International Journal of Science and Research Archive
eISSN: 2582-8185
Cross Ref DOI: 10.30574/ijsra
Journal homepage: https://ijsra.net/

(RESEARCH ARTICLE)

Check for updates

Synthesis, characterization and antibacterial activity of Ni (II) and Mn (II) cephalexin complexes

Ahmed Aliyu Maje [1,*] Ahmad Shu'aibu Babayo [2] and (Navy Capt.) Sa'idu IR [3]

[1] *School of Sciences, Department of Integrated Science, Jigawa State College of Education, Gumel, Nigeria.*
[2] *School of General Studies, Department of Science Education, Jigawa State College of Education, Gumel. Nigeria.*
[3] *Faculty of Military Science, Department of Cyber Security, Nigeria Defence Academy Kaduna, Nigeria*

International Journal of Science and Research Archive, 2025, 14(02), 248-257

Publication history: Received on 27 December 2024; revised on 02 February 2025; accepted on 05 February 2025

Article DOI: https://doi.org/10.30574/ijsra.2025.14.2.0375

Abstract

The increasing threat of antimicrobial resistance has necessitated the development of novel therapeutic strategies. This study focuses on the synthesis, characterization, and antimicrobial evaluation of divalent metal-cephalexin complexes involving Mn (II) and Ni (II). Cephalexin, a β-lactam antibiotic, was coordinated with these metal ions to enhance its stability and bioactivity. The complexes were synthesized through a reflux method and characterized using solubility tests, decomposition temperature analysis, Fourier Transform Infrared (FT-IR) spectroscopy, conductivity measurements, magnetic susceptibility, and Job's method of continuous variation. The results indicate that the metal complexes exhibit tetrahedral geometry and are non-electrolytic in nature. Antimicrobial screening against selected bacterial and fungal strains, including Staphylococcus aureus, Bacillus subtilis, Escherichia coli, Candida albicans, Tinea capitis, and Tinea pedis, demonstrated that the metal complexes retained antimicrobial activity, albeit lower than free cephalexin. The findings suggest that while metal complexation influences drug stability and coordination chemistry, further studies are needed to optimize their therapeutic efficiency.

Keywords: Antimicrobial resistance; Metal-cephalexin complexes; β-lactam antibiotics; Antimicrobial activity

1. Introduction

The rise of antimicrobial resistance (AMR) has made the search for new and more effective antimicrobial agents a top priority in medicinal chemistry. As traditional antibiotics become less effective, researchers are exploring innovative ways to enhance their potency. One promising approach is the synthesis of metal-drug complexes, which can improve the stability, bioavailability, and overall antimicrobial activity of existing antibiotics.

This thesis focuses on developing and evaluating divalent metal-cephalexin complexes to enhance the drug's therapeutic potential. Transition metals like copper (Cu), zinc (Zn), and silver (Ag) have shown great promise in strengthening antibiotic effectiveness by stabilizing the drug, improving its absorption, and increasing its reactivity [8]. These metal complexes work by disrupting bacterial cell membranes, interfering with enzyme functions, and generating reactive oxygen species (ROS), all of which contribute to stronger bactericidal effects [5]. By incorporating metals into cephalexin, this study aims to develop new compounds that could combat resistant bacterial strains more effectively.

Cephalexin, a first-generation cephalosporin antibiotic is one of the numerous polydentate ligands available, it is widely used to treat a variety of bacterial infections. Its mechanism of action involves inhibiting bacterial cell wall synthesis by binding to penicillin-binding proteins (PBPs), which are essential for the cross-linking of peptidoglycan chains in the bacterial cell wall. This action leads to cell lysis and death, effectively combating bacterial infections caused by both Gram-positive and some Gram-negative bacteria [6].

* Corresponding author: Ahmed Aliyu Maje

Cephalexin's chemical structure includes a β-lactam ring, which is crucial for its antibacterial activity, and various functional groups such as amine and carboxylic groups, which can act as ligands in coordination chemistry. These functional groups allow cephalexin to form stable complexes with metal ions, potentially enhancing its antimicrobial properties through unique metal-ligand interactions [1];[11]. The cephalexin monohydrate has the formula: $C_{16}H_{17}N_3O_4S$ (H_2O) and its structure is shown below.

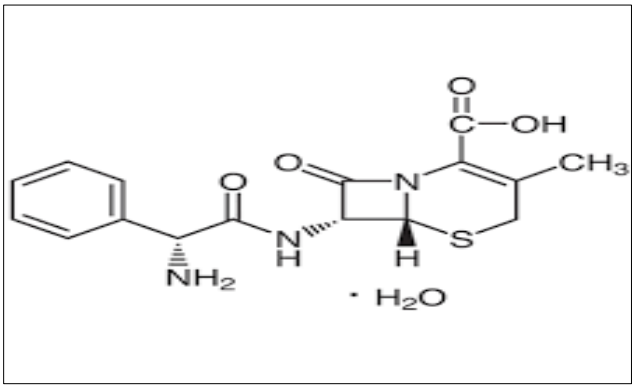

Figure 1 Structure of Cephalexin

2. Statement of the Problem

Antimicrobial resistance is making antibiotics like cephalexin less effective, creating a need for new strategies to enhance their potency. One possible solution is binding cephalexin with metals like ***Mn (II) and Ni (II)*** to improve its stability and effectiveness. However, it's unclear whether these metal complexes will actually enhance or weaken cephalexin's antimicrobial properties.

This study addresses three key questions:

- Can metal coordination make cephalexin more stable?
- Does it improve or reduce its antibacterial and antifungal activity?
- How do these metal complexes compare to regular cephalexin?

By synthesizing and testing Mn (II) and Ni (II) cephalexin complexes, this research aims to determine if metal-based modifications could be a promising approach to fighting resistant bacteria.

3. Scope of the Study

This study explores the potential of enhancing antibiotic effectiveness by combining cephalexin, a widely used β-lactam antibiotic, with transition metals—specifically Mn (II) and Ni (II). Given the growing concern over antimicrobial resistance, the research aims to determine how metal coordination affects the stability, structure, and antimicrobial properties of cephalexin.

The study is structured around three key areas:

3.1. Synthesis of Metal Complexes:

- Cephalexin is combined with Mn(II) and Ni(II) through a reflux process to form stable metal-drug complexes.
- The goal is to create new compounds that might offer improved drug stability and bioavailability.

3.2. Characterization of the Complexes:

- Various tests are conducted to understand the physical and chemical properties of the new compounds, including:
- **Infrared Spectroscopy (FT-IR):** Identifies how the metal binds to cephalexin.
- **Magnetic Susceptibility & Conductivity Tests:** Helps determine the geometry and electrical behavior of the complexes.
- **Solubility & Decomposition Temperature Tests:** Assesses the stability of the complexes.

3.3. Antimicrobial Evaluation

- The effectiveness of the metal-cephalexin complexes is tested against common bacteria and fungi, such as ***Staphylococcus aureus, Escherichia coli, and Candida albicans.***
- The results are compared with free cephalexin and standard antibiotics like amoxicillin and nystatin.

Objectives

The specific objectives include:

- Synthesis of cephalexin metal complexes by reacting $MCl_2 \cdot nH_2O$ (where M = Mn, and Ni) with cephalexin in a methanol solution.
- Characterization of the synthesized complexes using various techniques such as solubility tests, decomposition temperature analysis, FTIR spectroscopy, conductivity measurements, water of crystallization analysis, magnetic susceptibility, and Job's method of continuous variation.
- Evaluation of the antimicrobial activities of these metal (II)-cephalexin complexes against selected bacterial and fungal isolates.

4. Literature Review

Cephalexin and its derivatives are commonly utilized in the pharmaceutical and medicinal industry due to their biological and pharmaceutical activities, including anti-microbial, anti-cancer, anti-bacterial, and herbicidal activities as well as possessing high palatability and being useful for skin and joint infections. Interestingly, some organic drugs, including cephalexin, which exhibit toxicological and pharmacological properties, can be administered in forms of metal complexes. Many researchers have synthesized organic ligands derived from cephalexin in forms of Schiff bases and azo compounds which exhibited higher biological and medicinal properties when compared to cephalexin alone. One of the important features that make Schiff base more desirable when used for coordination complexation is possessing the ability to coordinate with the metal ions via forming chelating rings, which make them very effective when it comes to clinical and analytical applications. In this review, we present the latest and most promising studies that are related to synthesizing organic derivatives of cephalexin and their drug-metal complexes as well as the biological activity that is associated with these complexes [12]. A series of mixed ligand complexes of cephalexin and cefotaxime sodium were prepared. All complexes were characterized by molar conductivity, IR and UV-Visible spectroscopy. All the complexes have Oh geometry with general formula $\{M(L1)(L2)(H_2O)_2\}$, where M= Co(II), Cu(II), Ni(II), V(II), L1= cephalexin, L2= cefotaxime sodium. Antibacterial activity of all the synthesized complexes and ligands were tested against some bacteria. The antibacterial activities of all compounds in case of *Pseudomonas aeruginosa* at DMSO (10 mg/ml) concentration exhibit not active. The *Staphylococcus aureus*, *Escherichia coli, Salmonella,* some metal complexes exhibit more activity than ligand [10]. The interactions of cephalexin (Hcepha) with transition and d10 metal ions have been investigated. The complexes [M(cepha)Cl] nH2O [M¼Mn (II), Co (II), Ni (II), Cu (II), Zn (II), Cd (II), Hg (II)] were characterized by physicochemical and spectroscopic methods. The IR and 1 H NMR spectra of the complexes suggest that cephalexin behaves as a mono anionic tridentate ligand. In vitro antibacterial activities of Hcepha and the complexes were tested [4].

In a study by [17], cephalexin and two beta-lactam antibiotics were combined with four distinct aldehydes: 3-hydroxybenzaldehyde, 4-dimethylaminobenzaldehyde, 4- methoxybenzaldehyde, and 4-bromobenzaldehyde, to synthesize Schiff bases. The reaction between the free amino group of the acylamino side chain and the aldehydes resulted in the formation of four Schiff bases within the medication. Comprehensive characterization and surface examination were performed on each Schiff base. The biological activity of the synthesized compounds against *Bacillus pumilus* (Gram-positive bacteria) and *Candida albicans* (fungus) was evaluated using the agar diffusion disc method. The antibacterial screening tests revealed that the Schiff bases exhibited enhanced antibacterial activity against these microorganisms, indicating superior efficacy compared to the parent drugs. However, no significant inhibitory effect on the tested fungus was observed. Since the time Alexander Fleming discovered the penicillin in 1929 and the first starter of the sulpha medications by Domagk in 1932, the number of new antimicrobials presents increased dramatically between 1940 and 1960. The "period of antibiotic" droves to positive until the early 1970s, those contagious diseases may be well arranged and stopped, and mankind felt confident that the new drug would overcome it. However, contagion remains the second-main cause of death all over the world, producing more than 13 million deaths each year. This point is the result of the emergence of new illnesses, the return of diseases once arranged, and in particular, offers resistance of antimicrobial. Previously, antibiotics are chemicals created by diverse types of microorganisms that inhabit the evolution of other microorganisms and may ultimately damage them. In modernistic use, the term antibiotics have been extended to include both chemically adjusted normal antibiotics and fully synthetic materials that are

technically indicated to as agents of synthetic antimicrobial or semisynthetic. Antibiotics Antimicrobials can be sorted based on their purpose. “Tight -spectrum” antibiotics goal certain types of bacteria, like grams bacteria of -(-ive) or (+ive), but the wide spectrum of antibiotics discourages a broad bacteria zone. The discovery and amelioration of antibiotics are among the efficient achievements in technology and neoteric science and most effective in the fight versus contagious diseases. Nevertheless, the increasing emergence and distribution of antimicrobial resistance among strains of bacterial has decreased the effectiveness of therapy for large quantities of drugs. Mediators of Antimicrobial bacterial cell death can be classified as bacterial, represented by a bactericide or chloramphenicol by penicillin. Bactericidal agents cause the death of bacterial cells, while bacterial agents prevent bacteria from increasing. Semi-synthetic cephalosporin antibiotics have structures similar to that of penicillins, and both groups of compounds are characterized by similar properties and determined by the same methods. Most antibiotics, including cephalosporins and their decomposition products, contain electron donor groups that can bind naturally occurring metal ions in vivo. Cephalosporin antibiotics exhibit a change in their toxicological properties and biological performance when they were tested as metal complexes. The proposed reason for such a behavior is the capability of chelate binding of the cephalosporins to the metals. In an attempt to understand the coordination mode of metals with cephalosporins, different spectroscopic techniques such as IR, UV-visible, NMR spectroscopy and voltammetric measurements were carried out to elucidate the structure of the metal-cephalosporin complexes. Synthesis, characterization and biological screening of the cephalosporins and of the cephalosporin-metal complexes are discussed in this review. However, little information is available on the influence of the metal ions on the pharmacokinetics of the cephalosporin derivatives [3].

Also, in the work of [4], metal (II) coordination compounds of a cephalexin Schiff base (HL) derived from the condensation of cephalexin antibiotic with sulphathiazole were synthesized. The Schiff base ligand, mononuclear $[ML(OAc)(H_2O)_2]$ (M(II) = Mn, Co, Ni, Zn) complexes and magnetically diluted trinuclear copper(II) complex $[Cu_3L(OH)_5]$ were characterized by several techniques, including elemental and thermal analysis, molar conductance and magnetic susceptibility measurements, electronic, FT-IR, EPR and 1 H NMR spectral studies. The analytical and molar conductance values indicated that the acetate ions coordinate to the metal ions. The Schiff base ligand HL behaves as a monoanionic tridentate NNO and tetradentate NNOO chelating agent in the mono and trinuclear complexes respectively. The work of [2], shows copper (II) and zinc (II) complexes of Schiff bases obtained by condensation of amoxicillin and cephalexin with salicylaldehyde/pyridoxal were prepared and characterized by microanalytical, thermogravimetric, magnetic and spectroscopic data. All the complexes were found to be sixcoordinate and containing two water molecules. The electron paramagnetic resonance spectral lines exhibited rhombic distortion from axial symmetry, with $g > g\perp > ge$, in the copper (II) complexes. The geometry of the zinc (II) complexes appears to be octahedral. All the compounds under investigation showed antibacterial activity. The antibacterial activity showed the following trend: copper (II) complexes > zinc (II) complexes > Schiff base ligands > parent drugs. The copper (II) complexes with the Schiff bases derived from cephalexin showed substantially enhanced activity against Pseudomonas *aeruginosa* compared with the parent drug. All the copper complexes were also found to be active against kaolin paw oedema, whereas the parent drugs were inactive.

5. Methodology

5.1. Synthesis of Metal Complexes

The complexes were synthesized using the method adopted by [13].

0.027 mol of the ligand was dissolved in 70ml of hot methanol and 0.014 of each metal salt was dissolved in 35ml hot methanol. The two solutions were mixed with constant stirring and transferred into a round bottom flask. The mixture was refluxed for 3 hours.

The refluxed mixture was then transferred to an evaporating dish and left for the crystallization of the complex. The crystallized complex was washed with cold diethyl ether, and dried over fused phosphorous pentachloride.

$MCl_2.nH_2O + C_{16}H_{17}N_3O_4S.H_2O \longrightarrow [Mn(cepha)Cl].nH_2O$

Synthesis of Metal (II) Cephalexin Complexes

Where M= Mn and Ni.

5.2. Characterization Techniques

5.2.1. Solubility Test

Solubility test was done using nine different solvents such as distilled water, methanol, ethanol, benzene, acetone, diethyl ether, dimethyl sulfoxide, dimethyl formamide, and nhexane. About 0.2g of each complex was transferred into a test tube to which about 2ml of the solvent was added, and solubility observed.

Melting point and Decomposition Temperature

Melting point of Cephalexin as the decomposition temperature of the complexes by introducing a pinch of each into a capillary tube and then inserted into melting point apparatus. The temperature at which the ligand melted and complexes decomposed were recorded.

Molar Conductance Measurement of the Complexes

The molar conductance of the complexes was carried out by dissolving 0.0001M concentration of each complex in 60ml DMSO using a direct conductivity meter. The readings were taken at ambient temperature. The molar conductance was calculated using the formula as in schemes below:

$$\text{Molar conductance} = \frac{1000K}{\boldsymbol{C}}$$

Formula for calculating molar conductance.

Where; C = molar conductance, K = specific conductance

5.2.2. Magnetic Susceptibility:

Each of the prepared metal complexes was introduced into a separate capillary tube up to 1.8 – 2.0 cm mark. The capillary tube was then inserted into the magnetic susceptibility balance and the reading was recorded. The effective magnetic moment was calculated using the formula as in schemes below:

$$X_g = \frac{C_x L_x (\mathrm{R} - R_0)}{10^9 M}$$

Formula for calculating gram magnetic susceptibility

Where;

C= Constant= 1
L= Sample Length (cm)
R= Reading of sample in the tube
R_0= Reading of the empty tube
M= W_2-W_1= Mass of sample in the tube (mg)
W_1= weight of empty tube
W_2= weight of sample and tube
X_g= Gram magnetic susceptibility
Xm= Xg× molecular weight
Formula for calculating molar magnetic susceptibility

μeff = 2.828√Xm × T where Xm is the molar magnetic susceptibility

Formula for calculating effective magnetic moment

Fourier Transformed Infrared (FT-IR)

The infrared spectra of the ligand and complexes were recorded in the range of 650-4000 cm^{-1} for higher region and 400-1000 cm^{-1} for lower range.

5.2.3. Job's Method of Continuous Variation

A 0.001M stock solution of each complex and the ligand were prepared. Varying concentrations were then made and the absorbance was recorded at the maximum wavelength of each complex. The number of coordinated ligands was calculated using the formula as in scheme 3 below:

$$n = \frac{Xi}{1-Xi}$$

Formula for calculating number of coordinated ligands

Where; n = approximate number of coordinated ligands per metal ion, Xi = mole ratio of ligand

5.3. Antimicrobial Screening

Cephalexin and the complexes were screened against bacteria (Staphylococcus aureus, Escherichia coli, Bacillus subtilis) and fungi (Candida albicans, Tinea capitis, Tinea pedis), Ager well diffused method was adopted. The ligand and complexes were dissolved separately I dimethylsulfoxide (DMSO) to produce four different concentrations (4000 g/ml, 2000 g/ml, 1000 g/ml, 500 g/ml). Muller Hinton ager media was prepared for antibacterial (48 g/L) and Potato Dextrose ager (39 g/L) for antifungal. The culture was then transferred to a test tube containing normal saline until the turbidity of the suspension matched that of 0.5 McFarland Standard. The prepared media was sterilized by steaming method in auto cleave for 15 minutes at 121 ^{o}C and then poured into a petri-dish to solidify. The plates were incubated for 24 hours at 37 ^{o}C for the antibacterial and 72 hours at room temperature for the antifungal before measuring the inhibition zone in (mm), Amoxicillin and Nystatin were used as the standard control.

6. Results

Table 1 Percentage yield and physical properties of cephalexin and its metal (II) complexes

Ligand/Metal complexes	Color	% yield	Melting point ^{o}C	Decomposition Temperature ^{o}C
Cephalexin	White		326.8	
[Mn(cepha)Cl].3H_2O	Light Yellow	72		352
[Ni(cepha)Cl].4H_2O	Green	88		397

Cepha= Cephalexin ($C_{16}H_{17}N_3O_4S$. (H_2O)

Table 2 Solubility of ligands and complexes

Compounds	Distilled water	Methanol	Ethanol	Acetone	Benzene	DMSO	DMF	Diethyl ether	NHexane
[Mn(L)Cl].3H_2O	IS	SS	SS	SS	IS	S	S	IS	IS
[Ni(L)Cl].4H_2O	IS	SS	SS	IS	IS	S	S	IS	IS

L= Cephalexin ($C_{16}H_{17}N_3O_4S$. (H_2O); S= Soluble; SS= Slightly; IS= Insoluble; DMF= Dimethyl Formamide; DMSO= Dimethyl Sulfoxide

Table 3 Conductivity measurements of the complexes

Complexes	Concentration (Mol/dm^3) 10^3	Specific Conductance (Ω^{-1} cm^{-2}) 10^6	Molar Conductance (Ω^{-1} cm^2 mol^{-1})
[Mn(cepha)Cl].3H2O	1.0	11.20	11.20
[Ni(cepha)Cl].4H2O	1.0	13.24	13.24

Cepha= Cephalexin ($C_{16}H_{17}N_3O_4S$. (H_2O)

Table 4 Magnetic susceptibility measurement

Complexes	Xg (cm^3/g)	Xm(cm^3/mol)	μ_{eff} (BM)	Magnetic Property	Geometry
$[Mn(cepha)Cl].3H_2O$	3.03×10^{-5}	1.49×10^{-2}	5.96	Paramagnetic	Tetrahedral
$[Ni(cepha)Cl].4H_2O$	6.62×10^{-6}	3.40×10^{-3}	2.85	Paramagnetic	Tetrahedral

Cepha= Cephalexin ($C_{16}H_{17}N_3O_4S.(H_2O)$

Table 5 FT-IR bands of Cephalexin and its complexes

Compounds	$\upsilon(CO)_{lact}$	$\upsilon(CO)_{amide}$	υ(M-N)	$\upsilon(COO)_{assym}$	$\upsilon(COO)_{symm}$	υ(M-Cl)	υ(M-O)
Cephalexin	1752	1655		1580	1350		
$[MnLCl].3H_2O$	1637	1655	450	1525	1380	578	597
$[NiLCl].4H_2O$	1637	1655	467	1560	1400	500	615

L= Cephalexin ($C_{16}H_{17}N_3O_4S.(H_2O)$

Table 6 Percentage of water of crystallization

Complexes	Initial mass (g)	Final mass (g)	Loss in mass (g)	% of water of crystallization
$[Mn(cepha)Cl].3H_2O$	0.2	0.17878	0.02122	3
$[Ni(cepha)Cl].4H_2O$	0.2	0.17284	0.02716	4

Cepha= Cephalexin ($C_{16}H_{17}N_3O_4S.(H_2O)$

Table 7 Job's Method of Continuous Variation showing number of ligands

Complexes	X	1-X	$n = \frac{Xi}{1-Xi}$
$[Mn(cepha)Cl].3H_2O$	0.56	0.44	1.27
$[Ni(cepha)Cl].4H_2O$	0.42	0.58	0.72

Cepha= Cephalexin ($C_{16}H_{17}N_3O_4S.(H_2O)$

Table 8 Antibacterial Activity of Cephalexin and its metal complexes

Test Organisms used	Cephalexin				Mn(II)				Amoxicillin
	4000 (mg)	2000 (mg)	1000 (mg)	500 (mg)	4000 (mg)	2000 (mg)	1000 (mg)	500 (mg)	100 (mg)
Staphyloccocus aureus	21	19	17	14	14	12	10	8	33
Basillus subtilis	18	16	14	12	17	15	13	10	30
Eschericia coli	20	18	16	13	13	11	8	00	28

Test Organisms used	Cephalexin				Mn(II)				Nystatin
	4000 (mg)	2000 (mg)	1000 (mg)	500 (mg)	4000 (mg)	2000 (mg)	1000 (mg)	500 (mg)	100 (mg)
Candida albicans	17	15	13	10	14	12	10	9	31
Tinea capitis	19	17	15	12	16	14	12	10	27
Tinea pedis	20	18	17	15	19	17	15	12	26

Test Organisms used	Ni(II)				Amoxicillin
	4000 (mg)	2000 (mg)	1000 (mg)	500 (mg)	100 (mg)
Staphyloccocus aureus	14	12	10	8	33
Basillus subtilis	18	17	15	12	30
Eschericia coli	15	13	11	9	28

Test Organisms used	Ni(II)				Nystatin
	4000 (mg)	2000 (mg)	1000 (mg)	500 (mg)	100 (mg)
Candida albicans	17	15	13	11	31
Tinea capitis	13	10	7	00	27
Tinea pedis	15	14	12	10	26

7. Discussions

The complexes based on what is described in this research were synthesized by dissolving 0.027 mol of the ligand in 70ml of hot methanol and 0.014 of each metal salt in 35ml hot methanol. The two solutions were mixed with constant stirring and transferred into a round bottom flask. The mixture was refluxed for 3 hours. The refluxed mixture was then transferred to an evaporating dish and left for the crystallization of the complex. The crystallized complex was washed with cold diethyl ether, and dried over fused phosphorous pentachloride.

The complexes obtained were of varying colors (Table 1) with an appreciable percentage in yield of 72% and 88%. Ni recorded the highest yield than Mn. The cephalexin ligand melted at 326.8 ^{o}C whereas the complexes were found to have decomposing temperatures of 352 ^{o}C – 397 ^{o}C. This high decomposition values are an indication of the complex's stability. These colors result from the d-d transitions of the metal ions and the specific ligand field created by the cephalexin coordination.

The solubility test (Table 2) was carried on all the synthesized complexes in solvents namely; ethanol, nhexane, distilled water, methanol, diethyl ether, dimethyl sulfoxide, dimethyl formamide, acetone, and benzene.It was revealed that the complexes were soluble in dimethyl sulfoxide and dimethyl formamide, slightly soluble in acetone and ethanol with the exception of Ni complex which happened to be insoluble in acetone. And the complexes were insoluble in distilled water, methanol, diethyl ether, nhexane, and benzene.

The conductivity measurements are useful in investigating the existence of moving electrolytic species (ions) in the solution of complexes. It was measured at 10^{-3} M of each complex in dimethyl sulfoxide at room temperature. The molar conductance measurements (Table 3) in dimethyl sulfoxide solution carried out on the metal (II) complexes were found to be relatively low ranging from 11.20-13.24 Ω^{-1} cm^2 mol^{-1} when compared with molar conductance of strong electrolytes. This shows that the complexes are non-electrolytes.

The values of effective magnetic moment of metal complexes are shown in above in (Table 4). Manganese complex recorded an effective magnetic moment value of 5.96 BM. Nickel complex recorded a μeff of 2.85 BM. All values of effective magnetic moment fall within the range of tetrahedral geometry for the respective metal complexes.

The important FTIR spectral results of the ligand and complexes were displayed in (Table 5) above. The infrared spectral bands observed in the cephalexin ligand 1752 cm^{-1} is attributed to $\upsilon(C=O)_{lact}$ stretching and 1655 cm^{-1} which is attributed to amide carbonyl. This band of $\upsilon(C=O)_{lact}$ was observed to shift in the spectra of the synthesized metal complexes which further serve as an indication of the coordination of metals to the ligand.

The analysis of water of crystallization (Table 6) revealed that the complexes contain water molecules outside the coordination sphere, with the Ni (II) complex having the highest water content at 4%, and Mn (II) at 3%. This is indicative of hydrated metal complexes.

The metal to ligand ratio were shown in (table 7) determined by the Job's method of continuous variation. The results highlight the stoichiometric relationships in the metal-cephalexin complexes, showing a predominant 1:1 metal to cephalexin ratio with additional coordination from other ligands (chlorine). This mixed coordination environment is typical for metal complexes in aqueous solutions and aligns with the known chemistry of the involved metal ions. The variations in 'n' across different metals reflect the resulting stability of the complexes.

Table 8 shows the antimicrobial results of cephalexin and metal complexes against bacterial and fungal isolates. The antibacterial activity revealed that cephalexin was active against all bacterial strains at all concentrations. And the overall activity of cephalexin increases with increase in concentration. The highest activity was recorded against *Staphyloccocus aureus* at 4000mg/ml with inhibition zone of 21mm while the least activity was recorded against *Basillus subtilis* at 500mg/ml with inhibition zone of 12mm.

The complexes synthesized were active against the bacterial strains with the activity increasing with increase in concentration. They were largely lower in activity compared to the cephalexin ligand. The complexes were also presented to be less active than the control used; Amoxicillin.

The antifungal activity results revealed that cephalexin was active against all the fungal strains at all concentrations. The overall activity of cephalexin increases with increase in concentration. The highest activity was recorded against *Tinea pedis* at 4000mg/ml with inhibition zone of 20mm while the least activity was recorded against *Candida albicans* at 500mg/ml with inhibition zone of 10mm.

The complexes synthesized were active against the fungal strains with the activity increasing with increase in concentration. They were largely lower in activity compared to the cephalexin ligand. The complexes were also presented to be less active than the control used; Nystatin.

Generally, the above antimicrobial activity of the complexes is lower than that of cephalexin which might be as a result of coordination between the active site of the drug and metal (II) irons.

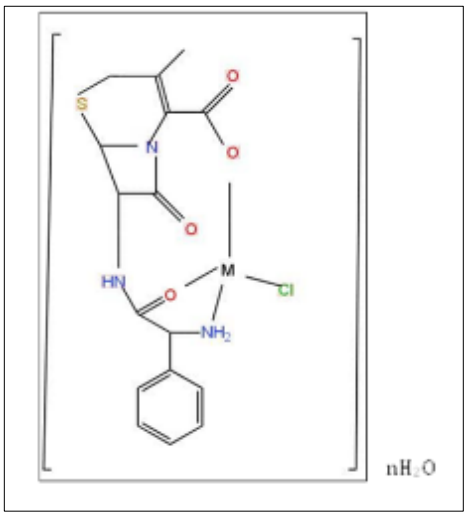

Figure 2 Structure of Metal Complexes

Where M= Mn and Ni

8. Conclusion

This study successfully synthesized and characterized Mn(II) and Ni(II) cephalexin complexes, confirming their tetrahedral geometry and non-electrolytic nature. While these complexes retained some antimicrobial activity, they were less effective than free cephalexin may be due to coordination between the metal ions and the active site of the ligand(beta-lactam carbonyl), suggesting that metal coordination does not necessarily enhance the drug's bioactivity. These findings highlight the potential of metal-based drug modifications while also emphasizing the need for further research to improve therapeutic outcomes. By deepening our understanding of how metal coordination affects antibiotics, this research contributes to the fight against antimicrobial resistance and opens the door for future studies to develop more effective, stable, and bioavailable drug-metal complexes for real-world medical applications.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of informed consent

Informed consent was obtained from Jigawa State College of Education Gumel for the use of laboratory.

References

[1] Anacona, J. R., & Rodriguez, I. (2004). Synthesis and antibacterial activity of cephalexin metal complexes. Journal of Coordination Chemistry, 57(15): 1263-1269.

[2] Ashoor, L. S., Mohaisen, I. K., & Al-Shemary, R. K. R. (2020). A review on versatile applications of transition metal complexes incorporating Schiff bases from amoxicillin and cephalexin. Asian Journal of Bio Science, 14, 7541-7550.

[3] Auda, S. H., Knütter, I., Bretschneider, B., Brandsch, M., Mrestani, Y., Große, C., & Neubert, R. H. H. (2009). Effect of different metal ions on the biological properties of cefadroxil. Pharmaceuticals, 2(3), 184–193

[4] Chohan, Z. H., Shaikh, A. U., Rauf, A., & Supuran, C. T. (2011). Antibacterial cobalt (II), copper (II), nickel (II), and zinc (II) complexes of cephalexin. Journal of Enzyme Inhibition and Medicinal Chemistry, 16(3): 175-184.

[5] Hrioua, A., Bougrin, K., Benhida, R., & Laghzizil, A. (2020). Synthesis, characterization, and antimicrobial activity of amoxicillin metal complexes. Journal of Coordination Chemistry, 73(1-2): 1-13.

[6] Kapoor, G., Saigal, S., & Elongavan, A. (2017). Action and resistance mechanisms of antibiotics: A guide for clinicians. Journal of Anaesthesiology Clinical Pharmacology, 33(3): 300-305.

[7] Nleonu E. C, Ezeibe A. U, Nwafor I. A, Nnaoma I. E (2022). Ligating Properties and Antimicrobial Studies of Metal (II) Complexes of Amoxicillin. Haya Saudi J Life Sci, 7(2): 66-69.

[8] Pang, Y. L., Bia, Z., & Wang, J. (2021). A review on the synthesis and applications of metal-drug complexes. Journal of Applied Pharmaceutical Science, 10(6): 78-92.

[9] Sharma, P. (2020). Antimicrobial resistance: A global challenge. Journal of Global Antimicrobial Resistance, 22, 5-7.

[10] Sultana, N., & Arayne, M. S. (2007). In vitro activity of cefadroxil, cephalexin, cefatrizine and cefpirome in presence of essential and trace elements. Pakistan Journal of Pharmaceutical Sciences.

[11] Ventola, C. L. (2015). The antibiotic resistance crisis: Part 1: Causes and threats. Pharmacy and Therapeutics, 40(4), 277–283.

[12] Zainulabdeen, K., Alsayed, R., Mahdi, S., Ahmed, D., Salman, I., Yaseen, A., Hairunisa, N., Mohammed, S., & Yousif, E. (2023). Evaluation of the antibacterial potential of cephalexin Schiff bases against Bacillus pumilus and Candida albicans. Applied Science Journal, 1(4): 384.