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Synthesis, Characterization and Antimicrobial Properties of Mixed-Ligand Complexes of Some Metal(II) Ions with Barbituric Acid and 1,10-Phenanthroline Ligands

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Abstract

Many pathogenic organisms have developed resistance to many antibiotics, which leads to an increase in the spread of many microbial infections. There is an urgent need to find more effective drugs to curb widespread transmission. Hence, this study synthesized and evaluated the antimicrobial activities of mixed-ligand complexes of Cu(II), Co(II), Ni(II), Mn(II), and Zn(II) ions with barbituric acid and 1,10 phenanthroline ligands in effort to find more effective antibiotics. The complexes were characterized using elemental analysis, metal analysis, melting points, solubility tests, and spectroscopic analyses (IR and UV-visible). The antimicrobial activities of the complexes were evaluated against two gram-positive bacteria (*Bacillus subtilis* and *Staphylococcus aureus*), two gram-negative bacteria (*Pseudomonas aeruginosa* and *Clostridium* spp.), and four pathogenic fungi (*Candida albicans, Aspergillus flavus, Aspergillus niger,* and *Saccharomyces cerevisiae*). The biological activities of the metal complexes were compared to the activities of some conventional antibiotics. The molecular formulas for the complexes in 1:1:1 (L-M-L) were established based on the results of the elemental and metal analyses. The IR spectroscopic data results showed the coordination of 1,10-phenanthroline to the metal ions through the nitrogen donor atom, while barbituric acid coordinated with the metal ions through nitrogen and oxygen atoms. The formation of the complexes was confirmed by UV-visible spectroscopic data. Many of the mixed-ligand metal complexes demonstrated higher biological activities than the standard drugs and also succeeded where the conventional antibiotics failed. Therefore, the metal complexes could be considered as more efficacious antibiotics that could be added to the arsenal of effective antibiotics for the prevention of the intrinsic problems of multidrug resistance.

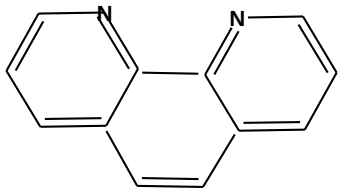
Keywords: Bacteria, Fungi, Ligands, Metal complexes, Multidrug resistance, Barbituric acid.

Introduction

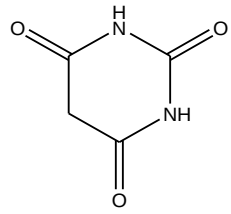
The development of resistance by pathogenic bacteria and fungi to many antibiotics has rendered the drugs ineffective, thereby leading to an increase in the spread of many microbial infections. This problem has been in occurrence for a very long time, and millions of deaths have been reported to occur worldwide as a result of the emergence of new infectious diseases and the re-emergence of diseases caused by multidrug-resistant strains of bacteria and fungi (Tegos

and Hamblin 2013, Borges et al. 2015, Campanini-Salinas et al. 2018). The intrinsic problem of the high rate of antibiotic resistance has become a global concern that requires the development of more effective new drugs, and this has led to a shift in research towards the synthesis and investigation of the antimicrobial activities of many metal complexes. Antimicrobial activities of many organic compounds have been reported to be enhanced upon coordination with metal ions. The development of coordination complexes with biological activities such as antimicrobial, anti-inflammatory, antioxidant, and anticancer has offered great potential to combat microbial resistance to organic antibiotics thereby reducing the spread of diseases and improving health conditions (Hambley 2007, Ronconi and Sadler 2007, Graf and Lippard 2012).

Many chelating ligands containing O, S, and N donor atoms and their metal complexes have been proven to exhibit distinct antimicrobial activities against many multidrug-resistant strains of bacteria and fungi (Colpas et al. 1990, Mandal et al. 1995, Islam et al. 2015). 1, 10-phenanthroline and barbituric acid (Figure 1) are chelating agents containing heterocyclic compounds with N and O donor atoms capable of forming chelates with metal ions. Metal complexes of the chelating agents with other ligands have been studied and found to serve as potential therapeutic agents such as antifungal and antibacterial drugs (Mahmudov et al. 2014, Krasnov et al. 2017, Radhi et al. 2019, Abbas et al. 2020).



1,10-phenanthroline



Barbituric acid

Figure 1: Structures of the chelating agents.

Many gram-positive bacteria, such as *Bacillus subtilis and Staphylococcus aureus,* and gram-negative bacteria, such as *Pseudomonas aeruginosa and Clostridium* spp., and fungi, such as *Candida albicans*, *Aspergillus flavus*, *Aspergillus niger, and Saccharomyces cerevisiae,* have been reported to resist the effects of many antibiotic drugs (Basak et al. 2016, Arendrup and Patterson 2017, Rhodes 2019, Vivas et al. 2019, Yang et al. 2021, Fisher et al. 2022). The conventional therapies for the control of microbial infections have suffered a major setback due to the occurrence of resistance by microorganisms to many antibiotics. Hence, there is a need for the development of more effective chemotherapeutic drugs. Therefore, coordination compounds of many pyrimidine derivatives are active against many microorganisms, and they are now being considered as replacements (Akinyele et al. 2020, Andrejević et al. 2022).

Antibacterial and antifungal activities of Cu(II) mixed ligand complexes of 1,10-phenanthroline and nonsteroidal anti-inflammatory drugs such as tolfenamic acid, mefenamic acid, and flufenamic acid against bacteria, *E. coli, S. aureus, and S. cerevisiae*, respectively, were investigated by Hudecova et al. (2020). The complexes were observed to show more activity against bacterial cells. A new series of mixed ligand complexes of Mn(II), Fe(II), Co(II), Cu(II), and Zn(II) with salicylic acid (SA) and 1,10-phenanthroline were synthesized and characterized using elemental analysis, IR, and UV-vis spectroscopic analysis by Lawal et al. (2017). Their antimicrobial activities against the bacteria *Escherichia coli*, *Staphylococcus aureus, Klebsiella pneumonia, Pseudomonas aeruginosa,* and the fungi *Candida spp.* were

also investigated. The complexes showed a diverse range of activities, with Cu(II) showing the highest antimicrobial activity, while the Fe(II) complex showed the least activity against bacteria and fungi.

Two complexes of ruthenium(III) from both 1,10-phenanthroline and guanide have been synthesized (Abebe and Hailemariam 2016). The in vitro antibacterial activities of the complexes against two gram-positive (*Staphylococcus aureus* and methicillin-resistant *Staphylococcus aureus*) and two gram-negative (*Escherichia coli* and *Klebsiella pneumoniae*) bacteria were evaluated. The complexes were found to exhibit better activities against the bacteria than the conventional chloramphenicol and ciprofloxacin antibacterial drugs. The mixed-ligand complex Cu(II) with bisimidazoles and 1,10-phenanthroline was synthesized, and the antibacterial properties of the complex were examined against the bacteria strains *Staphylococcus haemolyticus*, *Staphylococcus aureus*, *Proteus vulgaris*, *Escherichia coli*, *Pseudomonas aeruginosa*, and *Mycobacterium bovis* (Valle). The complex was found to be more effective against strains of *S. hemolyticus* and *S. aureus mycobacteria* (Plotnikov and Plotnikov 2018). A cadmium complex of barbiturate ligand was synthesized, and the complex was evaluated for its antimicrobial activities against various bacteria. The complex was found to exhibit stronger antibacterial activities than the ligand (Divya et al. 2022).

The emergence of multidrug-resistant pathogens has jeopardized many nations' capability to control many diseases and prevent fatality rates. Therefore, new and more effective antibiotics are needed to combat multidrug-resistant pathogens. Many researchers have investigated the antimicrobial activities of binary metal complexes of 1,10-phenanthroline, and barbituric acid against many multidrug-resistant microorganisms; however, the antimicrobial activities of the metal complexes are found to be limited (Yilmaza et al. 2008, Ikotun et al. 2011, Ismail et al. 2014, Palmucci et al. 2016, Akinyele et al. 2020, Andrejević et al. 2022).

Based on the literature review, no study has been carried out on the effects of mixed-ligand complexes of transition metal ions with 10-phenanthroline and barbituric acid on multidrug-resistant organisms. Therefore, regarding the antimicrobial activity displayed by binary metal complexes of 10-phenanthroline and barbituric acid, novel mixed-ligand complexes of 1,10 phenanthroline, and barbituric acid with five metal ions are synthesized, characterized and their biological activities against multidrug-resistant bacteria and fungi are evaluated in this study with a view to providing information on their biological activities, which could be exploited for combating the problem of multidrug resistance.

Materials and Methods

Reagents and equipment

The reagents and solvents used were of analytical grade; they were used without further purification. They included copper(II) acetate, zinc(II) sulphate heptahydrate, manganese(II) acetate, nickel(II) sulphate hexahydrate, cobalt(II) acetate, disodium-ethylenediaminetetraacetic acid, concentrated nitric acid, perchloric acid, murexide dye, solochrome black T, concentrated ammonia, ammonium chloride, sodium hydroxide, methanol, distilled water, dimethyl suphoxide, ethanol, chloroform, propan-2-ol, acetone, diethyl ether, ethylacetate, n-hexane, butan-1-ol, petroleum ether, sodium chloride, 1,10-phenanthroline monohydrate, barbituric acid, colistin, cotrimoxazole, augmentin, amoxicillin, and erythromycin.

The bacteria used included *Bacillus subtilis*, *Clostridium* spp., *Pseudomonas aeruginosa*, and *Staphytococcus aureus* while *Candida albicans*, *Aspergillus flavus*, *Aspergillus niger*, and *Saccharomyces cerevisiae* pathogenic fungi were employed.

Preparation of the mixed-ligand metal complexes

A weight of 0.256 g (0.002 mol) of barbituric acid was dissolved in 15 ml of 50% ethanol in a 100 ml beaker over a hot plate at

80 °C. Again, 0.397 g (0.002 mol) of 1,10-phenanthroline monohydrate was carefully weighed and dissolved in 15 ml of 50% ethanol in a separate beaker. The solutions of the two ligands were added simultaneously and dropwise to a stirring solution of 0.002 mol of each of the metal salts on a magnetic stirrer at 60 °C. The resulting solution was stirred for 2 hours, and the precipitated complex was removed by suction filtration, thoroughly washed with ethanol, and dried over silica gel in a desiccator.

Characterization of the complexes

The percentage of metal content in the complexes was determined by complexometric titration. Infrared spectra of all the ligands and complexes were recorded on the Perkin Elmer FT-IR Spectrum Bx spectrophotometer using a KBr disc in the range 400–4500 cm^{-1} at the Central Laboratory, Ladoke Akintola University of Technology, Ogbomoso. The electronic spectra of the solution of the ligands and complexes were taken on Spectro UV-Vis double beam pc scanning spectrophotometer UVD 2960 in the range of 190–900 nm at the Department of Chemistry, Ladoke Akintola University of Technology, Ogbomoso. Elemental (CHN) analysis was carried out at Atlantic Microlab Inc. Norcross, Georgia, USA.

Evaluation of antimicrobial activities of the metal complexes

Antibacterial assays

The antibacterial activity of the synthesized metal complexes was determined using a filter paper disc. Mueller-Hinton (MH) agar-base plates were used and prepared using sterile Petri dishes. The MH agar at 48 °C was inoculated with MH broth cultures of each bacterial species and poured over the base plates to form a homogeneous layer. Filter paper discs (Whatman No. 1) were sterilized in the oven at 85 °C for 1 h and cut into discs using a 5.0 mm sterile cork borer and blade. The dried sterile papers were dipped into 4 ml of the various samples, and the discs were placed on cultured plates and kept in the refrigerator for 24 h for proper diffusion of the samples into the media. The plates were incubated for 24 h at 37 °C for the organisms to grow and thereafter the zones of inhibition were observed and measured. The concentrations of each sample used were 5 mg/ml, 20 mg/ml, 50 mg/ml, 100 mg/ml and 250 mg/ml and dimethylsulphoxide (DMSO) was used in the dilution of sample (Jonathan and Fasidi 2003, Buwa and Staden 2006). Conventional antibiotics, colistin, cotrimoxazole, amoxicillin, erythromycin, and augmentin) were used as the reference drugs.

Antifungal assays

In the determination of antifungal activities of the complexes, Whatman filter paper No. 1 was cut into a disc using a 5.0 mm cork borer and sterile blade. These cut filter papers were sterilized in the oven at 85 °C for 1 h. The dried sterile papers were dipped into 4 ml of various extracts. Sterile Saboraud dextrose agar was poured into the Petri dishes and allowed to set. The plates were cultured with 24 h old organisms of *Aspergillus flavus*, *Aspergillus niger*, *Saccharomyces cerevisiae*, and *Candida albicans.* The plates were incubated at 30 °C for the organisms to grow. The filter papers containing the extracts were placed on the cultured plates. The plates were kept in the refrigerator for proper diffusion of the extracts into the media before incubating at 30 °C for 72 h (Jonathan and Fasidi 2003). The zones of inhibition were then measured. The experiments were conducted in duplicate, and cotrimoxazole was used as the reference drug.

Results and Discussion

The synthesized mixed-ligand complexes were characterized on the basis of solubility tests, percentage metal analysis, melting point, elemental analysis, and IR and UV-vis analyses. The physical properties and analytical measurements are shown in Table 1, while the solubility property of the metal complexes is reported in Table 2. The IR and Uv-visible bands are shown in Tables 3 and 4, respectively.

Table 1: Physical and analytical measurements

Complex	Molecular formula	% Yield	Melting point (°C)	Colour	Elemental analysis			
					% C Calc. (Found)	% H Calc. (Found)	% N Calc. (Found)	% M Calc. (Found)
L1	$C_4H_4N_2O_2$		245	Cream				
L2	$C_{12}H_8N_2$		114–117	White				
01	$C_{16}H_{24}N_4O_9Cu$	64.27	300	Green	40.05 (40.94)	5.04 (4.57)	11.67 (10.66)	13.24 (11.32)
02	$MnC_{16}H_{24}N_4O_9$	35.87	350	Cream	40.78 (38.59)	5.13 (4.30)	11.89 (13.28)	11.66 (8.87)
03	$ZnC_{14}H_{20}N_4O_{11}S$	33.60	285	White	32.48 (33.99)	3.89 (3.71)	10.83 (6.60)	12.64 (12.15)
04	$NiC_{16}H_{28}N_4O_{11}$	54.20	285	Pale-blue	37.60 37.09	5.52 4.70	10.96 12.72	11.49 (11.85
05	$CoC_{16}H_{26}N_4O_{10}Cl$	29.32	280	Pink	34.60 (37.09	4.64 (4.23)	9.93 (11.62)	10.45 (11.97)

L1= Barbituric acid (Barb), L2 = 1,10-phenanthroline (phen), 01 = $[Cu(Barb)(Phen)(H_2O)_2].4H_2O$, 02 = $[Mn(barb)(phen)(H_2O)_2].6H_2O$, 03 = $[Zn(Barb)(phen)(H_2O)SO_4].4H_2O$, 04 = $[Ni(barb)(phen)].8H_2O$, 05 = $[Co(barb)(phen)(H_2O)(Cl)].6H_2O$

Table 2: Solubility data for the complexes

Complex	Ac	EtOH	MeOH	$CHCl_3$	EtOAc	DH_2O	Hex	DMSO	DEE
01	I	SH	SH	I	I	I	I	S	I
02	I	I	I	I	I	I	I	S	I
03	I	I	I	I	I	S	I	S	I
04	I	SH	SH	I	I	SH	I	S	I
05	I	I	I	I	I	I	I	S	I

Key: S = Soluble, SH = Soluble when heated, SSH = Slightly soluble when heated, I = Insoluble Ac = Acetone, EtOH = ethanol, MeOH = Methanol, $CHCl_3$ = Chloroform, EtOAc = Ethylacetate, DH_2O = Distilled water, Hex = n-hexane, DMSO = dimethysuphoxide, and DEE = Diethyl ether.

Table 3: Infrared spectra data (cm^{-1}) for the metal complexes

Compound	$\nu_{C=C}$ (m-w)	$\nu_{C=N}$ (w-s)	ν_{C-N} (m-s)	$\nu_{C=O}$ (s)	ν_{N-H} (m)	ν_{O-H} (b)	ν_{S-O} (s)	ν_{M-N} (s)	ν_{M-O} (s)	ν_{M-Cl} (s)
L1	-	-	1350	1719	3477	-	-	-	-	
L2	1504 1639	1585	1315	-	-	3415	-	-	-	
01	1423 1622	1560	1300	1693	3426	-	-	546	426	
02	1593	1593	1294	1694	3379	3165	-	532	420	
03	1601	1442	1317	1720	3267	-	766	617	400	
04	1402	1402	1294	1699	3450	-	-	653	530	
05	1607	1355	1294	1686	3400	3400	-	530	434	725

Key: s = strong, m = medium, and w = weak.

Table 4: Electronic spectra data for the complexes

Complex	Band (nm)	Molar absorptivity ε,($mol^{-1}dm^3cm^{-1}$)	Assignment of transition(s)
L1	264		*n–π**
	246		*π–π**
	228		*π–π**
L2	264	37,879	*n–π**
	230	43,478	*π–π**
01	674	86.37	*d-d*
02	680	43.46	*d-d*
	596	62.36	*d-d*
	542	59.82	*d-d*
	454	64.73	*d-d*
03	602	685	MLCT
	580	708	
04	500	150	*d-d*
	370	950	*d-d*
05	594	259.64	*d-d*
	536	316	*d-d*

Antimicrobial activities of the metal complexes

The inhibitory zones of metal complex, antibacterial and antifungal activities displayed by the metal complexes and the standard drugs are shown in Figures 2, 3 and 4, respectively.

Physicochemical properties of the metal complexes

The microanalytical data and various colours of the mixed-ligand metal complexes of barbituric acid 1,10-phenanthroline are shown in Table 1. $[Zn(Barb)(Phen)(H_2O)(SO_4)].4H_2O$ was obtained in a white colour. The complexes of copper, manganese, nickel, and cobalt are green, cream, pale-blue, and pink, respectively. The percentage compositions of carbon, hydrogen, oxygen, and metal ions in the complexes were determined as shown in Table 1. The data obtained from the elemental and percentage metal analyses were in close agreement with the theoretical values and agreed with the proposed molecular formula and $ML_1–L_2$ composition of the metal(II) mixed-ligand complexes. The mixed-ligand complexes of Cu(II) and Co(II) ions gave the highest and lowest yields, respectively. The ligands barbituric acid (L_1) and 1,10-phenanthroline(L_2) melted at 100–240 °C and 98–100 °C, while their metal complexes melted between 280 and 300 °C (Table 1). This confirmed the coordination of the ligands to the metal ions and the purity of the complexes. The complexes are all soluble in DMSO but showed different degrees of solubility in other solvents (Table 2).

Infrared spectra

The relevant infrared spectra data for the free ligands and their mixed ligand metal complexes are given in Table 3. In the spectra of 1,10-phenanthroline monohydrate, the absorption bands at 3415 cm^{-1}, 1585 $cm^{-1,}$ and 1315 cm^{-1} were assigned to $\nu_{(O–H)}$, $\nu_{(C = N),}$ and $\nu_{(C–N)}$ stretching vibrations, respectively. The bands at 1600 cm^{-1} and 1504 cm^{-1} were assigned $\nu_{(C=C)}$ aromatic stretching vibrations corresponding to the aromatic rings in the ligand molecule. The band of 1315–1585 cm^{-1} was found to undergo a hypsochromic shift, which confirmed the coordination of the ligand to the central metal ions through the nitrogen donor atom (El-Ghamry et al. 2013, Triathi and Kamal 2015). The bands at 3477 cm^{-1}, 1719 cm^{-1}, and 1350 cm^{-1} in the barbituric acid spectra were assigned to $\upsilon_{(N-H)}$, $\upsilon_{(C=O),}$ and $\upsilon_{(C-N)}$ bands, respectively. Bands at 1640 cm^{-1} and 1344 cm^{-1} were assigned $\nu_{(C=N)}$ and $\nu_{(C–N)}$ stretching vibrations. The bands at 3477 cm^{-1} and 1719 cm^{-1} were

observed to undergo hypochromic shift confirming the coordination of the ligand to the central metal ions through nitrogen and oxygen atoms. The shifts and appearance of a new band in the region 400–800 cm^{-1} in the complexes established the formation of M-O, M-N, M-Cl, and M-S bonds (Venkatesh et al. 2016, Teleb et al. 2019).

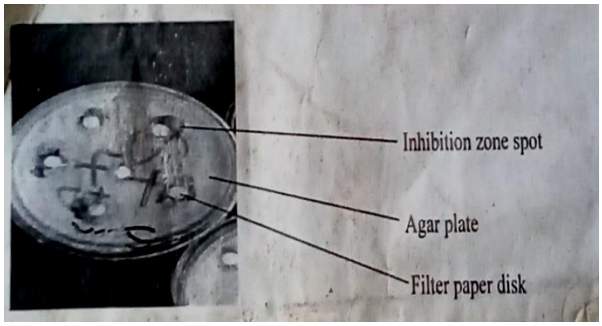
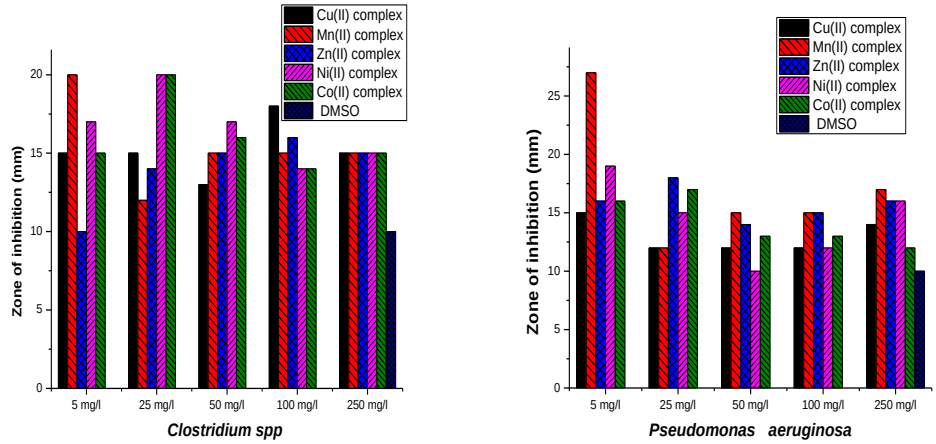
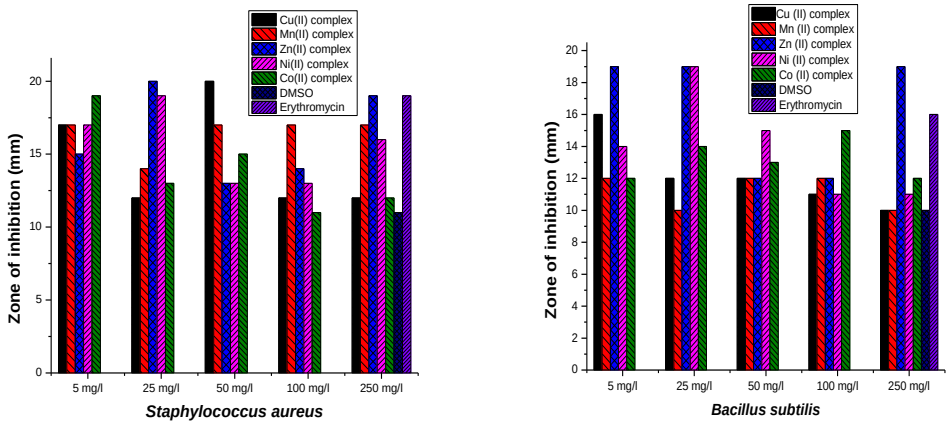


Figure 2: Spots of inhibitory zone of one of the metal complexes.



(a) Gram-negative bacteria



(b) Gram-positive bacteria

Figure 3: Histogram representation of antibacterial activities of the complexes and the standard drug.

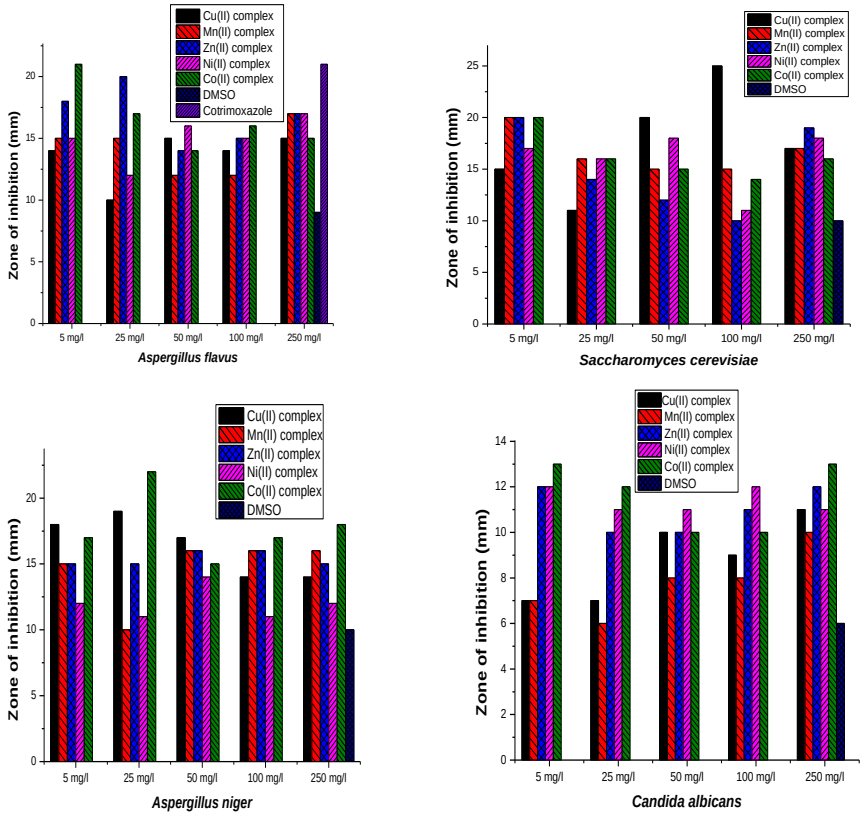


Figure 4: Histogram representations of antifungal activities of the complexes and the standard drug.

Electronic spectra

In the electronic spectra of barbituric acid, bands at 264 nm, 246 nm, and 228 nm were observed and attributed to n–π^* and π–π^* electronic transitions. Also, 1,10-phenanthroline showed two bands at 264 nm and 230 nm. The bands were assigned to n–π^* and π–π^* electronic transitions, respectively, as shown in Table 4. In the Cu(II) metal complex, an electronic band obtained at 674 nm was assigned to *d-d* (Nair et al. 2007). The electronic spectra of the mixed ligand of Mn(II) showed four bands at 680 nm, 596 nm, and 542 nm due to *d-d* electronic transitions (Koteswara and Reddy 1990, Reddy et al. 2008). In the spectra of the Zn(II) complex, two bands at 602 nm and 580 nm observed were attributed to MLCT transitions (Sathisha et al. 2008). Bands at 500 nm, 950 nm, 536 nm, and 594 nm were observed in the spectra of Ni(II) and Co(II) complexes, respectively. The bands were attributed to *d-d* electronic transitions (Rasool et al. 2014). These bands confirmed the formation of the metal complexes.

Antibacterial activities of the metal complexes

The metal complexes were tested against two gram-negative and two gram-positive bacteria at 5 mg/l, 25 mg/l, 50 mg/l, 100 mg/l, and 250 mg/l concentrations. The zones of inhibition of the complexes against the bacteria as measured over the disc plates are shown in Figure 2. The ligands at the concentrations were ineffective against the bacteria, while the complexes' antibacterial activities were measured and are represented using histograms shown in Figure 3. In Figure 3a, at the lowest concentration of 5 mg/l, the Mn(II) complex was found to exhibit the highest activity against

Clostridium spp., while the bacterium strain was resistant to the Zn(II) complex. The complexes of Ni(II) and Co(II) were found to exhibit the highest activity at 25 mg/l concentration, while the highest antibacterial activity at 50 and 100 mg/l concentrations was exhibited by Ni(II) and Cu(II) complexes, respectively. All the complexes exhibit the same activity at 250 mg/l. Different activities were shown by the complexes against *Pseudomonas aeruginosa.* The complexes displayed some degrees of activity against the bacterium, with the complex of Mn(II) showing the best activities at 5 mg/l, 50 mg/l, and 250 mg/l, Zn(II) complex displayed the best activity at 25 mg/l and the Ni(II) complex was inactive at 50 mg/l. The two gram-negative bacteria are resistant to cotrimoxazole and colistin drugs.

The metal complexes and the standard drugs (augmentin, amoxicillin, and erythromycin) were also examined for their effectiveness against two gram-positive bacteria at the concentrations (Figure 3b). At the different concentrations, distinct activities were exhibited by the metal complexes. At a concentration of 5 mg/l, Co(II) displayed the highest activity against the *Staphylococcus aureus* strain. Zn(II) complex showed pronounced activity against the bacterium at 25, and 250 mg/l, while the highest antimicrobial activities were exhibited by Cu(II) and Mn(II) complexes at 50 and 100 mg/l, respectively. The standard drugs were inactive at the concentrations except for erythromycin, which was observed to show the same activity as the Ni(II) complex. The Zn(II) and Cu(II) complexes showed more activities than the drug against the bacterium at 25 and 50 mg/l, respectively. The effects of the metal complexes and the standard drug observed against *Bacillus subtilis* are also presented in the figure. Zn(II) complex was observed to have pronounced activity against the bacterium at 5 mg/l and 250 mg/l. At 25 mg/l, Zn(II) and Ni(II) exhibited the same antimicrobial activities, while the Mn(II) complex was inactive. Ni(II) and Co(II) complexes were observed to display the best antibacterial activity against the bacterium at 50 and 100 mg/l, respectively. However, erythromycin was observed to exhibit antibacterial activity but lower than the metal complexes at a 250 mg/l concentration.

Antifungal activities of the metal complexes

The antifungal activities of the ligands, metal complexes, and standard drug cotrimoxazole at concentrations of 5 mg/l, 25 mg/l, 50 mg/l, 100 mg/l, and 250 mg/l were evaluated against four fungi (Figure 4). The ligands showed no activity against all the fungi. The complexes Co(II), Zn(II), Ni(II), and Co(II) showed good activities against the fungus *Aspergillus flavus* at concentrations of 5, 25, 50, and 100 mg/l, respectively, while the standard drug showed no activity at the concentrations. However, cotrimoxazole had the best activity at 250 mg/l against *Aspergillus flavus.* Different activities were exhibited by the metal complexes against *Saccharomyces cerevisiae* by the complexes, while the standard drug displayed no effect against the fungus. At a concentration of 5 mg/l, all the metal complexes were active against the fungus, with the Cu(II) complex showing the least effect on the fungus. Mn(II), Ni(II), and Co(II) complexes displayed the same activities against the fungus at 25 mg/l, while the Cu(II) complex displayed the lowest antimicrobial activity. At 50 and 100 mg/l, the Cu(II) complex demonstrated the best activity, and at 250 mg/l, Zn (II) was observed to be more effective than the other metal complexes. The fungus showed resistance to the standard drug.

All the complexes were active against *Aspergillus niger* at the different concentrations except Mn(II) at a concentration of 25 mg/l. The Cu(II) complex was found to be more active than the other metal complexes at 5 and 50 mg/l concentrations, while the Co(II) complex had more activities at 25, 100, and 250 mg/l against *Aspergillus niger*. The metal complexes exhibited different levels of activity against *Candida albicans* at the concentrations. The Co(II) complex was more active at concentrations of 5, 25, and 250 mg/l than other complexes against the

fungus. At the concentrations of 50 and 100 mg/l, the Ni(II) complex exhibited the best antimicrobial activity against the fungus. The standard drug was inactive against the fungus.

The metal complexes showed different degrees of activity against the microorganisms, and they were found to be more effective than the standard drugs against bacteria and fungi. The enhanced biological activities displayed by the metal complexes could be attributed to chelation. On chelation, the polarity of the metal atom is reduced due to the partial sharing of its positive charge with donor groups of the ligand and possible π-electron delocalization over the aromatic rings, leading to enhancement of the lipophilicity of the metal complexes. The increased lipophilicity improves the penetration of the complexes through the lipid membranes of the organism leading to the blocking of the metal binding sites in the enzymes of the microorganism (Teleb et al. 2019).

Conclusion

The mixed ligand complexes of barbituric acid (L1) and 1,10-phenanthroline (L2) with Co(II), Cu(II), Mn(II), Ni(II), and Zn(II) ions were synthesized, characterized and the in-vitro antibacterial and antifungal activities of the complexes were evaluated. The metal complexes demonstrated more antimicrobial activities than the standard drugs and also succeeded where the drugs failed. The metal complexes could be considered as more efficacious antibiotics that could be added to the arsenal of effective antibiotics for the prevention of widespread or intrinsic problems of multidrug resistance.

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