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Review Article

The Study of Antimicrobial Activities of Various Transition Metal Mixed Ligand Complexes Containing 1,10-Phenanthroline with Any Other Ligands

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Abstract: The widespread usage of antibiotics in recent years has resulted in a surge in drug-resistant bacteria resistant to a variety of medications. The identification of innovative and potent molecules against new targets is critical to combating the worrisome problem of microbial resistance to antibiotics. Numerous transition metal mixed ligand complexes have been explored as a result of this, with promising results. Because transition metals have different oxidation states and can interact with a variety of ligands, they play an essential role in medical inorganic chemistry. Metals' high activity has led to the recent creation of metal-based pharmaceuticals that are being explored as viable candidates for pharmacological and therapeutic purposes. This review focuses on research conducted over the last few decades that has sought to possess biological applications such as antimicrobial, antifungal, and antibacterial activities of synthetic mixed ligand transition metal complexes, and it focuses primarily on a small number of transition metal mixed ligand complexes such as Mn (II), Co(II), Cu(II), and Zn(II), Ru(III) that contain 1,10-Phenanthroline as a major ligand The majority of this article is devoted to nitrogen donor ligands that chelate transition metals and are employed in metallodrugs.

Keywords: 1,10-phenanthriline, Mixed Ligand Complexes, Biological Activities

1. Introduction

Transition metal ions have an essential part in biological processes in the human body today [1-3]. It is feasible to impose a set of desirable characteristics on transition metals in coordination with appropriate ligands for specific uses. Tailoring the kinds of ligands in complexes governs features such as oxidation state, stability, solvophilicity, and the electronic properties of metal ions [4-6]. Coordination modifies not just the characteristics of metal ions, but also the properties of the ligands themselves [5]. Because of their antibacterial and antifungal characteristics, metal complexes have received a lot of interest in modern medicine [7, 8]. Nowadays, bioinorganic chemists explore the pharmacology of heterocyclic ligands and their metal complexes as the primary focus of their research [9, 10]. Nitrogen-containing chemical molecules and their metal complexes display a wide spectrum of biological actions, including antibacterial, antifungal, anticancer, and antiviral properties. As DNA-binding agents, transition metal complexes have two different advantages [10, 11].

First and foremost, because of their well-defined coordination geometry, transition metal centers are highly appealing molecules for reversible recognition in nucleic acid studies. Furthermore, they frequently exhibit different electrochemical or photo-physical characteristics, boosting the functionality of the binding agent [10]. Indeed, these intelligent properties have fueled the complexes' employment in a wide range of applications, from fluorescent markers to DNA foot printing agents to electrochemical probes [12]. Many transition metal ion coordination compounds are amenable to nucleolytic cleavage. Mixed ligand-metal complexes have been discovered to be particularly effective in

this area due to their potential DNA binding capabilities [13]. Through stacking contacts, studies on the integration of excellent intercalators such as 1,10-Phenanthroline and 2,2′ -Bipyridine discovered significant affinity between DNA base pairs and their planar structure. The use of these metallo-intercalators for such research has the considerable benefit of allowing the ligands and metal ions to be altered in an easily controlled way to assist particular applications [13, 14]. Metal complexes exhibit stronger bioactivity than free ligands in most situations [3, 13, 15]. This is most likely owing to the complexes' higher lipophilicity. The enhanced activity of the metal chelate may be explained using harmonics and chelation theory [13, 16]. The topic of mixed ligand complexes has long piqued the interest of the chemical community. The synthesis of mixed ligand complexes is gaining popularity. This is due to the presence of at least two different types of ligands with differing characteristics related inside the complex's identical metal ion [3]. While coordinating, not only the metal's properties but also the characteristics of the ligands themselves are altered. For example, the pharmacological effects of free purines such as adenine, as well as their critical involvement in DNA/RNA base pairing via numerous hydrogen-bonding patterns, might vary dramatically after complex formation [17, 18]. The combined action of various ligands on the metal ion in a complex results in a set of new characteristics. This involves the stability of various oxidation states as well as the regulation of the metal ion's solvophilicity, electrophilicity, and nucleophilicity [19]. This piques the attention of researchers in the production of mixed ligand complexes with diverse characteristics. Many papers have been published in recent years devoted to the synthesis and characterization of mixed ligand complexes [20].

2. Biological Activities of Some Kinds of Mixed Ligands Complexes

Numerous mixed ligand transition metal complexes have been studied using various techniques, and their biological activities, which include antimicrobial, antiviral, anticonvulsant, anticancer, antimycobacterial, antimalarial, cysticidal, herbicidal, and anti-inflammatory activity, have been extensively studied [3, 21-24]. Chemical compounds biological characteristics are very sensitive to their chemical structure. One of the primary aims of medicinal chemistry is to comprehend such dependencies in terms of structure-activity correlations [25]. The drug action of biometals is enhanced by the formation of coordination with various bioactive ligands as a result of the stabilization of different oxidation states and modulation of the electronic properties of the metal ion, resulting in effective permeability of the drug into the site of action [26].

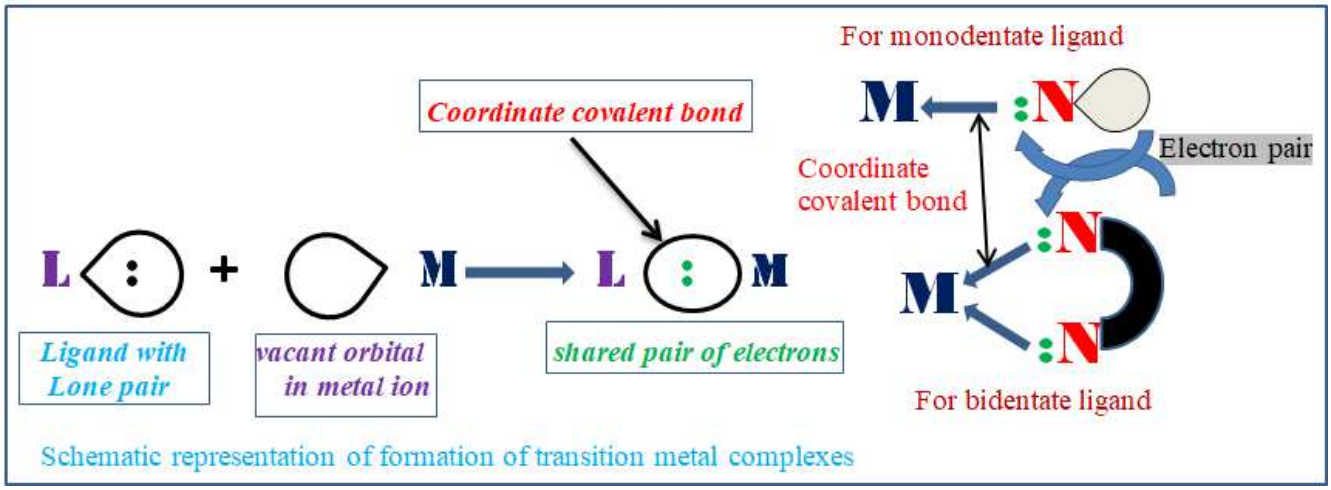

Figure 1. *Schematic representation of the formation of transition metal complexes [27].*

2.1. Antimicrobial Activities of Cobalt(II), Copper(II), and Zinc(II) Mixed-Ligand Complexes Containing 1,10-Phenanthroline and 2,2'-Bipyridine

$[Cu(Bpy)(Phen)(H_2O)_2](Cl)_2.2H_2O$, $[Co(Bpy)(Phen)_2](NO_3)_2.$ $2H_2O$ and $[Zn(Bpy)_2(Phen)]Cl_2.6H_2O$ was synthesized by Agwara et al. [1]. and investigated their antimicrobial properties. The antibacterial and antifungal activity of the ligands and complexes in vitro were assessed using the well-diffusion technique. Table 1 shows the findings of the sensitivity of these bacterial strains to the chemicals as measured by the inhibition zone growth diameter (IZ) are presented in table 1.

This study found that all produced mixed ligand complexes with IZ values ranging from 16 to 31 mm are active against all pathogens examined. The complexes provide poorer results than free 1,10-Phenanthroline and greater results than free Bipyridine ligand. It should be noted that the 1,10-phenan-throline has substantial antibacterial properties against the studied bacteria; nevertheless, it cannot be employed directly for therapeutic purposes owing to the cytotoxicity induced by its strong chelating nitrogen atoms binding with biometals and inhibiting metalloenzymes [28]. By coordinating with transition metals, toxicity has been minimized [4, 5, 25, 28]. Mixed ligand complexes offer the benefit of combining the respective bioactivities of

uncoordinated ligands and metal ions, potentially making them more effective antibacterial agents. Because water is the major component of the human body, the water-soluble compounds allow them to be used in humans. The copper-mixed ligand complex had the highest activity, whereas the zinc-mixed ligand complex had the lowest. In the descending sequence of activity, $[Cu(bpy)(phen)]Cl_2.\ 4H_2O$ > $[Co(bpy)(phen)_2](NO_3)_2.2H_2O$ > [Zn(bpy)2 (phen)] Cl_2.

Table 1. *Antimicrobial properties of ligands, metal salts, and metal mixed-ligand complexes.*

Bacteria	Antimicrobial activity (IZ diameter in mm)								
	1	2	3	4	5	6	7	8	RA
Enterobacter choacae	32	--	11	22	--	30	9	18	28
Staphylococcus aureus	31	9	10	24	7	30	8	20	30
Escherichia coli	31	14	13	22	8	29	9	22	22
Morganella morganii	30	--	11	23	--	29	--	20	27
Salmonella thyphi	32	9	12	25	--	31	9	17	30
Klebsiella pneumonia	28	--	11	20	7	26	10	17	29
Shigella flexineri	31	13	13	22	8	30	10	20	22
Citrobacter freundi	30	10	--	16	--	26	--	16	21
Pseudomonas aeruginosa	31	7	11	23	--	30	10	19	25

IZ=inhibition zone; 1=1,10-Phenanthroline (phen); 2=2,2'-bipyridine (bpy); 3=$Co(NO_3)_3.6H_2O$; 4=$[Co(bpy)(phen)_2](NO_3)_2.2H_2O$; 5=$CuCl_2.2H_2O$; 6=$[Cu(bpy)(phen)]Cl_2.\ 2H_2O$; 7=$ZnCl_2$; 8=$[Zn(bpy)_2(phen)]Cl_2.\ 6H_2O$; RA=reference antibiotics (gentamycin).

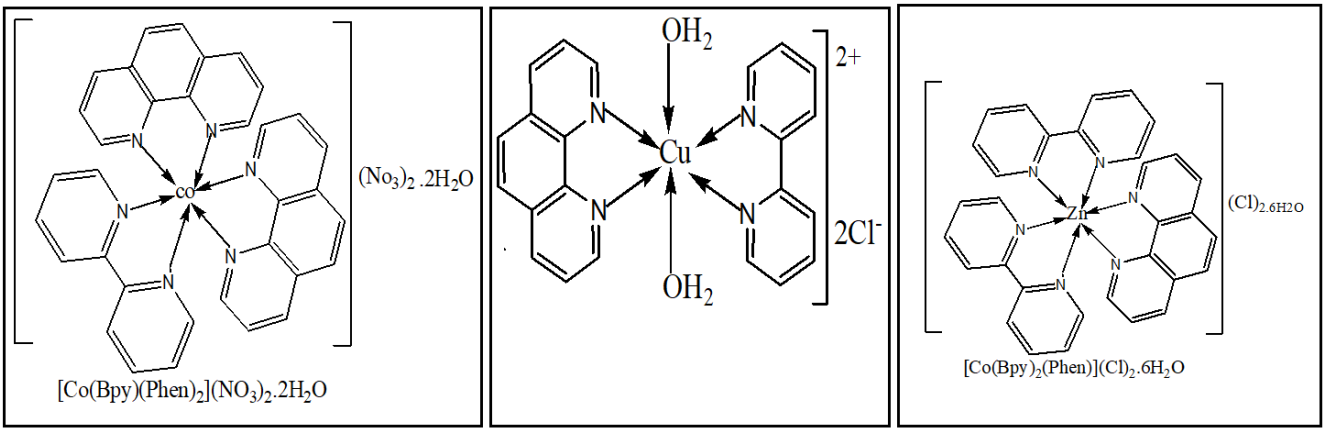

Figure 2. *The proposed structure of the complexes [1].*

2.2. Antimicrobial Activities of New Mixed Ligand Complexes of Copper (II) with 1,10-Phenanthroline and Thymine

Cu(II) mixed ligand complexes with 1,10-Phenanthroline and Thymine were synthesized and tested for antimicrobial activity against Staphylococcus aureus (ATCC 25923), Streptococcus pneumonia (SP) (clinical isolate), methicillin resistant Staphylococcus aureus (MRSA) (clinical isolate), Klebsiella pneumonia (KP) (clinical isolate), Escherichia coli (EC (ATCC12022). When evaluating biological activities, the complexes demonstrated improved antibacterial activity compared to the free metal salt, with thymine being less active than 1,10-Phenantroline. When compared to the commercially available antibiotics ciprofloxacin and chloramphenicol, the produced Cu(II) complexes demonstrated significant antibacterial activity [13].

Table 2. *Comparative antibacterial activities of ligands, synthesized complexes 1 and 2, metal salt, and commercially available antibiotics [13].*

Bacteria	Antibacterial activity (IZ diameter in mm)								
	1	2	3	4	5	6	7	8	9
SA	13.12±0.3	35.3±0.32	NA	25±0.23	35.0±0.4	NA	NA	24.0±0.32	27.3±0.21
SP	17.9±0.36	38.0±0.20	NA	24.7±0.3	34.0±0.2	NA	NA	24.0±0.21	26.7±0.35
MRSA	17.8±0.35	36.7±0.13	NA	27.7±0.2	31.3±0.2	NA	NA	23.3±0.22	26.3±0.24
EC	11.8±0.28	31.3±0.24	NA	22.7±0.2	28.8±0.3	NA	NA	21.3±0.31	28.7±0.26
KP	28.4±0.33	41.7±0.3	NA	24.7±0.4	40.0±0.2	NA	NA	28.3±0.32	32.3±0.23
SB	22.56±0.2	41.7±0.3	NA	30.0±0.2	27.3±0.3	NA	NA	25.0±0.41	27.3±0.21

Note: Relative standard deviation of all data is less than 5% (acceptable). 1=$CuCl_2\ \cdot 2H_2O$, 2=1,10-Phenanthroline, 3=thymine, 4=$[Cu(phen)_2(H_2O)_2]Cl_2$, 5=$[Cu(Phen)_2(thy)(H_2O)]Cl$, 6=water, 7=methanol, 8=reference antibiotic (ciprofloxacin), 9=reference antibiotic (chloramphenicol), and NA=no activity.

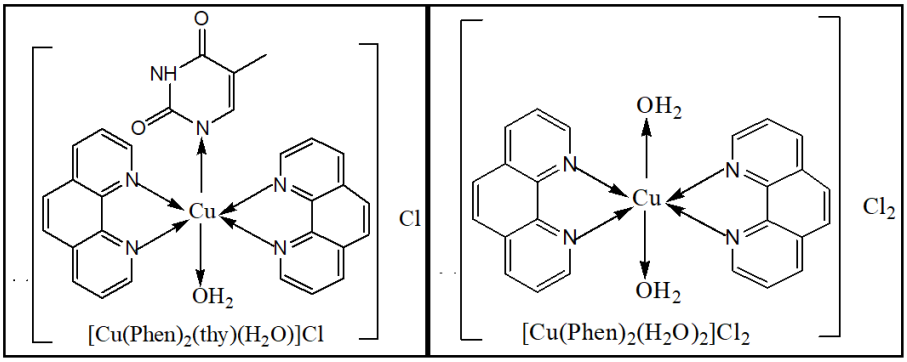

Figure 3. *The proposed structure of the Cu(II) complex.*

2.3. Antimicrobial activities of Mono and Binuclear Cobalt (II) Mixed-Ligand Complexes Containing 1,10-Phenanthroline, Acetamide, and Ethylenediamine

Getinet Tamiru et al. [29] created three mono-and binuclear mixed ligand complexes of cobalt(II) including 1,10-Phenanthroline, acetamide, and ethylenediamine spacer as $[Co(phen)_2(Act)(H_2O)]Cl_2.H_2O$ and $[Co(phen)_2(Act)(en)]Cl_2$) and binuclear $[Co_2(phen)_4(Act)_2(en)]Cl_4$. The complexes' antibacterial activity was evaluated in vitro on two Gram positive bacteria (Staphylococcus aureus and Streptococcus pyogenes) and two Gram negative bacteria (*Escherichia coli* and *Klebsiella pneumoniae*) using the disc diffusion technique. The findings demonstrated that all produced complexes have antibacterial activity.

The minimum inhibitory concentration (MIC) against each bacterium was determined by serial dilution of aqueous solutions of the complexes (100, 200, 300, 400,500, and 600 mg/L).

The minimum inhibitory concentration (MIC) is the lowest concentration that totally suppressed the growth of microorganisms for 24 hours. The MIC for $[Co(Phen)_2(Act)(H_2O)]Cl_2.H_2O$ was determined to be 100 g/L. In comparison to the two newly synthesized mononuclear mixed ligand complexes, the novel binuclear mixed ligand complex had the highest efficacy, outperforming the antibacterial activity of the commercially available medication gentamicin (Table 3). The binuclear mixed ligand complex's significant antibacterial activity is most likely owing to the bisintercalation caused by two planar intercalating 1,10-Phenanthroline ring systems covalently connected by ethylenediamine. Furthermore, the configurational freedom through the bridge likely increases its flexibility and, as a result, the complex's penetrating power [30]. All complexes were found water soluble, demonstrating their compatibility with normal human physiological systems and their potential for human treatment after in vivo cytotoxicity studies.

Table 3. *Results of the disc diffusion method of metal salt, ligands, and its metal complexes in 800 µg/L.*

COMPOUNDS	Bacteria with zone of inhibition(mm)			
	S. aureus (+)	S. pyog (+)	E. coli (-)	K. pne (-)
$[Co(Phen)_2(H_2O)_2]Cl_2.\ H_2O$	12±0.15	13±0.06	17±0.10	15±0.00
$[Co(Phen)_2(Act)(H_2O)]Cl_2.H_2O$	13±0.10	16±0.20	16±0.06	12±0.00
$[Co_2(Phen)_4(Act)_2(en)]Cl_4$	34±0.06	40±0.06	35±0.21	34±0.06
$[Co(Phen)_2(Act)(en)]Cl_2$	14±0.06	12±0.15	15±0.06	12±0.15

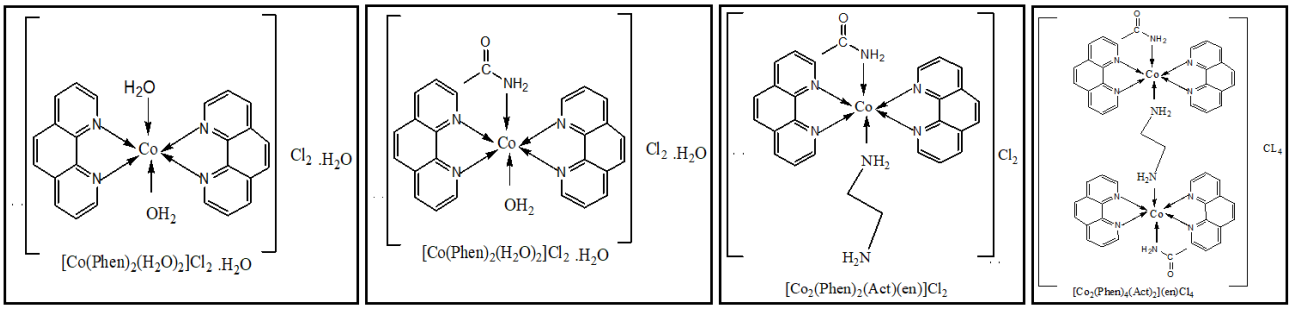

Figure 4. *The proposed structure of the Co (II) complex.*

2.4. Antifungal Activities of Mn(II), Co(II), Cu(II), and Zn(II) Mixed-Ligand Complexes Containing 1,10-Phenanthroline and 2,2`-Bipyridine

In an earlier work, Agwara et al. [1] reported on the synthesis, characterization, and antibacterial characteristics of mixed-ligand complexes of 1,10-Phenanthroline and 2,2'-bipyridine. They published a study in 2013 on the antifungal activity of mixed-ligand metal complexes including the two ligands mentioned above with Mn(II),

Co(II), Cu(II), and Zn(II) metal centers. Four Candida fungus species were utilized in the antifungal activity test: *Candida albicans*, *Candida parapsilosis, Candida krusei, and Cryptococcus neoformans*. This test was carried out by screening and selecting the best active substances based on their inhibition zone diameter prior to executing a MIC determination using the disc diffusion method. The antifungal properties of the compounds revealed that 1,10-Phenanthroline had the highest activity in all pathogens examined, with zones of inhibition ranging from 31 to 37 mm. 2,2'-bipyridine was also shown to have antifungal action, with zones of inhibition ranging from 25 to 35 mm. Metal complexes had strong activity, with inhibition zone values ranging from 13 to 30 mm, whereas the metal salts showed relatively low activity. The cobalt complex had the lowest activity against *Candida albicans* of all produced complexes. Each metal salt has a very modest activity when compared to the related complexes.

Table 4. *Antifungal activity (inhibition zone diameter (mm).*

Compounds	Candida krusei	Candida albicans	Cryptococcus Neoformans	Candida parapsilosis
1,10-Phenanthroline	37±0.2	31±1.1	35±1	32±0.6
2,2`-bipyridine	35±0	28±0.5	25±0	25±0.9
$[Mn(bpy)_2(phen)]Cl_2.2H_2O$	30±1.1	30±1.6	25±1	25±0.9
$[Co(bpy)(Phen)_2](NO_3)_2.2H_2O$	14±0.3	7±0	13±0	15±1.2
$[Cu(bpy)(phen)(H_2O)_2]Cl_2.2H_2O$	13±0.1	13±0.6	13±0.2	14±0.7
$[Zn(bpy)_2(phen)]Cl_2.6H_2O$	27±0.4	25±0.6	21±0.1	22±0.7
$Co(NO_3)_2.6H_2O$	14±1.2	13±0.6	0±0	17±1
$ZnCl_2$	0±0	5±0.1	0±0	0±0
$MnCl_2.4H_2O$	8±1.3	0±0	7±1.1	0±0
$CuCl_2.2H_2O$	12±1.4	11±1.3	16±0.7	14±0
Reference antibiotic (Nystatin)	13±0.8	20±1.1	20±0.7	14±0.7

Table 5. *Minimum inhibitory Concentration (MIC).*

Compounds	Fungi			
	Candida krusei	*Candida albicans*	*Cryptococcus Neoformans*	*Candida parapsilosis*
1,10-Phenanthroline	$1.9x10^{-2}$	$4.88x10^{-3}$	$3.9x10^{-2}$	$3.9x10^{-2}$
2,2`-bipyridine	$7.8x10^{-2}$	$7.8x10^{-2}$	$3.9x10^{-2}$	$7.8x10^{-2}$
$[Mn(bpy)_2(phen)]Cl_2.2H_2O$	$9.76x10^{-3}$	$4.88x10^{-3}$	$4.88x10^{-3}$	$9.76x10^{-3}$
$[Co(bpy)(Phen)_2](NO_3)_2.2H_2O$	$9.76x10^{-3}$	$4.88x10^{-3}$	$7.8x10^{-2}$	$1.9x10^{-2}$
$[Cu(bpy)(phen)(H_2O)_2]Cl_2.2H_2O$	$3.9x10^{-2}$	$4.88x10^{-3}$	$4.88x10^{-3}$	$3.9x10^{-2}$
$[Zn(bpy)_2(phen)]Cl_2.6H_2O$	$9.76x10^{-3}$	$4.88x10^{-3}$	$4.88x10^{-3}$	$3.9x10^{-2}$
Reference antibiotic (Nystatin).	$3.9x10^{-2}$	$1.9x10^{-2}$	$3.9x10^{-2}$	$3.9x10^{-2}$

2.5. Antibacterial Activities of Ruthenium (III) Mixed Ligand Complexes Containing 1,10-Phenanthroline and Guanide

Abebe and Hailemariam [5] created two novel Ruthenium (III) complexes from 1,10-Phenanthroline alone as $[Ru(phen)_2Cl_2]$ $Cl_2.H_2O$ and from 1,10-Phenanthroline and guanide as $[Ru(phen)_2(G)Cl]$ $Cl_2.H_2O$). (G=guanide), and they conducted the in vitro antibacterial screening on two Gram positive *Staphylococcus aureus* (S. aureus) and *methicillin-resistant Staphylococcus aureus* (MRSA) bacteria, as well as two Gram negative *Escherichia coli* (E. coli) and *Klebsiella pneumonia* (K. pneumoniae) bacteria. Even against the most drug resistant K.pneumoniae, the complexes outperformed commercially available Chloramphenicol and Ciprofloxacin. The compound $[Ru(phen)_2(G)Cl]Cl_2.H_2O$ inhibited S.aureus, MRSA, E. coli, and K. pneumoniae by 17.5%, 27.4%, 16.4%, and 52%, respectively, better than chloramphenicol. It also outperformed Ciprofloxacin in inhibiting infection by 5.9 percent, 5.1 percent, 2.3 percent, and 17.2 percent, respectively. Similarly, $[Ru(Phen)_2(Cl)_2]Cl_2.H_2O$ suppressed infections by 11 percent, 8.7 percent, 0.1 percent, and 31.2 percent better than chloramphenicol. The antibacterial properties of these two complexes were evaluated, and it was obvious that the ruthenium complexes had a broad range of activity, being active against all microorganisms examined. Tables 5 and 6 include antimicrobial data, respectively. As a result of in vivo cytotoxicity studies, these chemicals can be evaluated as possible antibacterial medicines.

Table 6. *Antibacterial activities of the complexes, free ligands, metal salt, and commercially available antibiotics.*

Compounds	Bacteria(Inhibition zone)			
	S. aureus (ATCC 25923)	MRSA (clinical isolate)	*E. coli* (ATC 255922)	*K. pneumonia* (ATCC 986605)
1,10-Phenanthroline	27.40±0.12	26.4±0.11	28.20±0.12	26.00±0.14
Guanine	—	—	—	—
$RuCl_3$	—	—	12.20±0.21	—
$[Ru(Phen)_2(Cl)_2]Cl{\cdot}2H_2O$	25.54±0.15	24.56±0.2	26.53±0.13	26.50±0.13
$[Ru(Phen)_2(G)(Cl)]Cl{\cdot}H_2O$	29.65±0.13	28.8±0.21	30.70±0.11	30.70±0.11
Ciprofloxacin	28.00±0.14	27.4±0.13	30.00±0.10	26.20±0.32
Chloramphenicol	25.24±0.14	22.6±0.15	26.50±0.23	20.20±0.35

Table 7. *The % activity index data of the complexes against the tested bacteria compared to (A) Chloramphenicol and (B) Ciprofloxacin.*

(A)

Compounds	Microorganisms			
	S. aureus	**MRSA**	***E. coli***	***K. pneumoniae***
$[Ru(Phen)_2(Cl)_2]Cl{\cdot}2H_2O$	11.00%	8.70%	0.10%	31.20%
$[Ru(Phen)_2(G)(Cl)]Cl{\cdot}H_2O$	17.50%	27.40%	15.85%	52.00%

(B)

Compounds	Microorganisms			
	S. aureus	**MRSA**	***E. coli***	***K. pneumoniae***
$[Ru(Phen)_2(Cl)_2]Cl{\cdot}2H_2O$	-8.80%	-10.00%	-12.00%	1.01%
$[Ru(Phen)_2(G)(Cl)]Cl{\cdot}H_2O$	5.90%	5.10%	2.30%	17.17%

2.6. Antibacterial Activities of Copper(II) Mixed-ligand Complexes Containing 1,10-Phenanthroline, Adenine, and Thymine

Antimicrobial [13, 16, 21, 31-33] and anticancer [34-36] activities have been described for copper (II) complexes in the literature. For example, Abebe et al. [37]. reported $[Cu(phen)_2(Thy)]Cl_2$ and $[Cu(phen)_2(Ad)]2Cl$ (phen=1,10 phenantroline, Ad=Adenine, and Thy=Thymine), and the antibacterial properties of the complexes were investigated in vitro using the Agar diffusion technique. Two Gram positive strains (*Staphylococcus aureus and Methicillin Resistant Staphylococcus aureus* (clinical isolate)) and two Gram negative bacteria (*Escherichia coli* (ATCC255922) and *Klebsiella pneumoniae* (ATCC986605) were employed in this investigation.

The results of this study's in vitro antibacterial activity were compared with commercially available antimicrobial agents (ciprofloxacin and chloramphenicol). The complex $[Cu(phen)_2(Thy)]2Cl$ inhibited the growth of *methicillin-resistant Staphylococcus aureus* (MRSA), *Escherichia coli* (E. coli), and *Klebsiella pneumoniae* (K. pneumonia) better than chloramphenicol by 11.25 percent, 19.41 percent, and 25.35 percent, respectively, and showed better activities on MRSA and K. pneumoniae than ciprofloxacine by 2. Similarly, $[Cu(phen)_2(Ad)]2Cl$ inhibited MRSA, E. coli, and K. pneumoniae by 11.24 percent, 2.48 percent, and 9.06 percent, respectively, better than chloramphenicol.

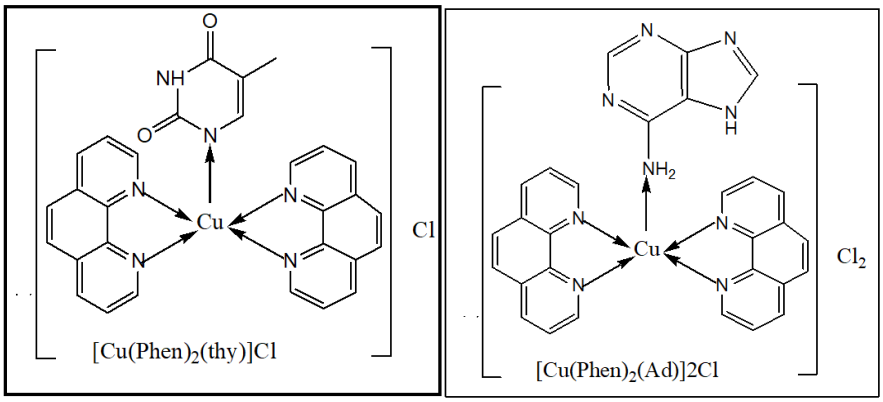

Figure 5. *The proposed structure of the complexes [37].*

Table 8. *Antibacterial activity of metal salt, ligands, metal complexes, and reference antibiotics.*

Compound tested	Antimicrobial activity (mean IZ diameter(mm)±SD)			
	S. aureus	**MRSA**	***E. coli***	***K. pneumoniae***
1	0±0	0±0	20.00±0.82	0±0
2	24.33±0.47	23.67±0.47	23.00±0.82	18.33±0.94
3	22.00±0	26.00±0.82	27.00±0.47	18.33±0.47
4	21.00±0.82	26.67±0.47	32.67±0.47	22.00±0.82
5	20.00±0.82	28.67±0.47	29.67±0.47	28.33±0.94
6	0±0	0±0	0±0	0±0
7	0±0	0±0	0±0	0±0
8	0±0	0±0	0±0	0±0
9	0±0	0±0	0±0	0±0
R1	26.67±0.94	26.00±0.82	34.67±0.94	19.33±0.47
R2	25.67±1.25	23.67±0.47	26.33±0.94	16.67±0.47

MRSA=*Methicilin resistant S. Aureus*, IZ=Inhibition zone. SD=Standard deviation, 1=$CuCl_2.2H_2O$, 2=$[Cu(phen)_2(H_2O)]2Cl$, 3=$[Cu(phen)_2(Ad)]2Cl$, 4=$[Cu(phen)_2(Thy)]2Cl$, 5=1,10-phenantroline, 6=Adenine, 7=thymine, 8=Methanol, 9=Distilled water, R1=Ciprofloxacin, R2=Chloramphenicol.

2.7. Antibacterial Activity of Mono and Binuclear Cobalt(II) Complexes Containing 1,10-Phenanthroline and Adenine Using 1,3-diaminopropane as a Spacer

Abebe et al. [4] synthesized three new cobalt(II) mixed ligand complexes with octahedral geometries: $[Co(L1)_2(H_2O)_2]Cl_2$, $[Co(L1)_2(L2)(H_2O)]Cl_2$, and $[Co_2(L1)_4(L2)_2(L3)]Cl_4$. L1 is 1,10-Phenanthroline, L2 is adenine, and L3 is 1,3-diamineprop-ane. Elemental analysis, conductivity measurement, infrared, and UV-Vis spectroscopy methods were used to describe these complexes. Using the disc diffusion method, the antibacterial activity of the ligands, metal salts, and metal complexes were investigated against four pathogenic bacteria (*Staphylococcus aureus, Salmonella typhus, Escherichia coli, and Staphylococcus epidermis*). Ciprofloxacin was used as a control antibiotic. Table 9 summarizes the complex's antibacterial activity data. Their findings demonstrated that all synthesized complexes have antibacterial action. Complex 3 was shown to have superior antibacterial activity than the precursor complexes 1 and 2 against all tested bacterial strains in this study (Table 10).

Table 9. *Antibacterial activity of $CoCl_2.6H_2O$, ligands, metal complexes, and reference antibiotics.*

Antimicrobial activity (mean IZ diameter (mm)±SD)				
	Escherichia coli	***Salmonella typhus***	***Staphylococcus aurous***	***Staphylococcus epidermis***
$CoCl_2.6H_2O$	10.50±0.00	11.33±0.58	12.08±1.01	13.92±0.14
L_1	27.33±0.57	35.33±0.28	34.83±0.29	27.28±0.29
L_2	0	0	0	0
L_3	40.00±0.00	50.17±0.29	54.50±0.50	43.92±0.14
$[Co_2(L1)_4(L2)_2(L3)]Cl_4$	23.76±0.57	23.92±0.14	23.25±0.66	22.50±1.32
$[Co(L1)_2(L2)(H_2O)]Cl_2$	21.33±0.57	20.50±0.00	19.53±0.50	20.17±0.29
$[Co(L1)_2(H_2O)_2]Cl_2$	20.67±0.57	19.50±0.50	18.67±0.58	19.25±0.43
Methanol	42.75±0.25	42.67±0.58	44.83±0.29	40.83±0.29
Water	0	0	0	0
Ciprofloxacin	35.25±0.25	40.50±0.50	29.92±0.38	36.08±1.0

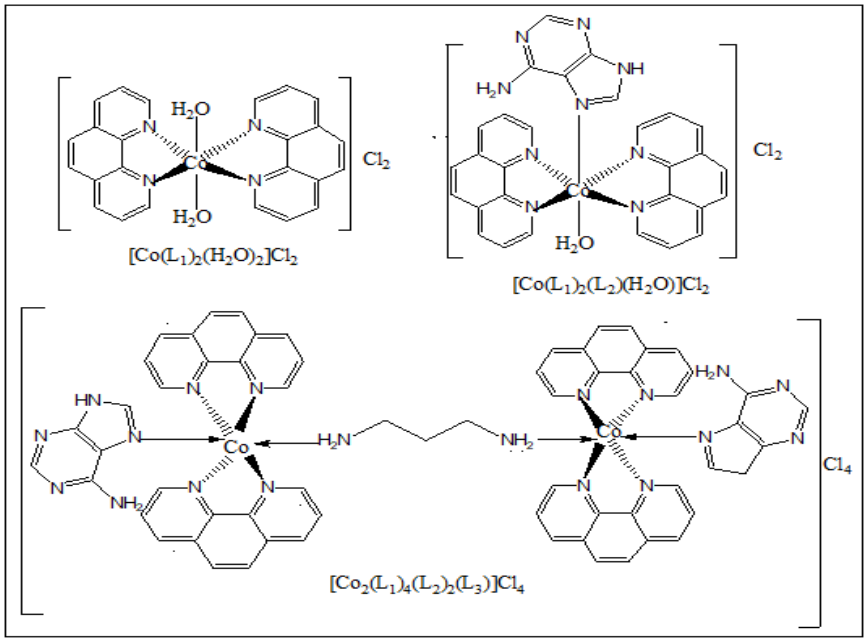

Figure 6. *The proposed structure of the three complexes.*

Table 10. *The percentage activity index data of the complexes against the tested bacteria compared with ciprofloxacin.*

Microorganism				
Compounds	***Escherichia coli***	***Salmonella typhus***	***Staphylococcus aurous***	***Staphylococcus epidermis***
$[Co_2(L_1)_4(L_2)_2(L_3)]Cl_4$	− 0.32	− 0.40	− 0.22	− 0.38
$[Co(L_1)_2(L_2)(H_2O)]Cl_2$	−0.39	− 0.49	− 0.35	− 0.44
$[Co(L_1)_2(H_2O)_2]Cl_2$	−0.41	− 0.59	− 0.38	− 0.47

3. Conclusions

The biological effects of a few transition metal mixed ligand complexes have been reviewed in this study. The use of bioinorganic chemistry in medicine is a fast expanding topic. Novel therapeutic and diagnostic metal complexes are beginning to have an impact on medical practice.

Bioinorganic chemistry advances are important for improving the design of molecules to prevent hazardous side effects and understanding their mechanisms of action. This review reveals that biologically active metals such as Mn(II), Co(II), Cu(II), Zn(II), and Ru(III) containing 1,10-Phenanthroline as a major ligand with any other ligands and their biological applications such as antimicrobial, antibacterial, and antifungal activities and these mixed ligand complexes are active against different microorganisms and could be a suitable strategy to develop novel therapeutic tool for medical treatment.

4. Recommendations

Microbial infections have now emerged as a serious clinical danger, resulting in considerable morbidity and death, owing to the emergence of microbial resistance to currently available antimicrobial treatments. Antibiotic resistance is a develop-ing concern since many bacterial illnesses increasingly resist all known antibiotics. New antibacterial compounds and metal complexes that can combat multiresistant microbes are obviously in high demand. As a result, a variety of metal mixed-ligand complexes including 1,10-Phenanthroline and other ligands have been reported in the literature for antimicrobial activity, however in some cases the antibacterial activity was lower in Gram negative bacteria than in Gram positive bacteria. Therefore, it's critical to supplement efforts to identify novel complexes comprising various ligands with various pr-operties. The ligands, in addition to non-covalent interactions with the DNA, increase the complex's efficacy against microorganisms through covalent interactions. Then, to combat the worrying problem of microbial resistance to antibiotics, synthesis and antimicrobial activity utilizing various ligands may be necessary. It is clear that by coordinating transition metals with appropriate ligands, a set of desirable characteristics may be imposed on them for specific uses. It is accomplished by modifying characteristics of metal ions such as oxidation state stability, solvophilicity, electrophilicity, and nucleophilicity. Tuning can be accomplished by varying the metal and selecting one of the several ligands available for complexation. Therefore, it is recommended that the synthesis of various mixed ligand coordination molecules containing one or more metal centers has become a fascinating and engaging study subject.

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