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Zn(II) and Cd(II) Complexes of Cephalosporin: Solvent-free and Solution-based Syntheses, Characterization and *in vitro* Antimicrobial Evaluation

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ABSTRACT

Rapid increase of microbial resistance to antibiotics is fast becoming a global concern. To overcome this alarming problem, the discovery of novel active compounds against new targets is a matter of urgency. Herein, solvent-free and solution-based synthesized Zn(II) and Cd(II) complexes of cephalosporin derivatives (cefixime and cefuroxime) have been described and compared. The complexes were characterized by solubility, melting point and conductivity measurements, infrared spectroscopy, UV/Visible and metal analysis. The complexes were either milky, yellow or brown in colour and had high decomposition temperatures (187-315˚C). The complexes were all air stable and generally soluble in dimethyl sulfoxide but insoluble in *n*-hexane. The molar conductivity values (10.3 – 16.6 Scm^2 mol^{-1}) for both solvent-free and solution-based complexes were found to below indicative of the complexes being non-electrolytic. The coordination of the metal ions to the ligands occurred through oxygen of the three $C=O$ in the ligands as it was evident from infrared spectroscopic analysis. The UV-Visible spectra for all the complexes formed showed a five-coordinate geometry around the ligands and two aqua molecules. In general, the characterization has evidenced the identical nature of the complexes obtained *via* the two synthesis techniques. The antimicrobial screening was carried out against four Gram-positive (*Staphylococcus aureus, S. pyogen,* Methicillin-resistance *Staphylococcus aureus (MRSA) and Bacillus subtilis)*, four Gram-negative (*Klebsiella pneumoniae, Escherichia coli, Salmonella typhi and Pseudomonas aeruginosa)* bacteria and one fungus (*Candida albicans)*. The results revealed that both ligands showed activity against all the micro-organisms tested except *Pseudomonas aeruginosa* and *Streptococcus pyogene* in the case of the ligand cefuroxime. Compared to the ligands, the other complexes were also more active against the micro-organisms. At all test concentrations, the complex $[Cd(CFU)Cl_2]$ showed increased activity against all tested micro-organisms. Similar results were reported for cefixime complexes which showed significantly enhanced antimicrobial and antifungal activities against microbial strains as compared to free ligand cefixime.

Keywords: Antimicrobial potency, Cefixime, Cefuroxime, Solvent-free synthesis

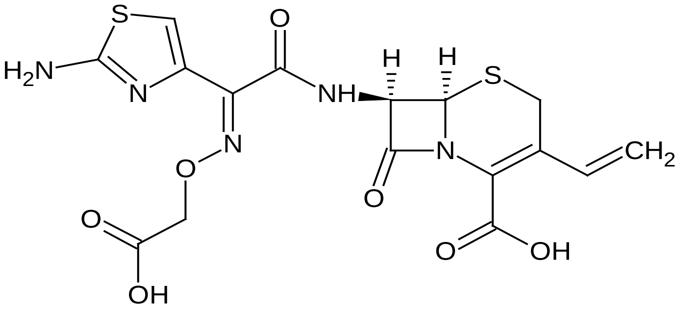
INTRODUCTION

The solvent-free synthesis of transition-metal complexes has recently gained considerable attention because it is more efficient and eco-friendly (Jia *et al.*, 2021). Basically, the interest in solvent-free conditions stems from the possibility of both solution-based and solvent-free methods giving rise to the same product (Tella *et al.*, 2016). Cephalosporins are a class of β-lactam antibiotics originally derived from the fungus Acremonium, which was previously known as Cephalosporium. Together with cephamycins, they constitute a subgroup of β-lactam antibiotics called cephems. The antibacterial spectrum of cephalosporins resembles that of cefuroxime. Most gram negative and gram-positive microorganisms are sensitive to cephalosporins (Hoque *et al.*, 2020).

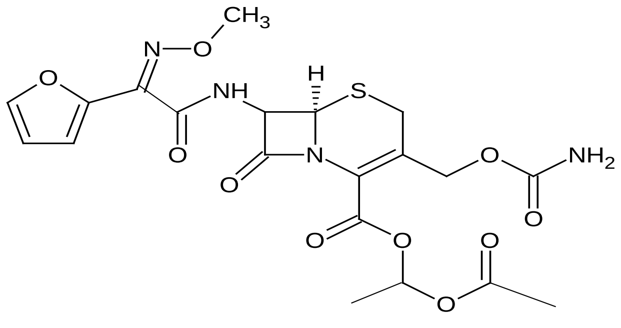
Cefixime (CFI) is a broad spectrum, third generation, cephalosporin class of antibiotic. Chemically, it is (6R,7R)-7-[2-(2-amino-4-thiazolyl)glyoxylamido]-8-oxo-3-vinyl-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-(Z)-[o-(carboxymethyl)-oxime] trihydrate as shown in Figure 1a (Ramadan *et al.*, 2013, Danish *et al.*, 2015). It is one of the essential medicines according to World Health Organization (Cirri *et al.*, 2021). It is Indian, British, United States, European, Japanese, and Martindale pharmacopeia recommended antibiotic (Keskar and Jugade, 2015).It is active against gram-positive and gram-negative bacterial infections and used to treat otitis media, pharyngitis, bronchitis, and urinary-tract infections. Cefixime is an antibiotic that is used for the treatment of a variety of bacterial infections, skin and urinary tract infections, pneumonia, and strep throat (Rubel *et al.*, 2019).

Cefuroxime (CFU) is an antibiotic used to treat and prevent a number of bacterial infections such asbronchitis (infection of the airway tubes leading to the lungs), gonorrhea, and infection of the skin, ears sinuses, throat, tonsils and urinary tract. It works by stopping the growth of bacteria, and sometimes it is used to treat pneumonia (Waziri *et al.*, 2018). It is used by mouth or by injection into a vein or muscle. It is the second generation of Cephalosporins. The chemical structure is shown in Figure 1b.

Antimicrobial resistance is fast becoming a global concern with rapid increases in multidrug resistant bacteria. Some previously treatable pathogens are now becoming untreatable, for example methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant enterococcus (VRE). MRSA (resistant to methicillin, cephalosporins, all beta lactams, and occasionally gentamicin, erythromycin and trimethoprim/sulfamethoxazole) VRE (resistant to vancomycin, ampicillin, and gentamicin) (Khan *et al.*, 2017). To overcome the alarming problem of microbial resistance to antibiotics, the discovery of novel active compounds against new targets is a matter of urgency. Herein, we report Zn(II) and Cd(II) complexes of cefixime and cefuroxime synthesized by solvent-free and solution-based techniques and evaluate their antimicrobial sensitivity against some clinical isolates.



(a)



(b)

Figure 1: Chemical Structure of Cefixime(a) and Cefuroxime(b)

MATERIALS AND METHODS

The chemicals used in this work are of analytical grade and were used without further purification. These include $CdCl_{2}.2^{1}/_{2}H_{2}O$, $ZnCl_{2}.2H_{2}O$, cefuroxime (CFU) and cefixime (CFI). Infrared spectral analyses of the complexes were carried out in the range of 500-4000 cm^{-1} on SHIMADZU Corporation FTIR-8400S Spectrophotometer. The metals estimation analysis was determined using Atomic Absorption Spectroscopy (AAS) on Buck scientific 210VGP. The UV/visible spectra of the complexes and the ligands were also carried out using UV-2550 SHIMADZU Spectrophotometer in the wavelength range of 200-800 nm.

Solvent-free Synthesis of the Metal(II) Complexes

Cefixime (10 mmol, 4.53 g) and metal(II) salts [$CdCl_{2}.2½H_{2}O$ (10 mmol, 2.25 g) and $ZnCl_{2}.2H_{2}O$ (10 mmol, 1.72 g)] each in the ratio of 1:1 (M:L) were carefully weighed and transferred into a mortar. Each of the metal salt and the ligand (cefixime) were crushed for 20 minutes to obtain a homogenous powder. The homogenous mixture (powder) were then transferred to a beaker and stored in a desiccator. Same procedure was used for cefuroxime (10mmol, 5.10g) and the metal(II) salts above (Ndahi *et al.*,2017).

Solution-based Synthesis of the Metal(II) Complexes

The complexes were synthesized by dissolving cefixime (10 mmol, 4.53 g) in 10 ml hot methanol. $CdCl_2.2½H_2O$ (10 mmol, 2.25 g) and $ZnCl_2.2H_2O$ (10 mmol, 1.72 g) were each dissolved in 10 mL hot methanol. The metal and cefixime solutions were mixed and refluxed for 2 hours with constant stirring. The mixture was carefully poured into a beaker and cooled to room temperature before filtration. The precipitate was washed three times with 5ml portions each of methanol, distilled water and dried in a desiccator over anhydrous calcium chloride for three days. Same procedure was used for cefuroxime with $CdCl_2.2½H_2O$ and $ZnCl_2.2H_2O$ (Obaleye *et al.*, 2007).

Antimicrobial Activity Assay

The antimicrobial activities of the antibiotics and their metal complexes were determined by using disc diffusion method against *Streptococcus pneumonia, Bacillus subtilis, Salmonella typhi, Klebsiella pneumoniae, Escherichia coli,* Methicillin-resistance *Staphylococcus aureus (MRSA), Pseudomonas aeruginosa and Staphylococcus aureus.* The suspensions containing speciesof the micro-organisms were freshly prepared using nutrient agar medium and poured into petri dishes and were allowed to set. The solutions of the antibiotics were introduced within various concentrations 30, 20 and 10 mg/mLof antibiotics and their metal complexes in methanol which were placed on the culture media and incubated for 24 hours at 37°C. Activities were determined by measuring the diameter of the zone of inhibition (mm) (Waziri *et al.*, 2018).

RESULTS AND DISCUSSION

Physical Characteristics of the Complexes

The physical properties of the ligands and their metal(II) complexes prepared by solvent-free and solution-based methods are shown in Tables 1 and 2 respectively. The complexes formed by both methods showed either milky, yellow or brown colour. Variations in colours among transition metal complexes can be rationalized from crystal field theory (CFT) or due to presence of chromophore (Muhammad and Saadatu, 2017). It may also be due to *d-d* electronic transition and as a result of charge transfer transition from ligand to metal ions within the complex molecule (Albert and Geoffrey, 1987).

The solvent-free synthesized complexes were obtained in excellent yields ranging from 79.6-89.8% whereas the solution-based complexes have a moderate yield ranging from 42.1 – 79.8%. Studies have shown that most solvent free synthesized complexes have high experimental yields. For example, the % yield for $[Cu(CHOOCH_3)_2(TMP)_2]$ prepared *via* solvent free technique was found to be 80.0% whereas that of solution-based synthesized complex of $[Cu(CHOOCH_3)_2(TMP)_2]$ was moderate with 64.0% yield (Tella *et al.*, 2016). Molar conductivity values of the synthesized (solvent-free and solution based) complexes are low (10.3–16.6 $Scm^2\ mol^{-1}$). The low values of conductivity indicate the non-electrolytic behavior of the complexes (Geary, 1971).

The metal content in the complexes has been determined. The experimentally obtained percentage agrees with the theoretically calculated values for both solution-based and solvent-free synthesized complexes. From the results, the complexes could be formulated as $[MLCl_2]$ (where M=Zn(II) or Cd(II) and L= cefixime or cefuroxime). The decomposition temperatures of the solvent-free synthesized complexes are in the range of 187-315˚C and those of solution-based occurs between 192 – 327˚C. These high temperatures indicate high thermal stabilities of the complexes (Ajayeoba *et al.*, 2017; Muhammad and Saadatu, 2017). Furthermore, the results revealed that the melting/decomposition temperatures of the ligands differ from those of the metal complexes which suggest the formation of new products.

The solubility of the complexes in some common organic solvents has been determined. The result reveals their solubility in methanol and dimethyl sulfoxide (DMSO) and insolubility in *n*-hexane which suggests that they may be polar complexes. Similar observation was reported by Ogunniran *et al.*(2008).

Table 1: Physical Properties of the Ligands and their Metal(II) Complexes Prepared by Solvent-free Method

Compound	Molecular Formula (Molar Mass) (gmol^{-1})	Colour	Yield(g) (%)	Decomposition Temperature (^{o}C)	Molar Conductivity (Scm^{2} mol^{-1})	Metal found (Cacld)
Cefixime	$C_{16}H_{15}N_5O_7S_2$ (453.451)	White	------	218-225	------	
Cefuroxime	$C_{20}H_{22}N_4O_{10}S$ (510.476)	White	------	135	------	
Zn(CFU)Cl_2	$Zn(C_{20}H_{22}N_4O_{10}S)Cl_2$ (646.856)	Brown	5.304 (82.0)	240	15.1	8.21 (8.88)
Zn(CFI)Cl_2	$Zn(C_{16}H_{15}N_5O_7S_2)Cl_2$ (589.831)	Milky	5.031 (85.3)	280	16.5	8.40 (9.38)
Cd(CFU)Cl_2	$Cd(C_{20}H_{22}N_4O_{10}S)Cl_2$ (693.877)	Milky	5.52 (79.6)	195	13.6	15.17 (15.28)
Cd(CFI)Cl_2	$Cd(C_{15}H_{15}N_5O_7S_2)Cl_2$ (636.862)	Yellow	5.319 (84.7)	315	10.3	14.04 (16.56)

Table 2: Physical Properties of the Ligands and their Metal(ll) Complexes Prepared by Solution-based Method

Compound	Molecular Formula (Molar Mass)	Colour	Yield(g) (%)	Decomposition Temperature (^{o}C)	Molar Conductivity (Scm^{2} mol^{-1})	% Metal found(Cacld)
Cefixime	$C_{16}H_{15}N_5O_7S_2$ (453.451)	White	------	218-225	------	------
Cefuroxime	$C_{20}H_{22}N_4O_{10}S$ (510.476)	White	------	135	------	------
Zn(CFU)Cl_2	$Zn(C_{20}H_{22}N_4O_{10}S)Cl_2$ (646.856)	Brown	3.45 (54.8)	258	16.6	7.85 (8.88)
Zn(CFI)Cl_2	$Zn(C_{16}H_{15}N_5O_7S_2)Cl_2$ (589.831)	Milk	4.707 (79.8)	272	12.4	8.38 (9.38)
Cd(CFU)Cl_2	$Cd(C_{20}H_{22}N_4O_{10}S)Cl_2$ (693.877)	Milk	2.923 (42.1)	268	12.4	13.81 (15.28)
Cd(CFI)Cl_2	$Cd(C_{15}H_{15}N_5O_7S_2)Cl_2$ (636.862)	Yellow	2.879 (45.2)	285	11.8	12.12 (11.03)

CFU=Cefuroxime, CFI=Cefixime, Cacld=Calculated

Infrared Spectra

The infrared spectra of the ligands and their corresponding metal complexes synthesized *via* solvent-free and solution-based methods are presented in Table 3 and 4 respectively. The band at 3402cm^{-1} which appeared in the free ligands and some of the metal(II) complexes prepared by solvent-free and solution-based synthesized complexes are characteristic of O-H stretching (Lever, 1984; Rotimi *et al.* 2017; Sheela, 2015 and Jassim *et al.,*2015). The bands at 3402 cm^{-1} observed in the free ligands were shifted (3394 – 3417 cm^{-1}) (Sankaranarayana and Pushpa, 2016). Infrared spectra for both the ligands, solvent-free and solution-based complexes show different bands intensities within the region of 2831–2931 cm^{-1} which are characteristic of amine group. Most of the spectra that are present in free ligands also appeared in their metal complexes due to structural similarities (Ngoshe *et al.,* 2018). In both the free ligands (cefuroxime and cefixime), weak bands appeared at 1643 cm^{-1} is a characteristic of (C=N) stretching (Muhammad and Saadatu, 2017). These bands remained unaffected in the spectra of the complexes prepared by both solvent-free and solution-based methods indicating non-involvement of the azomethine (C=N) in complexation. It can be seen from the result presented, the bands found at 1126 and 1134 cm^{-1} for cefixime and cefuroxime ligands assigned for C─N stretching was shifted to higher frequency 1141 cm^{-1} - 1149 cm^{-1} in some of the complexes. While Cd(CFU)Cl_2 of solvent-free complexes showed no shift either to lower or higher frequency. In the spectra of the ligands, the band due to C=O is observed at 1766 cm^{-1}. This band either disappeared or underwent shift to lower wavenumber of 1635 – 1643 cm^{-1} suggesting coordination via the carbonyl oxygen (Danish *et al.,* 2015). The spectra of the complexes showed new bands between 524 – 671 cm^{-1}assignable to M – O bond (Fayad *et al.,* 2012; Nishida *et al.,* 2009). This is probably due to the coordination of metal ion through oxygen atom. This mode of coordination has also been found in metal complexes of trimethoprim synthesized previously in solvent medium (Naldini *et al.*, 1984). It could to be inferred that the ligands act as tridentate coordinated to the metal ions through the oxygen atom of the three C=O group as shown in Figure 2.

Table 3: Infrared Bands of the Ligands and their Metal(II) Complexes Prepared by Solvent-free Method

Compound	$\nu(O-H)$	$\nu(N-H_2)$	$\nu(C=O)$	$\nu(C=N)$	$\nu(C-N)$	$\nu(M-O)$
Cefixime	3402_b	2924_w	1766_m	1643_w	1126_m	-----
Cefuroxime	3402_b	2916_w	----	1643_w	1134_m	-----
$Zn(CFU)Cl_2$	3394_b	2916_w	----	1635_w	1151_m	609_w
$Zn(CFI)Cl_2$	3402_b	2931_w	1735_m	1643_w	1141_m	540_w
$Cd(CFU)Cl_2$	3387_b	2916_w	----	1643_w	1134_m	547_w
$Cd(CFI)Cl_2$	3394_b	2924_w	1743_m	1643_w	1141_m	524_w

S=Strong, b=broad, m=medium, w=weak, sh=sharp

Table 4: Infrared Bands of the Ligands and their Metal(II) Complexes Prepared by Solution-based Method

Compound	$\nu(O-H)$	$\nu(N-H_2)$	$\nu(C=O)$	$\nu(C=N)$	$\nu(C-N)$	$\nu(M-O)$
Cefixime	3402_b	2924_w	1766_m	1643_w	1126_w	------
Cefuroxime	3402_b	2916_w	-----	1643_w	1134_m	------
$Zn(CFU)Cl_2$	3402_b	2931_w	-----	1643_m	1141_m	671_w
$Zn(CFI)Cl_2$	3349_b	2924_w	-----	1643_m	1149_m	609_w
$Cd(CFU)Cl_2$	3394_b	2916_w	-----	1643_w	1149_m	609_w
$Cd(CFI)Cl_2$	3417_b	2924_w	-----	1643_w	1149_m	578_w

s=strong, b=broad, m=medium, w=weak sh=sharp

UV-visible Spectral Data of the Ligands and their Metal(II) Complexes

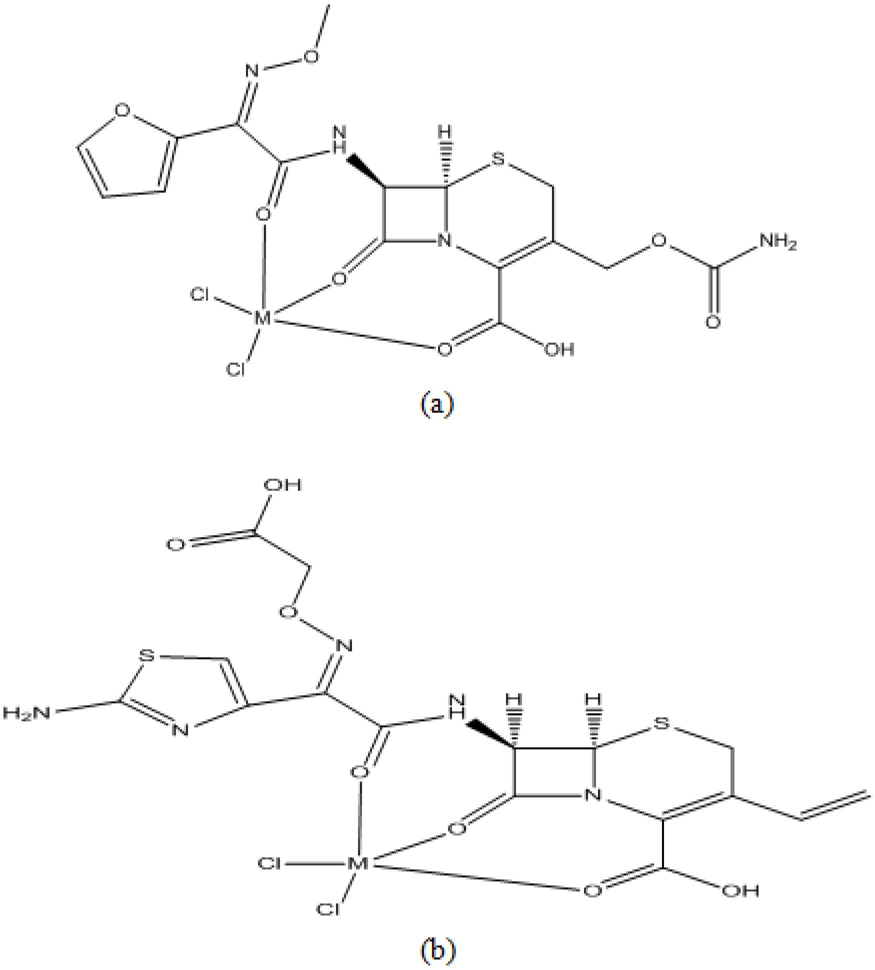
Tables 5 and 6 show UV-visible spectral data of the ligands and their metal(II) complexes. The UV-Visible absorption spectra of cefuroxime and cefixime gave absorption bands at 288 and 301 nm (34722 – 33222cm^{-1}) respectively, while the electronic spectra for the (solvent free and solution based) complexes displayed absorption bands between 290 nm (33482 cm^{-1}) to 301 nm (33222 cm^{-1}). Cefuroxime (CFU) complexes synthesized through solvent-free method and solution-based technique showed a shift to lower wave length (hypsochromic shift) as compared to the free ligand, while cefixime (CFI) complexes gave both hypsochromic and bathochromic shifts. Majority of the bands occurred at 280-300 nm. Bands in this range are attributed to intra-ligand transition π-π^* (Ajayeoba *et al.,* 2017; Babahan *et al.,* 2013; Omar *et al.,* 2012). In the absorption bands of the complexes, these transitions were assigned to ligand – metal charge transfer (LMCT) due to a weak interaction between the ligand and metal ions (Waziri *et al.,* 2018).

Table 5: UV-visible Spectral Data of the Ligands and their Metal(II) Complexes Prepared by Solvent-free Method

Compounds	λ_{max}(nm)	Ɛ (cm^{-1})	Assignment
CFI	297	33670	π-π^*
CFU	301	33222	π-π^*
$Zn(CFU)Cl_2$	290	34482	LMCT
$Zn(CFI)Cl_2$	291	34364	LMCT
$Cd(CFU)Cl_2$	289	34602	LMCT
$Cd(CFI)Cl_2$	294	34013	LMCT

Table 6: UV-visible Spectral Data of the Ligands and their Metal(II) Complexes Prepared by Solution-based Method

Compounds	λ_{max} (nm)	Ɛ (cm^{-1})	Assignment
CFI	297	33670	π-π^*
CFU	301	33222	π-π^*
$Zn(CFU)Cl_2$	291	34364	LMCT
$Zn(CFI)Cl_2$	296	25252	LMCT
$Cd(CFU)Cl_2$	290	33482	LMCT
$Cd(CFI)Cl_2$	296	33783	LMCT



Where M = Zn(II) or Cd(II)

Figure 2: Proposed Structure of Metal(II) Complexes of Cefuroxime (a) Cefixime(b)

Antibacterial Activities

The ligands and the synthesized complexes were tested against nine different micro-organisms which comprises of four Gram-positive (*S. aureus, S. pyogen, MRSA and B. subtilis)*, four Gram-negative (*K. pnemoniae, E. coli, S. typhi and P. aeruginosa)* bacteria and one fungus (*C. albicans)*. The results for the ligands and their solvent-free and solution-based synthesized complexes are presented in Tables 7 and 8 respectively. According to the data obtained for both the solvent-free and solution-based method, all the ligands showed activity against all the micro-organisms tested except *P. aeruginosa* and *S. pyogen* for cefuroxime. At all concentrations, the complex Cd(CFU)Cl_2 showed increased activity against all tested micro-organisms. The results also showed that the other complexes were active against the other micro-organisms as compared to the ligands. Similar result was recorded with cefixime which showed significantly enhanced antimicrobial and antifungal activities against microbial strains as compared to free ligands (Sankaranarayana and Pushpa, 2016).

The results of minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) for both the solvent-free and solution–based methods showed that only complexes of Cd(CFI)Cl_2 display increased activity against *C. albicans and P. aeruginosa* as compared to the ligand (cefixime) while all the tested cefuroxime complexes showed activity on all the micro-organisms except *K. pnemoniae, P. aeruginosa* and *B. subtilis* as compared to the ligand (cefuroxime).

Table 7: Antimicrobial Activities of the Ligands and their Metal(II) ComplexesPrepared by Solvent-free Method

Compound	Conc. (mg/mL)	*S. aureus*	*S. Pyogene*	*MRSA*	*K. pnemoniae*	*B. Subtilis*	*E.coli*	*S. typhi*	*C. albicans*	*P. aeruginosa*
CFI	10	10.3±04	20.0±0.0	13.3±04	18.7±0.4	24.7±0.4	9.7±.04	16.0±00	0.0±0.0	0.0±0.0
	20	15.7±04	25.0±0.0	18.3±04	24.3±0.4	30.0±0.0	20.3±04	21.7±04	8.0±0.0	0.0±0.0
	30	21.0±00	30.3±0.4	24.0±00	28.0±0.0	34.7±0.4	20.0±00	27.0±00	13.0±0.0	10.0±0.0
CFU	10	0.0±0.0	0.0±0.0	0.0±0.0	13.0±0.0	15.0±0.0	0.0±0.0	0.0±0.0	0.0±0.0	0.0±0.0
	20	8.0±0.0	0.0±0.0	7.0±0.0	19.7±0.0	20.0±0.0	8.0±0.0	10.0±00	7.0±0.0	0.0±0.0
	30	13.0±00	0.0±0.0	12.7±04	24.3±0.0	25.0±0.0	12.0±0.	15.0±00	11.0±0.0	0.0±0.0
Zn(CFU)Cl$_2$	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	0.0±0.0	0.0±0.0	0.0±0.0
	20	0.0±0.0	8.0±0.0	0.0±0.0	7.0±0.0	0.0±0.0	0.0±0.0	0.0±0.0	0.0±0.0	0.0±0.0
	30	0.0±0.0	10.7±0.4	0.0±0.0	9.7±0.4	0.0±0.0	0.0±0.0	0.0±0.0	0.0±0.0	0.0±0.0
Zn(CFI)Cl$_2$	10	0.0±0.0	7.0±0.0	0.0±0.0	7.0±0.0	7.0±0.0	0.0±0.0	0.0±0.0	0.0±0.0	0.0±0.0
	20	0.0±0.0	7.0±0.0	0.0±0.0	10.0±0.0	11.0±0.0	0.0±0.0	9.0±0.0	0.0±0.0	0.0±0.0
	30	0.0±0.0	10.0±0.0	0.0±0.0	14.0±0.0	15.7±0.0	0.0±0.0	13.3±04	8.7±0.0	0.0±0.0
Cd(CFU)Cl$_2$	10	12.7±00	0.0±0.0	7.6±0.4	8.0±0.0	9.0±0.0	11.7±00	14.6±04	25.3±0.4	12.6±0.4
	20	17.7±00	9.0±0.0	13.0±00	13.0±0.0	14.6±0.4	16.6±04	20.0±00	21.3±0.4	17.7±0.4
	30	23.0±00	14.3±0.4	17.6±04	18.0±0.0	20.0±0.0	21.7±04	24.6±04	27.0±0.0	23.0±0.0
Cd(CFI)Cl$_2$	10	15.3±04	16. ±0.4	12.0±00	8.6±0.4	14.3±0.4	9.3±0.4	10.0±00	19.0±0.0	7.0±0.0
	20	21.0±00	22.3±0.4	17.3±04	14.0±0.0	20.3±0.4	14.7±04	15.0±00	24.6±0.4	11.0±0.0
	30	26.0±04	28.0±0.0	22.0±00	19.3±0.0	26.0±0.0	20.0±00	20.3±04	30.0±0.0	16.0±0.0

S. aureus=Staphylococcus aureus, S. pyogene= Streptococcus pyogene, B. subtilis=Bacillus subtilis, E. coli=Escherichia coli, S. typhi=Salmonella typhi, K. pneumoniae=Klebsiella pneumoniae, MRSA=Methicillin-resistant *Staphylococcus aureus, C. albicans= Candida albicans*

Table 8: Antimicrobial Activities of the Ligands and their Metal(II) Complexes Prepared by Solution-Based Method

Compound	*Conc (mg/mL)*	*S. aureus*	*S. Pyogene*	*MRSA*	*K. pnemoniae*	*B. subtilis*	*E.coli*	*S. typhi*	*C. albicans*	*P. aeruginosa*
	10	10.3±0.4	20.0±0.0	13.3±0.4	18.7±0.4	24.7±0.4	9.7±0.4	16.0±0.0	0.0±0.0	0.0±0.0
CFI	20	15.7±0.4	25.0±0.0	18.3±0.4	24.3±0.4	30.0±0.0	20.3±0.4	21.7±0.0	8.0±0.0	0.0±0.0
	30	21.0±0.0	20.3±0.0	24.0±0.4	28.0±0.0	34.7±0.4	20.±0.0	27±0.0	13.±0.0	10.±0.0
	10	0.0±0.0	0.0±0.0	0.0±0.0	13.0±0.0	15.0±0.0	0.0±0.0	0.0±0.0	0.0±0.0	0.0±0.0
CFU	20	8.0±0.0	0.0±0.0	7.0±0.0	19.7±0.4	20.0±0.0	8.0±0.0	10±0.0	7.0±0.0	0.0±0.0
	30	13.0±0.0	0.0±0.0	12.7±0.4	24.3±0.0	25.0±0.0	12±0.0	15.0±0.0	11±0.0	0.0±0.0
	10	0.0±0.0	7.6±0.0	0.0±0.0	0.0±0.0	0.0±0.0	0.0±0.0	0.0±0.0	0.0±0.0	0.0±0.0
Zn(CFU)Cl$_2$	20	0.0±0.0	10.3±0.4	0.0±0.0	0.0±0.0	0.0±0.0	0.0±0.0	0.0±0.0	0.0±0.0	0.0±0.0
	30	0.0±0.0	13.0±0.0	0.0±0.0	8.0±0.0	0.0±0.0	0.0±0.0	0.0±0.0	8.0±0.0	0.0±0.0
	10	0.0±0.0	7.7±0.4	7.0±0.0	7.0±0.0	8.0±0.0	0.0±0.0	7.3±0.4	0.0±0.0	0.0±0.0
Zn(CFI)Cl$_2$	20	0.0±0.0	10.7±0.0	9.7±0.0	10.3±0.4	12.3±0.4	7.0±0.0	10.7±0.0	7.0±0.0	0.0±0.0
	30	0.0±0.0	13.7±0.0	14. ±0.	14.0±0.4	17.0±0.0	12.3±0.4	15.3±0.0	12.0±00	9.0±0.0
	10	15.3±0.4	10.3±0.4	0.00±0.0	9.3±0.4	7.6±0.4	0.0±0.0	13.3±0.4	7.3±0.4	13.0±0.0
Cd(CFU)Cl$_2$	20	20.0±0.0	14.6±0.4	9.00±0.0	14.0±0.0	11.6±0.4	8.3±0.4	18.3±0.4	12.6±04	17.3±0.4
	30	24.6±0.4	20.0±0.0	12.0±0.0	18.0±0.0	17.0±0.0	12.0±0.0	23.0±0.0	17.3±04	21.6±0.4
	10	16.3±0.4	9.0±0.0	7.0±0.0	14.0±0.0	8.3±0.4	11.3±0.0	14.0±0.0	11.3±04	13.0±0.0
Cd(CFI)Cl$_2$	20	21.0±0.0	13.6±0.4	10.6±0.4	19.3±0.4	13.0±0.0	15.6±0.0	18.6±0.4	16.3±04	18.3±0.4
	30	25.3±0.4	18.0±0.0	15.0±0.0	24.0±0.0	18.0±0.0	23.0±0.0	20.6±0.4	20.6±04	23.0±0.0

S. aureus=Staphylococcus aureus, S. pyogene= Streptococcus pyogene, B. subtilis=Bacillus subtilis, E. coli=Escherichia coli, S. typhi=Salmonella typhi, K. pneumoniae=Klebsiella pneumoniae, MRSA=Methicillin-resistan*t Staphylococcus aureus, C. albicans= Candida albicans*

CONCLUSION

Complexes of the antibiotics cefixime and cefuroxime as ligands were synthesized in 1:1 metal: ligand ratios using solvent-free and solution-based techniques. The complexes were all air stable and generally soluble in dimethyl sulfoxide (DMSO) but insoluble in *n*-hexane. The complexes were non-electrolytic and thermally stable as indicated by their high decomposition temperatures. Coordination occurred through oxygen of ν(C=O) of the ligands forming five - coordinate geometry. In general, the results showed that the complexes obtained by the two methods are virtually sameas similar IR peaks were observed in their spectra.The antimicrobial screening of the complexes revealed that only complex Cd(CFI)Cl$_2$ display increased activity against *C. albicans and P. aeruginosa* as compared to the antibiotic drug ligand (cefixime) while all the tested cefuroxime complexes showed activity against all the micro-organisms except *K. pneumoniae*, *P. aeruginosa* and *B. subtilis* in which case are less potent than the ligand (cefuroxime).

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