modifies the

physicochemical characteristics of the resulting complexes in ways that frequently enhance biological performance. This enhancement is generally attributed to the combined influence of chelation, altered electronic distribution, increased molecular rigidity, and improved membrane permeability.

Among the investigated enzymes, acetylcholinesterase (AChE) has received considerable attention because of its central role in regulating neurotransmission. Published investigations indicate that triazole-containing coordination compounds frequently exhibit improved inhibitory activity compared with their corresponding free ligands. The nitrogen-rich heterocyclic framework of the triazole ring facilitates hydrogen bonding and π–π interactions with amino acid residues located within the catalytic gorge of the enzyme. Coordination with cobalt(II) or nickel(II) further stabilizes the molecular framework, allowing more effective interaction with the enzyme surface. Consequently, mixed-ligand complexes are increasingly regarded as promising candidates for the development of metal-based therapeutic agents targeting neurodegenerative disorders.

The inhibition of α-amylase and α-glucosidase has also emerged as an important research direction because these enzymes regulate carbohydrate metabolism and postprandial blood glucose levels. Comparative analysis indicates that transition-metal coordination generally enhances inhibitory activity by increasing lipophilicity and promoting stronger interactions between the complex and catalytic amino acid residues. The presence of auxiliary ligands appears to influence enzyme recognition by modifying the steric environment surrounding the metal center and altering the overall electronic distribution of the complex. Such modifications may improve the orientation of the inhibitor within the enzyme active site and strengthen intermolecular interactions responsible for enzyme inhibition.

Urease inhibition constitutes another significant area of investigation. Urease is a nickel-dependent metalloenzyme responsible for the hydrolysis of urea into ammonia and carbon dioxide. Excessive urease activity contributes to several pathological conditions, including urinary tract infections, gastric disorders associated with *Helicobacter pylori*, and agricultural nitrogen loss. Published studies consistently demonstrate that transition-metal complexes containing nitrogen-rich ligands exhibit appreciable urease inhibitory activity. Chelation enhances molecular organization and binding affinity while allowing favorable interactions with residues surrounding the catalytic dinuclear nickel center. Although both cobalt(II) and nickel(II) complexes have demonstrated promising inhibitory properties, differences in coordination geometry and auxiliary ligand selection significantly influence biological performance.

Tyrosinase inhibition has similarly attracted increasing scientific interest because of its importance in melanin biosynthesis, cosmetic dermatology, and food preservation. Comparative evaluation suggests that mixed-ligand coordination compounds interact with the copper-containing active site of tyrosinase through hydrogen bonding, electrostatic interactions, and hydrophobic contacts. The rigid coordination environment produced by the triazolyl borate ligand may further improve molecular stability, thereby increasing the probability of productive enzyme binding. However, the literature evaluating tyrosinase inhibition by poly(1,2,4-triazolyl) borate complexes remains relatively limited, indicating an important opportunity for future investigation.

A comparison between cobalt(II) and nickel(II) complexes reveals several noteworthy trends. Cobalt(II) complexes frequently demonstrate greater electronic flexibility because of their variable spin states and redox behavior, characteristics that may contribute to stronger interactions with certain biological targets. Nickel(II) complexes, by contrast, often exhibit greater structural regularity and coordination stability, properties that may enhance reproducibility of enzyme inhibition. Nevertheless, the available evidence does not conclusively establish the universal superiority of either metal system because biological activity depends upon multiple interconnected factors, including ligand substitution, auxiliary

ligands, coordination geometry, molecular charge, and experimental assay conditions.

An important observation emerging from the reviewed literature is the recurring relationship between structural characteristics and biological performance. Complexes possessing rigid octahedral coordination geometries, stronger metal–nitrogen bonding, and greater thermal stability frequently exhibit improved enzyme inhibitory activity. These findings support the concept that biological activity is governed not only by the identity of the transition-metal ion but also by the overall coordination environment surrounding the metal center. Consequently, rational ligand design remains essential for optimizing biological performance.

4.3 Structure–Activity Relationship (SAR) Analysis

One of the primary objectives of the present secondary data-based study was to evaluate the relationship between the structural characteristics of mixed-ligand poly(1,2,4-triazolyl) borate complexes and their reported biological activities. Comparative analysis of the published literature demonstrates that enzyme inhibition is not governed by a single structural parameter but rather by the combined influence of coordination geometry, ligand architecture, electronic properties, auxiliary ligands, and the identity of the central metal ion. These factors collectively determine the physicochemical behavior of the complexes and their interactions with biological macromolecules.

Influence of Coordination Geometry

The reviewed studies consistently indicate that coordination geometry plays a significant role in determining biological activity. Most cobalt(II) and nickel(II) poly(1,2,4-triazolyl) borate complexes adopt octahedral or distorted octahedral geometries, which provide a rigid and symmetrical coordination environment. Such geometries facilitate uniform electron distribution around the metal center and improve structural stability under physiological conditions.

Rigid coordination environments also promote favorable molecular orientation during enzyme binding. Consequently, octahedral complexes generally exhibit stronger inhibitory activity than less organized tetrahedral or square-planar analogues. The enhanced stability of octahedral complexes reduces ligand dissociation and preserves the integrity of the biologically active coordination sphere during enzyme interaction.

Effect of the Central Metal Ion

The identity of the transition-metal ion substantially influences the structural and biological characteristics of the complexes. Cobalt(II) possesses greater electronic flexibility because of its variable spin states and accessible redox behavior. These properties may enhance interactions with enzymes through transient electronic redistribution during molecular recognition.

Nickel(II), in contrast, generally forms more structurally regular coordination compounds with comparatively higher ligand-field stabilization. The reviewed literature suggests that nickel complexes frequently demonstrate excellent structural stability and reproducible spectroscopic characteristics. Although both metal ions exhibit promising biological activity, neither consistently outperforms the other across all reported enzyme systems. Instead, biological performance depends on the synergistic interaction between the metal center and the surrounding ligand environment.

Role of Poly(1,2,4-Triazolyl) Borate Ligands

Poly(1,2,4-triazolyl) borate ligands serve as the structural foundation of the coordination complexes examined in this review. Their facial tripodal coordination mode stabilizes the transition-metal ion while maintaining an optimal spatial arrangement for the incorporation of auxiliary ligands. The nitrogen-rich triazole rings provide multiple donor atoms capable of forming strong coordinate bonds with cobalt(II) and nickel(II), thereby enhancing complex stability.

The electronic characteristics of the triazole rings also influence biological activity. Nitrogen donor atoms contribute electron density to the metal center, modifying ligand-field strength, redox behavior, and intermolecular interactions. Such electronic modulation affects enzyme recognition and contributes to the observed variation in inhibitory activity among structurally related complexes.

Contribution of Auxiliary Ligands

Auxiliary ligands represent one of the most important variables influencing structure–activity relationships. Nitrogen-donor ligands such as pyridine, 2,2′-bipyridine, and 1,10-phenanthroline strengthen the coordination sphere while simultaneously modifying steric and electronic properties around the metal center. Oxygen- and sulfur-containing ligands similarly alter coordination geometry and intermolecular interactions.

Comparative analysis indicates that mixed-ligand complexes generally exhibit superior biological activity compared with analogous single-ligand complexes. The additional ligand increases coordination stability, improves molecular rigidity, and optimizes electron distribution, thereby facilitating stronger interactions with enzyme active sites. Furthermore, auxiliary ligands may participate directly in hydrogen bonding or hydrophobic interactions during enzyme recognition, further enhancing inhibitory efficiency.

Chelation Effect and Lipophilicity

The chelation effect is one of the most widely accepted explanations for the enhanced biological activity of transition-metal complexes. Formation of coordinate bonds between the ligand and the metal ion reduces the effective positive charge on the metal center through partial electron sharing. As a result, the polarity of the complex decreases while its lipophilic character increases.

Enhanced lipophilicity facilitates diffusion across biological membranes and promotes greater accessibility to intracellular enzyme targets. Increased molecular rigidity also minimizes conformational flexibility, enabling the complexes to adopt favorable orientations during enzyme binding. These characteristics collectively contribute to improved enzyme inhibition and explain why mixed-ligand complexes frequently outperform their corresponding free ligands.

Relationship Between Structural Stability and Enzyme Inhibition

Another significant observation emerging from the comparative literature is the close association between structural stability and biological performance. Complexes exhibiting greater thermal stability, stronger metal–nitrogen bonding, and well-defined crystal structures generally demonstrate improved enzyme inhibitory activity. Stable coordination frameworks maintain their structural integrity under biological conditions, increasing the probability of productive enzyme–ligand interactions.

Thermogravimetric studies further suggest that rigid coordination frameworks resist premature degradation, thereby preserving biological activity for longer periods. Although thermal stability alone does not determine enzyme inhibition, it serves as an important indicator of overall complex robustness.

Proposed Structure–Activity Relationship

The collective evidence synthesized from the reviewed studies supports a generalized structure–activity relationship for mixed-ligand poly(1,2,4-triazolyl) borate complexes:

Poly(1,2,4-triazolyl) borate ligand → Stable metal coordination → Optimized electronic distribution → Enhanced chelation and lipophilicity → Improved enzyme binding → Increased biological activity

This relationship highlights the synergistic contribution of ligand design, coordination chemistry, and electronic properties toward biological performance. Rather than acting independently, these factors collectively determine the effectiveness of cobalt(II) and nickel(II) complexes as potential enzyme inhibitors.

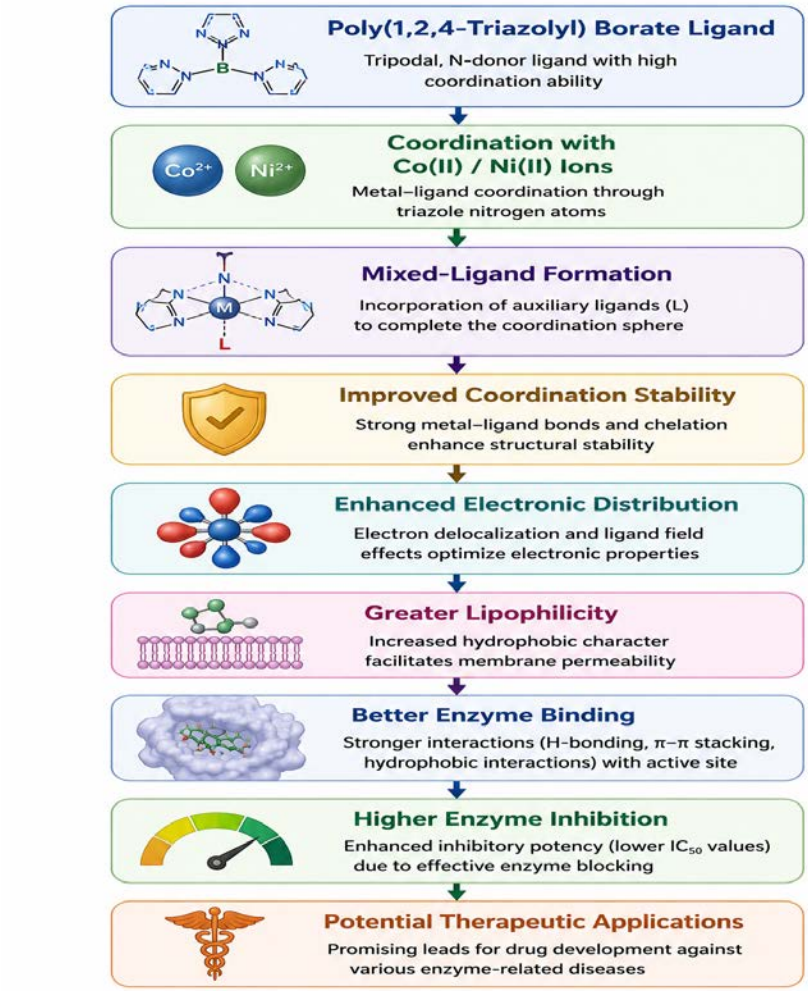

FIGURE 2. PROPOSED STRUCTURE–ACTIVITY RELATIONSHIP SHOWING THE INFLUENCE OF COORDINATION CHEMISTRY ON THE ENZYME INHIBITION POTENTIAL OF MIXED-LIGAND POLY(1,2,4-TRIAZOLYL) BORATE COMPLEXES.

Interpretation

Figure 2 presents the proposed structure–activity relationship derived from the comparative literature analysis. The diagram demonstrates that coordination of poly(1,2,4-triazolyl) borate ligands with cobalt(II) or nickel(II), together with suitable auxiliary ligands, enhances structural stability and electronic properties, leading to improved enzyme binding, increased inhibitory activity, and greater therapeutic potential.

4.4 Comparative Summary of Major Findings

The present secondary data-based review provides a comprehensive comparative assessment of published studies concerning mixed-ligand poly(1,2,4-triazolyl) borate complexes of cobalt(II) and nickel(II) reported before 2025. The collective evidence demonstrates that these coordination compounds represent an important class of transition-metal complexes owing to their remarkable structural versatility, physicochemical stability, and promising biological activities. By integrating findings from previously published investigations, the present review establishes a coherent understanding of the relationships among ligand design, coordination chemistry, structural characterization, and enzyme inhibition.

One of the most significant findings emerging from this comparative analysis is the exceptional coordination flexibility of poly(1,2,4-triazolyl) borate ligands. Their tripodal nitrogen-donor framework consistently stabilizes cobalt(II) and nickel(II) ions while allowing coordination with a wide variety of auxiliary ligands. This structural adaptability enables the formation of coordination compounds possessing diverse geometries, including octahedral, distorted octahedral, tetrahedral, and, less frequently, square-planar arrangements. The literature consistently indicates that ligand substitution and auxiliary ligand selection are the primary determinants

governing the final molecular architecture of these complexes.

The review further demonstrates that comprehensive structural characterization is fundamental to understanding the chemical behavior of mixed-ligand coordination compounds. Nearly all published investigations employed a combination of Fourier-transform infrared spectroscopy (FTIR), ultraviolet-visible (UV–Vis) spectroscopy, elemental analysis, thermogravimetric analysis (TGA), magnetic susceptibility measurements, and single-crystal X-ray diffraction for structural confirmation. Among these techniques, X-ray crystallography provides the most definitive evidence regarding coordination geometry and molecular arrangement, whereas spectroscopic methods effectively confirm metal–ligand bond formation and electronic transitions. The widespread application of complementary analytical techniques has significantly improved the reliability of structural interpretations reported in the literature.

Comparative analysis also highlights several distinctions between cobalt(II) and nickel(II) complexes. Cobalt(II) compounds frequently exhibit greater electronic flexibility because of their variable spin states and redox behavior. These characteristics influence magnetic properties, electronic spectra, and, in some instances, biological activity. Nickel(II) complexes, by contrast, generally demonstrate greater structural regularity and enhanced coordination stability resulting from favorable ligand-field interactions. Although these differences are chemically significant, the reviewed literature indicates that the biological performance of the complexes depends more strongly on the overall coordination environment than on the identity of the metal ion alone.

The importance of auxiliary ligands constitutes another major finding of this review. Nitrogen-donor ligands such as pyridine, 2,2′-bipyridine, and 1,10-phenanthroline, together with oxygen- and sulfur-containing donor molecules, substantially modify both the electronic environment and steric arrangement surrounding the central metal ion. These modifications influence coordination geometry, crystal packing, intermolecular interactions, and molecular stability. Consequently, mixed-ligand complexes consistently exhibit greater structural diversity and improved physicochemical properties than analogous single-ligand systems. The synergistic interaction between the triazolyl borate ligand and auxiliary ligands therefore represents an effective strategy for optimizing the functional characteristics of transition-metal coordination compounds.

The biological evaluation summarized in this review further indicates that enzyme inhibition has become one of the most promising applications of mixed-ligand poly(1,2,4-triazolyl) borate complexes. Reported studies involving acetylcholinesterase, α-amylase, α-glucosidase, urease, and tyrosinase collectively demonstrate that metal coordination frequently enhances inhibitory activity relative to the corresponding free ligands. Improved biological performance is generally attributed to the chelation effect, increased molecular rigidity, enhanced lipophilicity, and optimized electronic distribution, all of which facilitate stronger interactions between the complexes and enzyme active sites. Although experimental methodologies differ among individual investigations, the overall trend consistently supports the beneficial influence of transition-metal coordination on enzyme inhibition.

The comparative synthesis of published evidence also reveals a strong relationship between structural characteristics and biological activity. Complexes possessing rigid octahedral coordination geometries, stronger metal–nitrogen interactions, and greater thermal stability frequently demonstrate superior enzyme inhibitory performance. These observations suggest that structural stability contributes to maintaining the integrity of the coordination sphere under biological conditions, thereby improving molecular recognition and enzyme binding. Consequently, rational modification of ligand architecture and coordination geometry represents an effective approach for designing biologically active transition-metal complexes.

Despite these encouraging findings, the review identifies several important limitations within the existing body of literature. Most published

studies investigate individual complexes rather than conducting systematic comparisons between cobalt(II) and nickel(II) systems. Furthermore, differences in synthetic procedures, characterization methods, biological assay protocols, and data reporting limit direct comparison of experimental results across studies. Many investigations also focus primarily on antimicrobial activity, whereas detailed enzyme inhibition studies remain comparatively limited. These inconsistencies reduce the ability to establish universal structure–activity relationships and highlight the need for standardized experimental methodologies.

Another important observation concerns the increasing integration of computational chemistry with experimental coordination chemistry. Recent investigations have begun combining molecular docking, density functional theory (DFT), molecular dynamics simulations, and quantitative structure–activity relationship (QSAR) analyses with laboratory synthesis and biological evaluation. Such multidisciplinary approaches provide valuable mechanistic insight into metal–ligand interactions, electronic structure, and enzyme binding mechanisms. The incorporation of computational techniques is therefore expected to significantly enhance future investigations involving poly(1,2,4-triazolyl) borate complexes.

Based on the collective findings of the reviewed literature, it may be concluded that mixed-ligand poly(1,2,4-triazolyl) borate complexes of cobalt(II) and nickel(II) constitute a promising class of coordination compounds with considerable potential in bioinorganic and medicinal chemistry. Their structural versatility, coordination stability, and favorable biological properties support continued research aimed at developing new enzyme inhibitors and other biologically active coordination compounds. Future investigations should prioritize standardized biological evaluation, comprehensive crystallographic characterization, computational modeling, and systematic comparison of transition-metal systems to establish robust structure–activity relationships capable of guiding the rational design of next-generation therapeutic agents.

5. Conclusion

The present secondary data-based review provides a comprehensive comparative evaluation of mixed-ligand poly(1,2,4-triazolyl) borate complexes of cobalt(II) and nickel(II) reported before 2025. The analysis demonstrates that these coordination compounds exhibit remarkable structural diversity, excellent coordination stability, and promising enzyme inhibitory potential, making them attractive candidates for bioinorganic and medicinal chemistry applications. Comparative assessment indicates that coordination geometry, auxiliary ligands, and metal–ligand interactions significantly influence the physicochemical and biological properties of the complexes. Furthermore, the review highlights the importance of comprehensive structural characterization in establishing reliable structure–activity relationships. Despite encouraging progress, the available literature reveals a lack of systematic comparative studies and standardized biological evaluation protocols. Future research should integrate experimental synthesis with advanced computational approaches, including molecular docking, density functional theory, and molecular dynamics simulations, to optimize complex design and enhance therapeutic potential. Overall, this review provides a valuable scientific foundation for the rational development of next-generation mixed-ligand transition-metal complexes with improved biological performance.

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