Synthesis and Pharmacological Evaluation of Oxygen-Bridged Metal Complexes

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Abstract

This research investigates the synthesis, characterization, and pharmacological evaluation of oxygen-bridged metal complexes with significant antimicrobial and anticancer activities. The study involved the synthesis of novel oxygen-bridged complexes using transition metals including copper(II), nickel(II), cobalt(II), and iron(III) with various organic ligands. The objective was to develop metal complexes with enhanced bioactivity compared to their free ligands. Methodologically, complexes were synthesized via conventional condensation methods and characterized using spectroscopic techniques including IR, UV-Vis, NMR, and mass spectrometry. The pharmacological evaluation was conducted through antimicrobial assays against Gram-positive and Gram-negative bacteria, antifungal testing, and cytotoxicity studies against cancer cell lines. Results demonstrated that oxygen-bridged metal complexes exhibited superior antimicrobial activity with MIC values ranging from 1.56-32 μg/mL against various bacterial strains, significantly outperforming standard antibiotics. Anticancer evaluation revealed IC50 values in the range of 2.0-34 μM against different cancer cell lines, with selectivity indices exceeding 10, indicating preferential toxicity toward cancer cells over normal cells. The enhanced bioactivity was attributed to the synergistic effect of metal coordination, improved membrane permeability, and generation of reactive oxygen species. Discussion revealed that the oxygen-bridging mode enhanced stability and bioavailability of the complexes. In conclusion, oxygen-bridged metal complexes represent promising therapeutic agents with dual antimicrobial and anticancer properties, warranting further clinical investigation.

Keywords: *Metal complexes, Oxygen-bridged, Antimicrobial activity, Cytotoxicity, Coordination chemistry*

1. Introduction

Metal complexes have emerged as promising therapeutic agents in medicinal chemistry due to their unique properties including variable oxidation states, diverse coordination geometries, and ability to interact with biological molecules (Omer et al., 2024; Karati et al., 2024). The field of medicinal inorganic chemistry has witnessed significant advancement since the serendipitous discovery of cisplatin by Rosenberg in 1965, which revolutionized cancer treatment and opened new avenues for metal-based drug discovery (Kumar, 2022; Gonzalez-Cano et al., 2024). Oxygen-bridged metal complexes represent a unique class of coordination compounds where oxygen atoms serve as bridging ligands between metal centers, creating distinctive structural architectures and electronic properties (Bourget-Merle et al., 2017; Kumar et al., 2010). These complexes have gained considerable attention due to their enhanced stability, improved bioavailability, and synergistic effects between the metal center and organic ligands (Linoj et al., 2024). The oxygen-bridging motif not only stabilizes the metal complex but also facilitates specific interactions with biological targets, leading to enhanced pharmacological activity.

The increasing prevalence of antimicrobial resistance and the need for novel anticancer agents have prompted researchers to explore metal-based compounds as alternatives to traditional organic drugs (Frei et al., 2023; Balewski et al., 2024). Metal complexes offer unique advantages including multiple mechanisms of action, ability to overcome drug resistance, and potential for targeted therapy (Chohan et al., 2005; Egger et al., 2009). The coordination of bioactive ligands to metal centers often results in enhanced biological activity compared to the free ligands, attributed to improved cellular uptake, altered pharmacokinetics, and novel mechanisms of action. Recent studies have demonstrated that transition metal complexes exhibit significant antimicrobial activity through various mechanisms including membrane disruption, enzyme inhibition, and generation of reactive oxygen species (Jain & Mehata, 2017; McKenzie et al., 2019). Similarly, metal complexes have shown promising anticancer activity through DNA binding, mitochondrial targeting, and induction of apoptosis (Gurgul et al., 2020; Hosny et al., 2024). The development of oxygen-bridged metal complexes represents a strategic approach to combine the beneficial properties of metal coordination with enhanced stability and bioactivity.

2. Literature Review

The field of metal-based therapeutics has experienced remarkable growth over the past decades, with extensive research focusing on the development of novel metal complexes for various medical applications. Recent studies have shown significant progress in utilization of transition metal complexes as drugs to treat several human diseases. Transition metals exhibit different oxidation states and can interact with negatively charged molecules, making them attractive candidates for drug development.

2.1 Historical Perspective and Development

The journey of metal complexes in medicine began with traditional mineral medicine and evolved into modern metallodrug development (Karati et al., 2024). The transition from traditional applications to scientifically-based metallodrugs represents a significant milestone in pharmacology. One of the most notable examples is cisplatin, a platinum-based chemotherapeutic agent that revolutionized cancer treatment (Omer et al., 2024). This discovery paved the way for extensive research into metal-based therapeutic agents across various medical applications.

2.2 Mechanisms of Action

Metal complexes exhibit diverse mechanisms of biological activity that differ significantly from organic compounds. Transition metal complexes are gaining prominence as strategic antimicrobial candidates to combat the global crisis of microbial resistance, driven by the declining efficacy of conventional antibiotics (Frei et al., 2023). These complexes can overcome drug resistance through various mechanisms including generation of reactive oxygen species and penetration of biological membranes. Three-dimensional configurations of metal complexes formed by the coordination of organic ligands with the metal allow the complexes to react more effectively with biological molecules (Haas & Franz, 2009). The type of ligand has a significant effect on the chemical activities and subsequent medical applications of metal complexes, allowing for fine-tuning of their properties.

2.3 Antimicrobial Applications

The antimicrobial potential of metal complexes has been extensively studied, with particular focus on their ability to combat resistant pathogens (Jain & Mehata, 2017). Silver and its complexes have shown cytotoxic effects against Gram-positive/Gram-negative bacteria and fungi, much is not known about the exact mechanism of action of silver

except for its strong affinity to react with thiol groups (Chohan et al., 2005). 1,2,3-Triazoles and their molecular derivatives are well known for a plethora of physiological activities, including antibacterial and antifungal (Frei et al., 2023). The coordination of these bioactive ligands to metal centers often results in synergistic antimicrobial effects, with the complexes showing enhanced activity compared to the free ligands.

2.4 Anticancer Applications

The anticancer potential of metal complexes has been a major focus of research, particularly following the success of platinum-based drugs (Gurgul et al., 2020). Metal-based complexes have demonstrated significant anticancer effects and have emerged as candidates with great potential for cancer therapy (Omer et al., 2024). These agents are effective in a variety of cancers, including those resistant to conventional chemotherapeutic agents. Metal chelation to bioactive small molecules is a well-established strategy to enhance the biological activity of the resulting complexes (Balewski et al., 2024). The coordination of metal ions to hydroxylated organic cores often improves their natural bioactivities, including anticancer and antimicrobial effects.

2.5 Oxygen-Bridged Systems

Oxygen-bridged metal complexes represent a specialized class of coordination compounds with unique structural and electronic properties (Bourget-Merle et al., 2017). Among synthetic systems, the subclass of μ3-oxo-centered carboxylate-bridged trinuclear complexes has drawn particular interest for its redox activity, unique spin configurations, and well-defined supramolecular architectures (Linoj et al., 2024). These compounds have been investigated for their catalytic, magnetic, and biological properties. The copper(II) and nickel(II)-salicylaldoxime complexes have been used as complex ligands in the synthesis of oxygen bridge complexes and have shown significant activity against test bacteria (Kumar et al., 2010). The oxygen-bridging motif provides enhanced stability and can lead to improved biological activity through specific molecular interactions.

3. Objectives

The primary objectives of this research were:

1. To synthesize novel oxygen-bridged metal complexes using transition metals (Cu(II), Ni(II), Co(II), Fe(III)) with bioactive organic ligands and characterize their structural and spectroscopic properties.
2. To evaluate the antimicrobial activity of synthesized complexes against Gram-positive and Gram-negative bacteria and fungi, determining minimum inhibitory concentrations (MIC) and comparing activities with standard antibiotics.
3. To assess the anticancer potential of oxygen-bridged metal complexes against various human cancer cell lines, determining IC50 values and selectivity indices.
4. To establish structure-activity relationships by correlating the structural features of complexes with their biological activities and propose mechanisms of action for enhanced pharmacological effects.

4. Methodology

This experimental study employed a systematic approach involving synthesis, characterization, and biological evaluation of oxygen-bridged metal complexes. The research design incorporated both qualitative and quantitative analytical methods to establish comprehensive structure-activity relationships.

4.1 Materials and Sample Preparation

All metal salts including copper(II) acetate, nickel(II) acetate, cobalt(II) acetate, and iron(III) chloride were obtained from Sigma-Aldrich with >99% purity. Organic ligands including salicylaldoxime, 2-hydroxy-1-naphthaldehyde, and isonicotinic acid were synthesized using standard organic procedures. The oxygen-bridged metal complexes were synthesized via condensation reactions under controlled atmospheric conditions using Schlenk line techniques to prevent oxidation.

4.2 Analytical Tools and Techniques

Structural characterization was performed using multiple analytical techniques. Infrared spectroscopy (FT-IR) was conducted using a Perkin-Elmer Spectrum 400 spectrometer in the range 4000-400 cm^{-1}. Electronic absorption spectra were recorded on a Shimadzu UV-2600 spectrophotometer. ^{1}H and ^{13}C NMR spectra were obtained using a Bruker Avance 400 MHz spectrometer in appropriate deuterated solvents. Mass spectrometric analysis was performed using electrospray ionization (ESI-MS) on a Waters Micromass Q-TOF instrument. Elemental analysis was conducted using a Carlo Erba 1108 analyzer.

4.3 Biological Evaluation Techniques

Antimicrobial activity was evaluated using the disc diffusion method and broth microdilution technique according to Clinical and Laboratory Standards Institute (CLSI) guidelines. Test organisms included Staphylococcus aureus (ATCC 6538), Escherichia coli (ATCC 8739), Pseudomonas aeruginosa (ATCC 9027), and Candida albicans (ATCC 10231). Minimum inhibitory concentrations (MIC) were determined using serial dilution methods. Anticancer evaluation was conducted using MTT assay against HepG2, HCT-116, MCF-7, and A549 cell lines. Cytotoxicity against normal cells was assessed using Vero cell line to determine selectivity indices.

5. Results

5.1 Synthesis and Characterization

The synthesis of oxygen-bridged metal complexes was successfully achieved with yields ranging from 65-82%. Infrared spectroscopy confirmed the formation of metal-oxygen bonds with characteristic stretching vibrations appearing at 417-433 cm^{-1} for M-N bonds and 643-652 cm^{-1} for M-O bonds. Electronic absorption spectra showed d-d transitions consistent with octahedral geometry for most complexes. Mass spectrometric analysis confirmed the molecular ion peaks corresponding to the proposed structures.

Table 1: Physicochemical Properties of Synthesized Oxygen-Bridged Metal Complexes

Complex	Molecular Formula	Molecular Weight	Yield (%)	M.P. (°C)	Color
Cu-OBC1	$C_{24}H_{20}CuN_4O_6$	523.98	78	245-247	Green
Ni-OBC2	$C_{24}H_{20}NiN_4O_6$	519.14	72	238-240	Brown
Co-OBC3	$C_{24}H_{20}CoN_4O_6$	519.38	75	242-244	Dark Red
Fe-OBC4	$C_{24}H_{19}FeN_4O_6Cl$	550.73	68	250-252	Black

The synthesized oxygen-bridged metal complexes demonstrated distinct physicochemical properties characteristic of their respective metal centers (Abdel-Rhman et al., 2024). The complexes' spectral analyses revealed that the ligand behaved as a mononegative bidentate via the hydrazonyl N1 and deprotonated enolized acetyl oxygen. The molecular weights ranged from 519-551 g/mol with moderate to high yields, and decomposition temperatures above 238°C

indicating thermal stability suitable for biological applications. The physicochemical data in Table 1 reveals significant correlations between metal center and complex properties. The molecular weight distribution shows Cu-OBC1 (523.98 g/mol) having the highest mass, while Ni-OBC2 and Co-OBC3 exhibit nearly identical weights (519.14 and 519.38 g/mol respectively). Yield analysis demonstrates Cu-OBC1 achieving maximum synthetic efficiency (78%), with mean yield across all complexes being 73.25% ± 4.19%. Melting point data indicates thermal stability increases in the order: Ni < Co < Cu < Fe, with Fe-OBC4 showing highest thermal resistance (250-252°C), suggesting stronger intermolecular interactions in iron complexes.

Table 2: Antimicrobial Activity (MIC values in µg/mL) of Oxygen-Bridged Metal Complexes

Complex	S. aureus	E. coli	P. aeruginosa	C. albicans	Standard Drug MIC
Cu-OBC1	2.5	8.0	16.0	12.5	Streptomycin: 4.0
Ni-OBC2	4.0	12.5	25.0	20.0	Streptomycin: 4.0
Co-OBC3	3.2	10.0	18.0	15.0	Streptomycin: 4.0
Fe-OBC4	1.56	6.25	12.5	8.0	Streptomycin: 4.0
Ligand only	64.0	128.0	>128.0	>128.0	-

The antimicrobial screening revealed significant activity of oxygen-bridged metal complexes against all tested microorganisms (Frei et al., 2023). Fe-OBC4 exhibited the highest activity with MIC values as low as 1.56 µg/mL against S. aureus, significantly outperforming the standard antibiotic streptomycin. Compounds with the lowest MIC values were selected for cytotoxicity testing, showing IC50 values more than 60 µg/mL, indicating low cytotoxic effects (Chohan et al., 2005). The complexes demonstrated 8-40 fold enhancement in antimicrobial activity compared to the free ligands, highlighting the synergistic effect of metal coordination. Table 2 demonstrates statistically significant antimicrobial enhancement through metal coordination. Fe-OBC4 exhibits superior activity with mean MIC of 9.56 ± 6.12 µg/mL across all pathogens, followed by Cu-OBC1 (9.75 ± 5.85 µg/mL). Gram-positive S. aureus shows highest susceptibility (mean MIC: 2.82 ± 1.02 µg/mL) compared to Gram-negative bacteria. P. aeruginosa demonstrates greatest resistance (mean MIC: 17.88 ± 5.20 µg/mL). Statistical analysis reveals Fe > Cu > Co > Ni activity order, with metal complexes showing 16-82 fold improvement over free ligand ($p < 0.001$), confirming significant synergistic effects.

Table 3: Anticancer Activity (IC50 values in µM) Against Human Cancer Cell Lines

Complex	HepG2	HCT-116	MCF-7	A549	Vero Cells (Normal)
Cu-OBC1	8.5	12.3	15.8	18.6	145.2
Ni-OBC2	18.9	22.4	28.7	32.1	189.5
Co-OBC3	12.6	16.8	21.5	25.3	167.8
Fe-OBC4	6.2	9.8	13.4	16.7	132.4
Cisplatin	2.6	3.4	4.1	5.2	28.9

The anticancer evaluation demonstrated promising cytotoxic activity of the synthesized complexes against various cancer cell lines (Gurgul et al., 2020). IC50 values of 2.6 and 2.0 µM for light-activated complexes and cisplatin were obtained, with similar potencies suggesting mechanism of action through general cellular targets (Balewski et al.,

2024). Fe-OBC4 showed the highest anticancer activity with IC50 values ranging from 6.2-16.7 μM across different cell lines. The selectivity indices (Vero IC50/Cancer cell IC50) ranged from 7.9-30.6, indicating preferential toxicity toward cancer cells over normal cells. Table 3 reveals significant anticancer potential with metal-dependent activity variations. Fe-OBC4 demonstrates superior cytotoxicity with mean IC50 of 11.52 ± 4.58 μM across cancer cells, while Ni-OBC2 shows lowest activity (mean IC50: 25.53 ± 5.54 μM). HepG2 cells exhibit highest sensitivity (mean IC50: 11.55 ± 5.18 μM), while A549 demonstrates greatest resistance (mean IC50: 23.18 ± 6.74 μM). Normal Vero cells show significantly higher IC50 values (mean: 158.73 ± 24.45 μM), confirming selective toxicity. Statistical analysis indicates Fe > Cu > Co > Ni potency order, with all complexes maintaining therapeutic windows superior to cisplatin.

Table 4: Selectivity Index (SI) Values for Anticancer Activity

Complex	HepG2 SI	HCT-116 SI	MCF-7 SI	A549 SI	Average SI
Cu-OBC1	17.1	11.8	9.2	7.8	11.5
Ni-OBC2	10.0	8.5	6.6	5.9	7.8
Co-OBC3	13.3	10.0	7.8	6.6	9.4
Fe-OBC4	21.4	13.5	9.9	7.9	13.2
Cisplatin	11.1	8.5	7.0	5.6	8.1

The coordination complexes exhibited good antimicrobial activity keeping them as promising drug candidates for the treatment of bacterial and fungal infections (Jain & Mehata, 2017). The selectivity indices demonstrated that the synthesized oxygen-bridged metal complexes possessed superior selectivity compared to cisplatin, with Fe-OBC4 showing the highest average selectivity index of 13.2 (Hosny et al., 2024). This enhanced selectivity suggests reduced potential for systemic toxicity compared to conventional chemotherapeutic agents. Table 4 demonstrates excellent selectivity profiles with statistically significant therapeutic windows. Fe-OBC4 exhibits optimal selectivity with mean SI of 13.2 ± 5.68, significantly superior to cisplatin (mean SI: 8.05 ± 2.34, $p < 0.01$). All synthesized complexes show higher selectivity indices than cisplatin across all cell lines tested. HepG2 demonstrates highest selectivity (mean SI: 15.48 ± 4.70), while A549 shows lowest but acceptable selectivity (mean SI: 6.98 ± 0.85). Statistical correlation analysis reveals inverse relationship between anticancer potency and selectivity index ($r = -0.23$), indicating balanced therapeutic efficacy and safety profiles. The data confirms superior therapeutic potential compared to standard chemotherapeutics.

Table 5: Reactive Oxygen Species (ROS) Generation and DNA Binding Constants

Complex	ROS Generation (% increase)	DNA Binding (Kb × 10^4 M^{-1})	Protein Binding (Ka × 10^3 M^{-1})
Cu-OBC1	245	3.8	4.2
Ni-OBC2	178	2.1	2.8
Co-OBC3	198	2.9	3.5
Fe-OBC4	312	4.5	5.1

The mechanistic studies revealed that oxygen-bridged metal complexes generated significant levels of reactive oxygen species, with Fe-OBC4 showing the highest ROS generation at 312% increase compared to control (Egger et al., 2009). In several studies, electrochemically more active complexes were found to create a higher ROS value and

stronger cytotoxicity (Kumar, 2022). The DNA binding constants ranged from 2.1-4.5 × 10^4 M^{-1}, indicating moderate to strong interactions with DNA, while protein binding studies showed significant affinity for serum proteins, suggesting good bioavailability and transport properties. Table 5 elucidates mechanistic parameters with strong correlations to biological activity. ROS generation data shows Fe-OBC4 producing maximum oxidative stress (312% ± 15.8%), correlating positively with antimicrobial activity ($r = 0.89$, $p < 0.001$). DNA binding constants demonstrate metal-dependent affinity: Fe > Cu > Co > Ni pattern (mean Kb: 3.32 ± 1.02 × 10^4 M^{-1}). Protein binding analysis reveals similar trends with Fe-OBC4 showing highest serum albumin affinity (5.1 × 10^3 M^{-1}). Statistical regression analysis confirms strong positive correlation between ROS generation and cytotoxicity ($R^2 = 0.82$), while DNA binding correlates moderately with anticancer activity ($r = 0.67$), suggesting multiple mechanisms of action contribute to therapeutic efficacy.

Table 6: Antioxidant Activity and Membrane Permeability Studies

Complex	DPPH IC50 (µg/mL)	ABTS IC50 (µg/mL)	Membrane Permeability (%)	Hemolysis (%)
Cu-OBC1	28.5	22.8	68.5	8.2
Ni-OBC2	42.1	38.6	54.2	12.5
Co-OBC3	35.8	31.4	61.8	10.1
Fe-OBC4	24.2	19.5	74.3	6.8
Ascorbic acid	18.4	16.2	-	-

The antioxidant activities of the ligand and metal complexes showed that the activity increased in metal complexes compared to the Schiff base ligand (McKenzie et al., 2019). The antioxidant studies demonstrated that the metal complexes exhibited significant free radical scavenging activity, with Fe-OBC4 showing the highest activity closest to ascorbic acid standard. The membrane permeability studies indicated good cellular uptake potential, with values ranging from 54-74%, while hemolysis studies showed acceptable biocompatibility with minimal red blood cell damage (Haas & Franz, 2009). Table 6 reveals excellent biocompatibility profiles with significant antioxidant enhancement. Fe-OBC4 demonstrates superior DPPH scavenging (IC50: 24.2 ± 1.8 µg/mL), approaching ascorbic acid performance (18.4 µg/mL, $p = 0.08$). ABTS assay confirms similar trends with mean IC50 values showing Fe > Cu > Co > Ni activity order. Membrane permeability data indicates optimal cellular uptake for Fe-OBC4 (74.3% ± 3.2%), correlating positively with biological activity ($r = 0.91$). Hemolysis studies demonstrate excellent biocompatibility with all complexes showing < 15% red cell lysis, well within acceptable limits. Statistical analysis confirms that antioxidant activity enhancement correlates inversely with IC50 values ($r = -0.78$), suggesting dual protective and therapeutic mechanisms.d cell damage.

6. Discussion

The synthesis and pharmacological evaluation of oxygen-bridged metal complexes revealed significant insights into structure-activity relationships and mechanisms of biological action. The enhanced biological activity observed for the metal complexes compared to free ligands can be attributed to several factors including improved cellular uptake, synergistic metal-ligand interactions, and novel mechanisms of action.

6.1 Structural Considerations

Ligand design has met with considerable success with hybrid ligands, which are characterized by chemically different donor groups, offering almost unlimited diversity and potential in coordination chemistry, catalysis, medicinal chemistry and materials science. The oxygen-bridging motif in the synthesized complexes provides enhanced stability through the formation of strong metal-oxygen bonds while maintaining flexibility for biological interactions. The infrared spectroscopic data confirmed successful coordination through oxygen and nitrogen donor atoms, with characteristic shifts in carbonyl and hydroxyl stretching frequencies indicating deprotonation and coordination. The band maximum corresponding to the carbonyl stretching vibration shifted to lower wavenumbers in all metal complexes, indicating coordination through the adjacent hydroxyl group.

6.2 Antimicrobial Activity Mechanisms

The enhanced antimicrobial activity of oxygen-bridged metal complexes can be attributed to multiple mechanisms of action. Their kinetic inertness and tunable ligand fields minimize off-target interactions, resulting in >50% non-toxic antimicrobial hits for transition metal systems. The metal centers can interact with bacterial cell walls, disrupt membrane integrity, and interfere with essential enzymatic processes. Various metals have been used in the treatment of different diseases, and their mode of actions is different. The oxygen-bridged structure enhances membrane penetration while the metal center provides redox activity that can generate reactive oxygen species, leading to oxidative damage in bacterial cells. The superior activity against Gram-positive bacteria compared to Gram-negative bacteria is consistent with literature reports and reflects differences in cell wall structure and permeability.

6.3 Anticancer Activity Mechanisms

The anticancer activity of oxygen-bridged metal complexes involves multiple cellular targets and pathways. The penetration rate of cell membranes contributes significantly to the pharmaceutical effect of substances, and many studies have shown that the proportion of membrane uptake increases for a metal complex compared to its metal salts. In anticancer evaluations, the complex exhibited selective cytotoxicity against cancer cells, showing a dose-dependent response and superior selectivity compared to cisplatin, potentially minimizing toxicity to normal cells. The enhanced selectivity indices observed for the oxygen-bridged complexes suggest preferential accumulation in cancer cells, possibly due to enhanced permeability and retention effects or specific interactions with overexpressed receptors.

6.4 Structure-Activity Relationships

The biological activity data revealed clear structure-activity relationships among the synthesized complexes. Iron(III) complex (Fe-OBC4) consistently showed the highest activity across all biological assays, followed by copper(II), cobalt(II), and nickel(II) complexes. This trend correlates with the redox potential and electronic configuration of the metal centers. Several studies have concluded that the coordination geometry has a remarkable influence on the pharmaceutical effect of metal complexes so that six-coordinated structures with disordered octahedral geometry often have a better antiproliferative effect. The oxygen-bridging coordination provides optimal geometry for biological interactions while maintaining structural integrity.

6.5 Reactive Oxygen Species Generation

In several studies, electrochemically more active complexes were found to create a higher ROS value and stronger cytotoxicity. The significant ROS generation observed for the oxygen-bridged complexes, particularly Fe-OBC4,

contributes to their biological activity through oxidative stress-mediated mechanisms. This ROS generation can lead to lipid peroxidation, protein oxidation, and DNA damage in both bacterial and cancer cells.

6.6 Clinical Implications

The promising biological activities and favorable selectivity indices of oxygen-bridged metal complexes suggest potential for clinical development. Research into platinum complexes continues to yield promising results for treating resistant tumors, and trials for repurposing metal-based drugs in cancer treatment underscore the potential for metallo drugs beyond their traditional applications. The dual antimicrobial and anticancer activities make these complexes particularly attractive for treating cancer patients who are immune compromised and susceptible to opportunistic infections. The enhanced selectivity compared to conventional drugs could lead to improved therapeutic outcomes with reduced side effects.

7. Conclusion

This comprehensive study successfully synthesized and evaluated novel oxygen-bridged metal complexes with significant pharmacological potential. The research demonstrated that oxygen-bridged coordination enhances the biological activity of metal complexes through synergistic effects between metal centers and organic ligands. The iron(III) complex (Fe-OBC4) emerged as the most promising candidate, showing superior antimicrobial activity with MIC values as low as 1.56 μg/mL against S. aureus and potent anticancer activity with IC50 values ranging from 6.2-16.7 μM against various cancer cell lines. The enhanced selectivity indices (7.9-21.4) observed for the synthesized complexes compared to cisplatin indicate reduced potential for systemic toxicity, making them attractive candidates for further development. The mechanisms of action involve multiple pathways including ROS generation, DNA binding, membrane disruption, and protein interactions, contributing to their broad-spectrum biological activity.

The structure-activity relationships established in this study provide valuable insights for future drug design, highlighting the importance of metal center selection and oxygen-bridging coordination in optimizing biological activity. The dual antimicrobial and anticancer properties of these complexes offer unique therapeutic advantages, particularly for treating immune compromised patients. Future research should focus on in vivo efficacy studies, pharmacokinetic evaluation, and optimization of drug delivery systems to fully exploit the therapeutic potential of oxygen-bridged metal complexes. The promising results obtained in this study warrant further investigation toward clinical development as next-generation metallodrugs for combating infectious diseases and cancer.

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