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Effect of Mechanochemically Synthesized Copper (II) and Silver (I) Complexes on Some Cephalosporin Resistant Bacteria

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Abstract:
Complexes of Cu (II) and Ag (I) with cefixime and cefradine as ligands have been mechanochemically (solvent free) synthesized and characterized by physico-chemical methods which includes: infrared, UV/Visible, elemental analysis, melting point, solubility and conductivity. Based on the elemental analysis, the complexes were proposed to have the formula [Cu(CFI)2H_2O], [Cu(CFA)2H_2O], [Ag(CFI)NO_3] and [Ag(CFA)NO_3] where CFI = cifixime and CFA = cefradine. The antimicrobial activities of the synthesized complexes were tested using disc diffusion method, against different strains of bacteria such as Strepto coccus pneumonia, Bacillus subtillus, Salmonella typhi, Klebsiellapnuemoniae, Escherichia coli,Methicillin-resistance staphylococcus aureus (MRSA),Pseudomonas aeruginosa and Staphlylococcus aureus. It has been observed that the complexes have higher activity than the free ligand.The IR spectral data indicates that both CFI and CFA coordinate to the metal ion through ν(COO) and ν(C=O) due to their structural similarities. The melting point, colour and electronic spectra of the complexes were different from that of the ligands, which suggest formation of coordination compounds.

Keywords: *Mechanochemical, Cephalosporin, Resistance and Bacteria*

1. Introduction

Mechanochemistry refers to reactions, normally of solids, induced by the input of mechanical energy, such as by grinding in ball mills. It is becoming more intensely studied partly because it can promote reactions between solids quickly and quantitatively, with either no added solvent or only nominal amounts. Historically it has been a sideline approach to chemical synthesis, and solution-based methods have been adopted by default [1]. However, mechano chemistry could in future become a more mainstream technique for two reasons. Firstly, it is increasingly clear that it is effective, and even advantageous, in ever-widening types of synthesis. Secondly, our current dependence on solvents appears increasingly unsustainable since it is wasteful of fossil-derived materials (e.g. 85% of chemicals used in the pharmaceutical industries are solvents and even if recycled typical recovery rates are only 50-80%), environmentally problematic, hazardous and energy-demanding with regard to solvent production, purification and recycling [2].Cephalosporin are bactericidal and have the same mode of action as other β-lactam antibiotics (such as penicillin), but are less susceptible to β-lactamases. Cephalosporin disrupt the synthesis of the peptidoglycan layer forming the bacterial cell wall. The peptidogly can layer is important for cell wall structural integrity. The final transpeptidation step in the synthesis of the peptidoglycan is facilitated by trans-peptidases known as penicillin-binding proteins (PBPs).The cephalosporin nucleus can be modified to gain different properties. Cephalosporin are sometimes grouped into "generations" by their antimicrobial properties. The first cephalosporin was designated first-generation cephalosporin, whereas, later, more extended-spectrum cephalosporin was classified as second-generation cephalosporin. Each newer generation has significantly greater Gram-negative antimicrobial properties than the preceding generation, in most cases with decreased activity against Gram-positive organisms. Fourth-generation cephalosporin, however, have true broad-spectrum activity [3].Resistance to cephalosporin antibiotics can involve either reduced affinity of existing PBP components or the acquisition of a supplementary β-lactam-insensitive PBP. Currently, some *Citrobacterfreundii*, *Enterobacter cloacae*, *Neisseria gonorrhea*, and *Escherichia coli* strains are resistant to cephalosporin. Some *Morganellamorganii*, *Proteus vulgaris*, *Providencia rettgeri*, *Pseudomonas aeruginosa* and *Serratiamarcescens* strains have also developed resistance to cephalosporin to varying degrees [4].Cephalosporin antibiotics have long been known to behave as relatively efficient chelating agents [5].Cephalosporin can interact with a variety of biomolecules, which may result in inhibition of the biochemical or biophysical processes associated with the

biomolecules. Metal complexes of antibiotics in particular offer great promise for such novel activity [6].In several cases, the metalchelates have been found to be more antimicrobialthan the chelating agents themselves [7].Most of the antibiotics, including cephalosporin, and their decomposition products contain electron donor groups that can bind naturally-occurring metal ions *in vivo*. Metal ions form chelates with these antibiotics and reduce their intestinal absorption [8]. Therefore, this research seek look at the effect of some antibiotics (Cephalosporin) when bind to metals such as copper (II) and silver (I) on cephalosporin resistance bacteria.

2. Experimental

All the reagents and chemicals were of analytical grade and were used without further purification. The ligands used are cifixime and cefradine, while the metal salts are copper chloride dihydrate [$CuCl_2.2H_2O$] and silver nitrate [$AgNO_3$]. IR spectra of the complexes in KBr pellets were obtained in the range of 4000-400cm^{-1} using FTIR spectrometer. Metal analysis was determined by atomic absorption spectroscopy using perkin-Elmer Spectrometer, model 3110. UV-Vis spectra were obtained on UV-2550 Shimazu Spectrophotometer in the wavelength range of 200-800nm.

2.1. Synthesis of the Complexes

Literature procedure [9] was modified and used for the synthesis of all the metal complexes by mechanochemical method. [Cifixime(10mmol, 4.535g) orcefradine (10mmol, 3.64g)] and[$CuCl_2.2H_2O$ (10mmol, 1.705g) or Ag (NO_3) (10mmol, 1.699g)]were weighed carefully and transferred into a mortar. The two reactants in each case were then crushed (ground) for twenty (20) minutes to obtain homogenous powder. The powder was removed from the mortar and stored in a desiccator.

2.2. Antimicrobial Screening

The *in-vitro* antimicrobial activities of the antibiotics and their metal complexes were assayed using disc diffusion method against the following microorganisms; *Strepto coccus pneumonia, Bacillus subtillus, Salmonella typhi, Klebsieliapnuemoniae, Escherichia coli,MRSA,Pseudomonas aeruginosa and Staphylococcus aureus.* The suspension of each micro-organism was added to a sterile nutrient agar medium, then spread on the sterile Petri dish plates and allowed to set. Different concentrations (30, 20 and 10)µg/ml of antibiotics and their metal complexes in methanol were placed on the culture media and incubated for 24hrs at 37°C. Activities were determined by measuring the diameter of the zone of inhibition(mm). The antibiotics and their complexes that showed zone of inhibition of 10mm and above were further assayed for minimum inhibitory concentration (MIC) and minimum bactericidal concentration(MBC) using samples concentration of (6,4 and 2)µg/ml in methanol using same bacterial species in peptone water [10].

3. Results and Discussion

The Cu(II) and Ag(I) complexes of cifixime and cefradine were synthesized by solvent freemethod through reaction of metal salts of Cu(II) and Ag(I) with cifixime and cefradine. The complexes were characterized by solubility, conductivity, melting point, TLC, AAS, infrared and UV-Vis spectroscopy. The complexes were found to be soluble in distilled water, methanol, ethanol and DMSO, except Cu(II) complexes which are slightly soluble in ethanol. All the complexes are insoluble in non-polar organic solvents. The solubility of the complexes in polar solvents, suggest that the complexes might be probably polar. The complexes are colored ranging from green to light brown and milky which typical of transition metal complex. The complexes are air and light stable with melting point ranging from 110 to 140^{0}C. The complexes of Cu(II) and Ag(I) with cifixime had melting points lower than that of the parent drug, while complexes of cefradine have melting point lower than that of the parent drug which might be due to complexation (Table 1). The molar conductivity of the complexes in DMSO (10^{-3}M) are in the range of 2.0-4.8 Scm^2/mol, which suggest that they are non-electrolyte (Table 1).

Compounds	**Molecular formula (Molar mass)**	**Color**	**Yield (*g*) *(%)***	**M.pt (°C)**	**Conductivity *(Scm^2/mol)***	**TLC RF Values**
Cifixime	$[C_{16}H_{15}N_5O_7S_2]$ (453.452)	White	-	218	-	05
Cefradine	$[C_{16}H_{17}N_3O_5S]$ (363.389)	White	-	140	-	0.9
[Cu-CFI].$2H_2O$	$[CuC_{16}H_{19}N_5O_9S_2]$ (552.95)	Green	5.27 (82.8)	110	2.8	0.7
[Cu-CFA].$2H_2O$	$[CuC_{16}H_{21}N_3O_7S]$ (462.89)	Green	5.24 (98.1)	130	4.6	0.8
[Ag-CFI].NO_3	$[AgC_{16}H_{15}N_6O_{10}S_2]$ (623.34)	Light brown	5.54 (88.9)	110	2.0	0.6
[Ag-CFA].NO_3	$[AgC_{16}H_{17}N_4O_8S]$ (533.28)	Milky	5.14 (96.4)	110	4.0	0.5

Table 1: Analytical data of the Antibiotics and their metal complexes
CFI=Cifixime, CFA= Cefradine

Ligands/Complexes	Formula	Wavelength (nm)	Energies (cm^{-1})	Assignments
CFI	$C_{16}H_{15}N_5O_7S_2$	320	3125	$\pi\rightarrow\pi^*$
CFA	$C_{16}H_{17}N_3O_5S$	330	3030	$\pi\rightarrow\pi^*$
$[Cu(CFI)2H_2O]$	$[Cu(C_{19}H_{15}N_5O_9S_2)]$	316 700	3165 1429	MLCT $^2E_g\rightarrow{}^2T_{2g}$
$[Cu(CFA)2H_2O]$	$[Cu(C_{16}H_{21}N_3O_7S)]$	301 308 314	3322 3247 3333	$n\rightarrow\pi^*$ MLCT
$[Ag(CFI)\ NO_3]$	$[Ag(C_{16}H_{15}N_6O_{10}S_2)]$	202 250 300	4950 4000 3333	$n\rightarrow\pi^*$ $n\rightarrow\pi^*$ MLCT
$[Ag(CFA)\ NO_3]$	$[Ag(C_{16}H_{17}N_4O_8S)]$	306 350	3268 2857	$n\rightarrow\pi^*$ MLCT

Table 2: UV-Vis Spectra of the Antibiotics and their metal complexes

3.1. Electronic Spectra

The UV-Visible spectra of the antibiotics and their metal complexes in methanol are presented in Table 2. From the results obtained, the antibiotics (CFI and CFA) showed one absorption maxima at 320nm and 330nm assigned to $\pi\rightarrow\pi^*$transition. The Cu(CFI) complex exhibit two bands at 316 and 700nm assigned to MLCT and $^2E_g\rightarrow{}^2T_{2g}$. Cu(CFA) also showed three bands at 301, 308 and 314nm which corresponds to $n\rightarrow\pi^*$ and MLCT [8]. The Ag (I) complexes show absorption bands at (202, 250, 300, 306 and 350nm), which indicate a bathochromic shift relative to the free ligands (320 and 330nm) indicating weak interaction between the ligand and silver ion [11].

Compounds	ν(O-H)	ν(N-H)	ν(C=O)	ν(NH_2)	ν(C=N)	ν(C-S)	ν(C=C)	ν(N-O)	ν(M-O)
CFI	3216	1662	1021	3526	1534	2050	15191	-	-
CFA	3020	1565	1028	3535	1545	2063	1554	-	-
$[Cu(CFI)2H_2O]$	3526	1669	1025	3183	1534	1900	1587	-	634
$[Cu(CFA)2H_2O]$	3410	1684	1021	3500	1533	2079	1558	1353	667
$[Ag(CFI)\ NO_3]$	3526	1669	1025	3190	1534	2117	1587	-	797
$[Ag(CFA)\ NO_3]$	3023	1610	1208	3567	1567	2050	1558	1353	670

Table 3: Infrared spectral data of the antibiotics and their metal complexes

Compounds	Molecular formula (Molar mass)	Microanalysis: found (calculated)%			
		C	H	N	M
$[Cu(CFI)2H_2O]$	$[CuC_{16}H_{19}N_5O_9S_2]$ (552.95)	34.68 (34.72)	3.48 (3.44)	12.62 (12.66)	11.60 (11.48)
$[Cu(CFA)2H_2O]$	$[CuC_{16}H_{21}N_3O_7S]$ (462.89)	41.50 (41.48)	4.51 (4.54)	9.08 (9.07)	13.65 (13.72)
$[Ag(CFI)NO_3]$	$[AgC_{16}H_{15}N_6O_{10}S_2]$ (623.34)	30.90 (30.80)	2.38 (2.41)	13.48 (13.48)	17.25 (17.29)
$[Ag(CFA)NO_3]$	$[AgC_{16}H_{17}N_4O_8S]$ (533.28)	36.01 (36.00)	3.20 (3.19)	10.46 (10.50)	20.17 (20.21)

Table 4: Microanalysis of Cu(II) and Ag(I) complexes

3.2. Infrared Spectra

The infra-red spectral data of the complexes and their ligands (antibiotics) are presented in Table 3. The band assignments are based on comparison with similar studies on mixed ligand complexes and some drug based metal complexes [12]. The bands that appear in the free ligands were found to be present in the complexes because of the similarity in their structures. The bands at (3020 and 3216) cm^{-1} in the free ligands were assigned to ν(O-H) band, the bands shifted to higher frequencies in the complexes. The appearance of new bands in the spectra of the complexes at (634-670) cm^{-1}suggest deprotonation of hydroxyl group and formation of ν(M-O) bond, which also suggest formation of complex.

3.3. Microanalysis

The microanalysis of the metal complexes is presented in Table 4. The results revealed that the % C, H and N are in good agreement with the proposed structures. From the data obtained, it appears that the complexes analyzed as $[Cu(L)\ 2H_2O]$ and $[Ag(L)NO_3]$. Where L= CFI and CFA.

3.4. Antibacterial Activity

The antibacterial activity of the newly synthesized complexes and their parent drugs were investigated using disc diffusion method [13]. Different strains of bacteria which includes both gram positive and negative. The results show that the copper complexes had no significant improvement compared to the parent drugs while silver complexes showed greater activity when compared with the parent drugs against the microorganisms tested. However, the highest zone of inhibition of 34±1.0 mm was recorded from the parent drug at 30 *mg/ml* against *B.subtilis.*

Compounds	**Conc. mg/mL**	***MRSA***	***S.aureus***	***S.pneumoniae***	***B.subtilis***	***E.coli***	***S.typhi***	**K.*pneumoniae***	***p.aeruginosa***
CFA	10	13±0.1	22±1.0	0.0±0.0	24±1.0	0.0±0.0	14±0.5	16±0.3	8.0±0.6
	20	17±0.6	25±0.6	0.0±0.0	29±1.0	9.0±0.6	19±0.6	22±0.5	11±1.0
	30	19±1.0	29±1.0	0.0±0.0	34±1.0	13±1.0	25±1.0	28±1.0	14±0.4
CFI	10	0.0±0.0	0.0±0.0	0.0±0.0	9.0±0.6	12±0.2	13±0.6	0.0±0.0	7.0±0.8
	20	0.0±0.0	0.0±0.0	8.0±0.2	12±1.0	16±1.0	18±0.4	7.0±0.5	11±0.0
	30	0.0±0.0	0.0±0.0	11±0.4	15±0.7	19±0.7	22±1.0	11±0.6	14±1.0
[Cu(CFA)2H_2O]	10	0.0±0.0	0.0±0.0	0.0±0.0	0.0±0.0	0.0±0.0	0.0±0.0	8.0±0.8	0.0±0.0
	20	0.0±0.0	0.0±0.0	0.0±0.0	0.0±0.0	0.0±0.0	0.0±0.0	12±0.3	0.0±0.0
	30	0.0±0.0	0.0±0.0	0.0±0.0	0.0±0.0	0.0±0.0	0.0±0.0	17±0.4	0.0±0.0
[CuCFI)2H_2O]	10	0.0±0.0	13±1.0	7.0±0.5	9.0±0.6	9.0±0.8	0.0±0.0	7.0±0.5	0.0±0.0
	20	0.0±0.0	18±0.6	9.0±0.5	13±0.5	12±0.3	8.0±0.4	11±1.0	0.0±0.0
	30	0.0±0.0	22±0.5	12±0.4	17±1.0	17±0.6	10±0.6	15±0.6	0.0±0.0

Table 5: Antimicrobial activities of antibiotics and their Cu(II) complexes on some bacteria

MRSA= Methicillin-resistance *staphylococcus aureus, s.aureus = staphylococcus aureus, s.pneumoniae = Strepto coccus pneumonia, B.subtilis=Bacillus subtilis, E.coli= Escherichia coli, S.typhi= Salmonella typhi, K.pneumoniae=Klebsiella pneumonia and P.aruginosa= Psuedomonas aeruginosa.*

Compounds	**Conc. mg/mL**	***MRSA***	***S.aureus***	***S.pneumoniae***	***B.subtilis***	***E.coli***	***S.typhi***	**K.*pneumoniae***	***p.aeruginosa***
CFA	10	13±0.1	22±1.0	0.0±0.0	24±1.0	0.0±0.0	14±0.5	16±0.3	8.0±0.6
	20	17±0.6	25±0.6	0.0±0.0	29±1.0	9.0±0.6	19±0.6	22±0.5	11±1.0
	30	19±1.0	29±1.0	0.0±0.0	34±1.0	13±1.0	25±1.0	28±1.0	14±0.4
CFI	10	0.0±0.0	0.0±0.0	0.0±0.0	9.0±0.6	12±0.2	13±0.6	0.0±0.0	7.0±0.8
	20	0.0±0.0	0.0±0.0	8.0±0.2	12±1.0	16±1.0	18±0.4	7.0±0.5	11±0.0
	30	0.0±0.0	0.0±0.0	11±0.4	15±0.7	19±0.7	22±1.0	11±0.6	14±1.0
[Ag(CFA) NO_3]	10	20±0.7	10±0.3	17±0.7	16±1.0	10±0.3	12±0.4	13±0.3	10±0.2
	20	25±0.5	13±0.3	22±0.5	21±0.3	12±1.0	17±0.5	19±0.6	13±0.3
	30	32±0.8	17±0.3	27±0.4	26±0.6	16±0.6	22±0.8	23±0.5	18±0.4
[Ag(CFI)] NO_3]	10	0.0±0.0	9.0±0.7	0.0±0.0	11±0.4	0.0±0.0	11±0.5	0.0±0.0	0.0±0.0
	20	0.0±0.0	12±1.0	0.0±0.0	16±0.3	8.0±0.8	16±0.4	0.0±0.0	0.0±0.0
	30	0.0±0.0	17±1.2	0.0±0.0	20±0.6	10±0.9	22±0.3	0.0±0.0	0.0±0.0

Table 6: Antimicrobial activities of the antibiotics and their Ag(I) complexes on some bacteria

Compounds	Conc. mg/mL	*MRSA*	*S.aureus*	*B.subtilis*	*S.typhi*	K.*pneumoniae*	*p.aeruginosa*	*E.coli*	*S.pneumoniae*
CFA	1	R	R	R	R	R	R	NA	NA
	2	R	S	S	R	R	R	NA	NA
	4	R	S	S	S	S	R	NA	NA
	6	S	S	S	S	S	R	NA	NA
	8	S	S	S	S	S	R	NA	NA
	10	S	S	S	S	S	S	NA	NA
CFI	1	NA	NA	R	R	NA	NA	R	NA
	2	NA	NA	R	R	NA	NA	R	NA
	4	NA	NA	R	S	NA	NA	S	NA
	6	NA	NA	S	S	NA	NA	S	NA
	8	NA	NA	S	S	NA	NA	S	NA
	10	NA	NA	S	S	NA	NA	S	NA
[Cu(CFA)2H_2O]	1	NA	NA	NA	NA	R	NA	NA	NA
	2	NA	NA	NA	NA	R	NA	NA	NA
	4	NA	NA	NA	NA	R	NA	NA	NA
	6	NA	NA	NA	NA	R	NA	NA	NA
	8	NA	NA	NA	NA	S	NA	NA	NA
	10	NA	NA	NA	NA	S	NA	NA	NA
[Cu(CFI)2H_2O]	1	NA	R	R	NA	R	NA	R	NA
	2	NA	R	R	NA	R	NA	R	NA
	4	NA	R	R	NA	R	NA	R	NA
	6	NA	S	R	NA	R	NA	R	NA
	8	NA	S	S	NA	R	NA	S	NA
	10	NA	S	S	NA	S	NA	S	NA

Table 7: Minimum inhibitory concentration (MIC) of the antibiotics and their Cu(II) complexes
R= resistant, S= susceptible and NA= not applicable

Compounds	Conc. Mg/mL	*MRSA*	*S.aureus*	*B.subtilis*	*S.typhi*	K.*pneumoniae*	*p.aeruginosa*	*E.coli*	*S.pneumoniae*
CFA	1	R	R	R	R	R	R	NA	NA
	2	R	S	S	R	R	R	NA	NA
	4	R	S	S	S	S	R	NA	NA
	6	S	S	S	S	S	R	NA	NA
	8	S	S	S	S	S	R	NA	NA
	10	S	S	S	S	S	S	NA	NA
CFI	1	NA	NA	R	R	NA	NA	R	NA
	2	NA	NA	R	R	NA	NA	R	NA
	4	NA	NA	R	S	NA	NA	S	NA
	6	NA	NA	S	S	NA	NA	S	NA
	8	NA	NA	S	S	NA	NA	S	NA
	10	NA	NA	S	S	NA	NA	S	NA
[Ag(CFA) NO_3]	1	R	R	R	R	R	R	R	R
	2	S	R	R	R	R	R	R	R
	4	S	R	S	R	R	R	R	S
	6	S	R	S	S	S	R	R	S
	8	S	S	S	S	S	S	S	S
	10	S	S	S	S	S	S	S	S
[Ag(CFI) NO_3]	1	NA	R	R	R	NA	NA	NA	NA
	2	NA	R	R	R	NA	NA	NA	NA
	4	NA	R	R	R	NA	NA	NA	NA
	6	NA	R	S	S	NA	NA	NA	NA
	8	NA	S	S	S	NA	NA	NA	NA
	10	NA	S	S	S	NA	NA	NA	NA

Table 8: Minimum inhibitory concentration (MIC) of the antibiotics and their Ag(I) complexes

Compounds	Conc. Mg/mL	*MRSA*	*S.aureus*	*B.subtilis*	*S.typhi*	K.*pneumoniae*	*p.aeruginosa*	*E.coli*	*S.pneumoniae*
CFA	2	NA	R	R	NA	R	NA	R	NA
	4	NA	R	R	NA	R	NA	R	NA
	6	NA	S	R	NA	R	NA	R	NA
	8	NA	S	S	NA	R	NA	S	NA
	10	NA	S	S	NA	S	NA	S	NA
CFI	2	NA	NA	R	S	NA	NA	S	NA
	4	NA	NA	S	S	NA	NA	S	NA
	6	NA	NA	S	S	NA	NA	S	NA
	8	NA	NA	S	S	NA	NA	S	NA
	10	NA	NA	S	S	NA	NA	S	NA
[Cu(CFA)2H_2O]	2	NA	NA	NA	NA	R	NA	NA	NA
	4	NA	NA	NA	NA	R	NA	NA	NA
	6	NA	NA	NA	NA	R	NA	NA	NA
	8	NA	NA	NA	NA	R	NA	NA	NA
	10	NA	NA	NA	NA	S	NA	NA	NA
[Cu(CFI)2H_2O]	2	NA	R	R	NA	R	NA	R	NA
	4	NA	R	R	NA	R	NA	R	NA
	6	NA	S	R	NA	R	NA	R	NA
	8	NA	S	S	NA	R	NA	S	NA
	10	NA	S	S	NA	S	NA	S	NA

Table 9: Minimum Bactericidal concentration (MBC) of the antibiotics and their Cu(II) complexes

Compounds	Conc. Mg/mL	*MRSA*	*S.aureus*	*B.subtilis*	*S.typhi*	K.*pneumoniae*	*p.aeruginosa*	*E.coli*	*S.pneumoniae*
CFA	2	NA	R	R	NA	R	NA	R	NA
	4	NA	R	R	NA	R	NA	R	NA
	6	NA	S	R	NA	R	NA	R	NA
	8	NA	S	S	NA	R	NA	S	NA
	10	NA	S	S	NA	S	NA	S	NA
CFI	2	NA	NA	R	S	NA	NA	S	NA
	4	NA	NA	S	S	NA	NA	S	NA
	6	NA	NA	S	S	NA	NA	S	NA
	8	NA	NA	S	S	NA	NA	S	NA
	10	NA	NA	S	S	NA	NA	S	NA
[Ag(CFA)NO_3]	2	R	R	R	R	R	R	R	R
	4	S	R	R	R	R	R	R	S
	6	S	R	S	S	S	R	R	S
	8	S	S	S	S	S	S	S	S
	10	S	S	S	S	S	S	S	S
[Ag(CFI)NO_3]	2	NA	R	R	R	NA	NA	NA	NA
	4	NA	R	R	R	NA	NA	NA	NA
	6	NA	R	R	S	NA	NA	NA	NA
	8	NA	S	S	S	NA	NA	NA	NA
	10	NA	S	S	S	NA	NA	NA	NA

Table 10: Minimum Bactericidal concentration (MBC) of the antibiotics and their Ag(I) complexes

3.5. Structure of the Complexes

The infrared spectroscopic results of this study revealed that coordination of both cefixime and cefradine to the metal ions occurs through oxygen atom of the carboxylate anion, oxygen atom of water molecule for [Cu(CFI)2H_2O] and [Cu(CFA)2H_2O] complexes to give five coordination number, with the ligand acting as tridentate. Similar trend was also reported [11], while complexes of [Ag(CFI)NO_3] and [Ag(CFA)NO_3], had their coordination through oxygen atom of the nitrate ion in addition to the oxygen atom of the carboxylate ion.

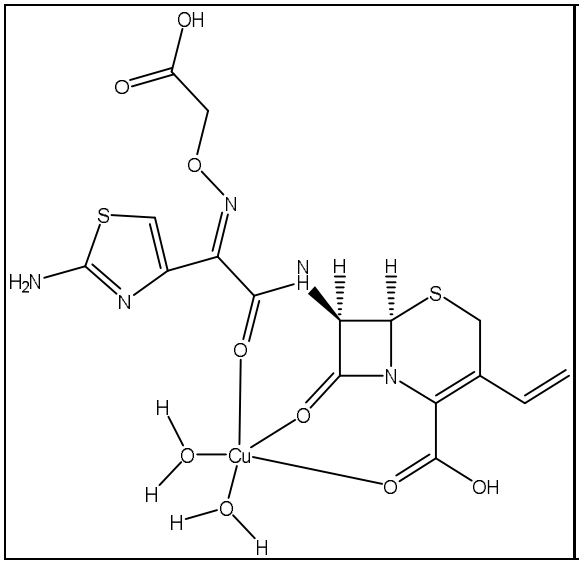

Figure 1: [Cu(CFI)2H$_2$O]

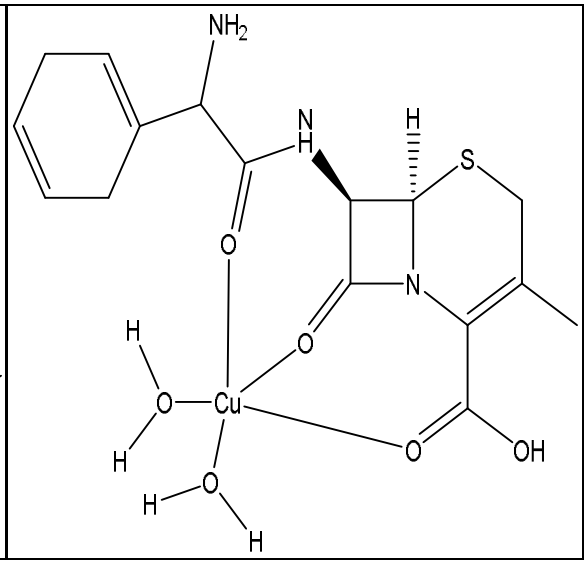

Figure 2:[Cu(CFA)2H$_2$O]

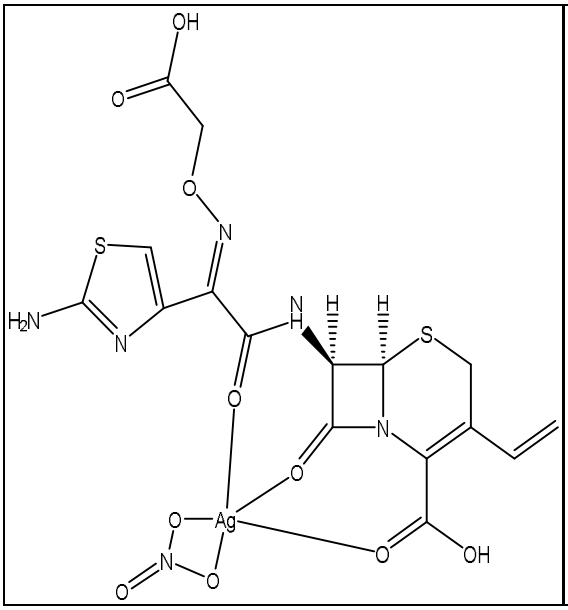

Figure 3: [Ag(CFI)NO$_3$]

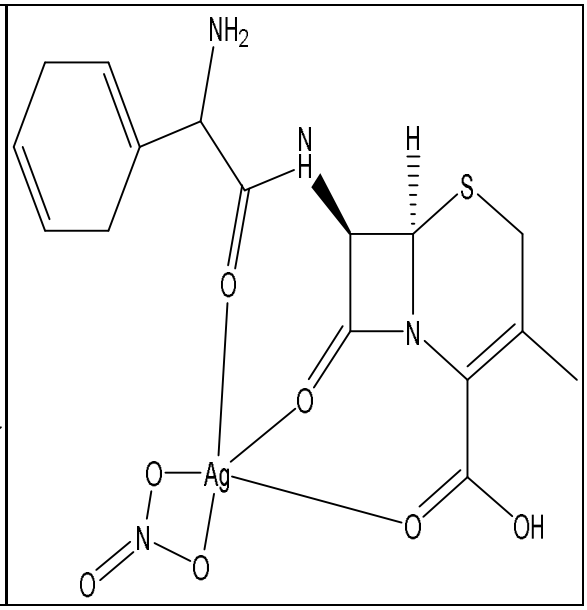

Figure 4:[Ag(CFA)NO$_3$]

4. Conclusion

Copper and silver complexes of cefixime and cefradine have been synthesized by grinding solid cefixime and cefradine molecules with copper chloride and silver nitrate. From the results obtained, its shows that all the complexes have five coordination number (Figure 1-4). The results of antibacterial activity of the complexes and their parent drugs, showed that the complexes of silver showed greater activity when compared with the parent drug. However, copper complexes showed less activity against the parent drug.

5. Acknowledgments

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