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Synthesis and Biological Utility of Binary and Mixed Metal Complexes Based on Ceftriaxone

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ABSTRACT

Here, the binary ceftriaxone metal complex of Cr (III) and five mixed metal complexes of $[CrM(ceft.)_2Cl(H_2O)_3]$, where M = Co(II), Mn(II), Ni(II), Cu(II), and Cd(II) were prepared. The prepared complexes were characterized by Fourier transform infrared (FT-IR), UV-Vis spectroscopy, magnetic measurements, molar conductance, ICP (Inductive coupled plasma), and microanalytical (C, H, and N) analysis were all used to describe the complexes. The shape, morphology, and size calculations have been examined using TEM. Thermogravimetric analysis (TGA) of the binary Cr(III) complex was also investigated. Several microorganisms have been tested for the antibacterial activity of the complexes, and the outcomes are contrasted with ceftriaxone's activity. The results indicated that all complexes displayed higher activity toward *Bacillus cereus* and *Escherichia coli* except $[CrCd(ceft)_2Cl(H_2O)_3]$, which has nearly the same activity compared to ceftriaxone. Also, all complexes displayed higher activity toward *pseudomonas aeruginosa* than the activity of ceftriaxone. However, they have lower activity toward *Micrococcus luteus, Sarratia marcescens, and Staphylococcus aureus.*

INTRODUCTION

Ceftriaxone is an antibiotic and belongs to the third generation of cephalosporins with a chemical structure as in **Figure 1**. Its bactericidal activity is typically caused by its inhibition ability toward the bacterial cell wall. The structural integrity of the cell wall is generally disrupted by ceftriaxone, which suppresses peptidoglycan cross-linking by forming a stable acyl-enzyme intermediate. In neonatal therapy, ceftriaxone is stable against β-lactamases, produced by the majority of Gram-positive and Gram-negative bacteria. Pseudomonas pneumonia, gram-negative sepsis, Streptococcal endocarditis, melioidosis, penicillinase-producing Neisseria gonorrhea, chancroid, gram-negative

osteomyelitis, Lyme disease, and gram-negative meningitis can all be effectively treated with third-generation cephalosporins. This activity explains their indications, mechanisms of action, and contraindications. [1-5]. Combining β-lactams with β-lactamase inhibitors is one method of increasing their antibacterial action. However, this approach is limited due to the variety of β-lactamase [6]. Targeting the bacterial regulatory systems responsible for β-lactamase expression is considered a promising strategy. Recently, the synthesis of complexes comprising various metal ions received great attention as a promising and simple approach to improving the antibacterial activity of antibiotics [7]. The prepared metal complexes of ceftriaxone usually display toxicological catalytic, bioinorganic relevance and pharmacological properties. Ceftriaxone and metal ions can interact to cause precipitation, leading to severe adverse pharmacological effects [8-12]. Ceftriaxone complexes can be used in wastewater treatment processes to decrease bacterial contamination. These complexes can effectively target and eliminate harmful bacteria present in wastewater helping to reduce the environmental impact of bacterial pollution [13].

Ceftriaxone overuse may cause a deficiency of minerals and serious physiological disorders. Pathogens became resistant toward parent compounds, thus, modification in existent molecules is required. Our novel compounds are highly efficient for testing pathogens. In the current study, ceftriaxone was reacted with essential trace elements to synthesize respective metal complexes. The novel compounds were characterized by different spectroscopic techniques like UV, FT-IR, elemental analysis, magnetic and molar conductivity.

Here, the binary Cr(III) and mixed metal (Cr(III), M) (M=Co(II), Mn(II), Ni(II), Cu(II) and Cd(II)) ceftriaxone complexes synthesized and characterized. Additionally, their anti-bacterial activity toward various bacteria was examined, and the outcomes contrast with the activity of ceftriaxone. The binary and mixed metal complexes show higher activity toward *Bacillus cereus*, *Pseudomonas aeruginosa* and *Escherichia coli* compared to the activity of ceftriaxone antibiotic.

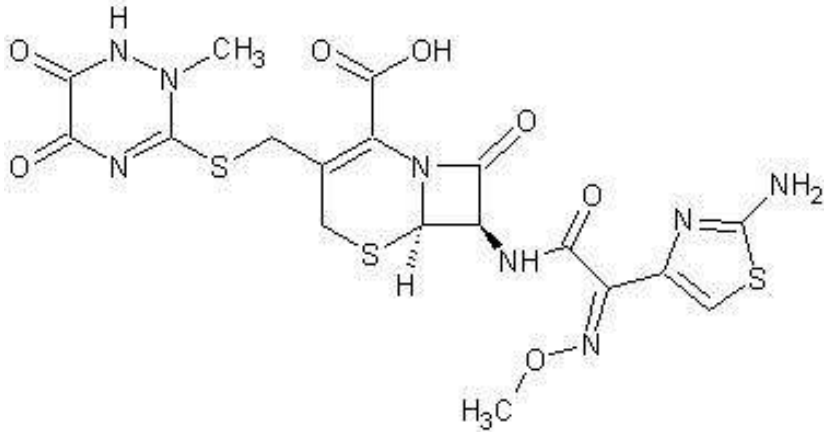

Figure 1: Chemical structure of Ceftriaxone antibiotic.

MATERIALS AND METHODS

Materials

Ceftriaxone antibiotic ($C_{18}H_{18}N_8O_7S_3$) was obtained from T3A Pharmaceutical Company, Assiut, Egypt. $CrCl_3.6H_2O$, $NiCl_2.6H_2O$, $CuCl_2.2H_2O$, $CoCl_2.6H_2O$, $MnCl_2.4H_2O$, $CdCl_2.H_2O$ were purchased from Sigma-Aldrich. All the reagents were of analytical purity and used without any purification. All preparations in our study have been performed with distillated water obtained from an ultra-pure purifier (ultrapure, resistivity $\geq$ 18.2 MΩ).

Characterizations

FT-IR spectroscopy was applied to determine the functional groups. The FT-IR analysis was performed on a Nicolet spectrophotometer (model 6700), and the spectrum was recorded in the 4000−400 cm^{-1} at a resolution of 2 cm^{-1}. TGA/DTA analysis was performed under N_2 atmosphere by using a NETZSCH-TGA/ STA 405 CD in a temperature range of 25 to 1000 °C with a heating rate of 5K/min. The absorbance spectra in the solution were determined by ultraviolet-visible (UV-Vis) spectroscopy, the spectra were carried out using thermo scientific evolution-300 in the wavelength of 200-900 nm. The morphology of the prepared complexes was performed by transmission electron microscopy (TEM) using a JEM-2100F; JEOL Ltd., Japan) with an accelerating voltage of 200 kV. Elemental analysis for C, H, N, and S was carried out on a Perkinelmer 240C instrument. A magnetic susceptibility balance of the MSB-Auto type was used to measure magnetic moments. Pascal's constants were used to adjust molar susceptibilities for the component atoms' diamagnetism. Hg $[Co(SCN)_4]$ was the calibrant that was employed. The metal percentage of the complexes was measured by using an inductively coupled plasma- optical emission spectroscopy (ICP-OES), thermo scientific -iCAP 6200 dual-view ICP emission spectrometer.

Preparation of a binary complex of ceftriaxone

$[Cr(ceft)Cl_2(H_2O)_2]H_2O$ was prepared by mixing 40 mL ceftriaxone (0.5 g) with 20 mL of $CrCl_3.6H_2O$ (0.23 g), and the mixture stirring for 24 h at room temperature. The obtained precipitate in dark green color was filtered, washed with distilled water several times and finally subjected to drying at 80 °C overnight [14].

Preparation of mixed metals [CrM(ceft.)$_2$Cl (H2O)3], M= Co(II), Mn(II), Ni(II), Cu(II), or Cd(II).

To prepare these complexes, 0.5 g ceftriaxone dissolved in 40 mL distilled water was slowly added to a solution of 0.23 g $CrCl_3.6H_2O$ dissolved in 20 mL distilled water, and the mixture was stirred for 24 h at room temperature. Various metal salts (X = 0.206 g of $CoCl_2.6H_2O$, 0.1716 g of $MnCl_2.4H_2O$, 0.206 g of $NiCl_2.6H_2O$, 0.1478 g of $CuCl_2.2H_2O$, and 0.17458 g of $CdCl_2.H_2O$)) were separately dissolved in 20 mL solutions and added to the above mixture, and the mixture was stirred for 24 h at room temperature. The obtained precipitate was filtered, thoroughly washed with distilled water, and finally subjected to drying at 80 °C for 12 h [14].

Biological activity

The bacterial activities of the prepared complexes have been carried out against pathogenic bacteria like *Staphylococcus aureus, Bacillus cereus, Micrococcus luteus, Pseudomonas aeruginosa, Serratia marcescens, and Escherichia coli* by the disc diffusion method using nutrient agar medium (Oxoid, Ireland), which was prepared by adding 1000 mL of distilled water to 28 g of media and sterilized in autoclave at 121 °C for 15 min on sterilized Petri dishes. After allowing the plates to harden for five minutes, a uniform 0.1% inoculum suspension was swabbed, and the inoculum was let dry for five minutes. Each substance was dissolved using dimethylformamide (DMF) to create a solution of concentration 10^{-3} M. Prepare the solution of chemicals by adding 0.5 ml of DMF and then vortex until complete solubility and put 50 µl solution in pores in agar media and incubate for 24 h (Kirby-Bauer method). After incubation, the former inhibition zones around the disc were measured with a transparent ruler in millimetres. Minimum Inhibitory Concentration (MIC) was carried out by determining the zone of inhibition of the complexes. Then compare it with that of the ceftriaxone against Gram negative and Gram-positive microorganisms. The serial dilution method was employed, and zone sizes were performed by the diffusion disk method [15,16].

RESULTS AND DISCUSSION

1. Elemental analysis and molar conductance

To investigate the formula and the composition of the binary and mixed metal complexes, the contents of C, H, N, and S were determined. The estimated contents of each element, as well as the physical properties and molar conductance in DMF, are listed in **Table 1Error! Reference source not found.**. The elemental analysis indicates that the prepared binary Cr(III) and mixed metal complexes displayed high purity. Moreover, the metal: ligand ratio of the binary Cr(III) metal complexes is 1:1, and mixed metal complexes display a 1:1:2 (Cr(III): metal ion: ligand) ratio. The complexation process indicates that ceftriaxone acts as a bi-and tetradentate ligand. All the obtained complexes are colored, and the obtained solid complexes are stable in the air and are non-hygroscopic. Additionally, these complexes are insoluble in water and in famous organic solvents, but they displayed observable solubility in DMF and DMSO solutions. The Λ_o values of the prepared binary Cr(III) and mixed metal complexes measured in $1x10^{-3}$ M DMF are in the range of 8.0-53.0 Ohm^{-1} cm^2 mol^{-1}. The non-electrolytic property of these complexes due to the reasonable range of 1:1 electrolytes in DMF is 65.0-90.0 $Ohm^{-1}cm^2$ mol^{-1} as in **Table 1** [17].

Table 1: Elemental analysis, and the Λo of all prepared complexes.

Complexes (Empirical formula)	Color	$\left(\frac{Calculated}{Found}\right)\%$					Λ_o ($Ohm^{-1}cm^2mol^-$)
		C	N	S	H	M	
$[Cr(ceft)Cl_2(H_2O)_2]H_2O$ **($C_{18}H_{22}CrN_8O_{10}S_3Cl_2$)**	Dark green	29.52 (29.90)	15.31 (15.49)	13.12 (12.99)	3.00 (2.97)	7.13 (7.03)	53.0
$[CrCo(ceft)_2Cl(H_2O)_3]$ **($C_{36}H_{48}CrCoN_{16}O_{17}S_6Cl$)**	Pale pink	32.99 (32.72)	17.11 (16.99)	14.66 (14.64)	3.66 (3.56)	Cr 3.95 (4.10) Co 4.48 (4.51)	24.0
$[CrMn(ceft)_2Cl(H_2O)_3]$ **($C_{36}H_{48}CrMnN_{16}O_{17}S_6Cl$)**	Grey	33.08 (33.11)	17.15 (17.30)	14.70 (14.62)	3.67 (3.65)	Cr 3.96 (3.99) Mn 4.19 (4.21)	46.0
$[CrNi(ceft)_2Cl(H_2O)_3]$ **($C_{36}H_{48}CrNiN_{16}O_{17}S_6Cl$)**	Pale green	32.99 (32.86)	17.10 (17.32)	14.66 (14.60)	3.66 (3.60)	Cr 3.95 (4.01) Ni 4.46 (4.43)	16.0
$[CrCu(ceft)_2Cl(H_2O)_3]$ **($C_{36}H_{48}CrCuN_{16}O_{17}S_6Cl$)**	Pale green	32.87 (32.55)	17.04 (17.20)	14.61 (14.80)	3.65 (3.59)	Cr 3.94 (4.01) Cu 4.81 (4.95)	33.0
$[CrCd(ceft)_2Cl(H_2O)_3]$ **($C_{36}H_{48}CrCdN_{16}O_{17}S_6Cl$)**	Grey	31.69 (31.71)	16.43 (16.49)	14.08 (14.15)	3.52 (3.49)	Cr 3.80 (3.86) Cd 8.21 (8.18)	8.0

2. FT-IR spectra of ceftriaxone and binary Cr (III) complex.

FT-IR spectra is a powerful technique to understand the molecular structure and the type of the metal-based complexes, The relevant FT-IR bands spectra of the Ceftriaxone and the $[Cr(ceft)Cl_2(H_2O)_2]H_2O$ complex are in **Figure l**, and their repellent bands are listed in **Table 2**. The FT-IR spectra of Ceftriaxone and $[Cr(ceft)Cl_2(H_2O)_2]H_2O$ complex displayed some observations; (i) all Cr(III)-based Ceftriaxone complexes showed broad band at 3333 cm^{-1} suggesting the coordination with water molecules. This also evidenced by the elemental analysis of the complexes [18]. (ii) The band at 3428 cm^{-1} for the N-H in Cr(III) complex. [19]. (iii) The band at 1750 cm^{-1} for the C=O group for free ceftriaxone is shifted to 1773 cm^{-1} in $[Cr(ceft)Cl_2(H_2O)_2]H_2O$. The amide group in ceftriaxone displayed a band at 1650 cm^{-1} ,while the complex showed a band at 1648 cm^{-1}, suggesting coordination between the ceftriaxone ligand with metal ions through the oxygen from the lactam carbonyl group rather than the amide carbonyl group, where the

shifting was not significant [20]. (iv) The band due to υ_{C-N} of β-lactam (1221 cm^{-1}), υ_{C-O} of methoxy group (1105 cm^{-1}) and υ_{N-O} of oxime (1038 cm^{-1}) in the free ligand unchanged after complexation [6]. (v) The band at 1610 cm^{-1} for the carboxylate asymmetrical stretching of the ceftriaxone shifted to a lower wavenumber indicates the complexation by that group. A carboxylate ligand could bind to the metal ions either monodentate or bidentate as changing in their positions. The separation value in the FTIR spectra of the complexes is >200, which indicates a monodentate carboxylate. Additionally, the carboxylate bands υ_{COO} (symm), γ(COO), ρ(COO) and ω(COO), located at 1350, 763, 607 and 541 cm^{-1}, respectively, also changes after coordination [21]. (vi) The υ_{C-O} of triazolic band for the free ceftriaxone, and the metal complex located at 1537, and 1535 cm^{-1}, respectively. [20].

Table 2: Fundamental FT-IR bands of ceftriaxone and binary Cr(III) complex.

Function groups	Frequency (cm^{-1}) Ceftriaxone	Frequency (cm^{-1}) $[Cr(ceft)Cl_2(H_2O)_2]H_2O$
υ_{O-H} of H_2O	-	3333
υ_{C-H} of β-lactam ring	2937	2936
$\upsilon_{C=O}$ (β-lactam ring)	1750	1773
$\upsilon_{C=O}$ amide	1650	1648
υ_{COO} (asymm)	1610	1542
υ_{COO} (symm)	1350	1340
υ_{C-O} (triazolic ring)	1537	1535
υ_{C-N} (β-lactam ring)	1221	1214
υ_{C-O} of methoxy group	1105	1104
υ_{C-O} of oxime	1038	1043
γ (COO)	763	808
ω (COO)	607	659
ρ(COO)	541	566

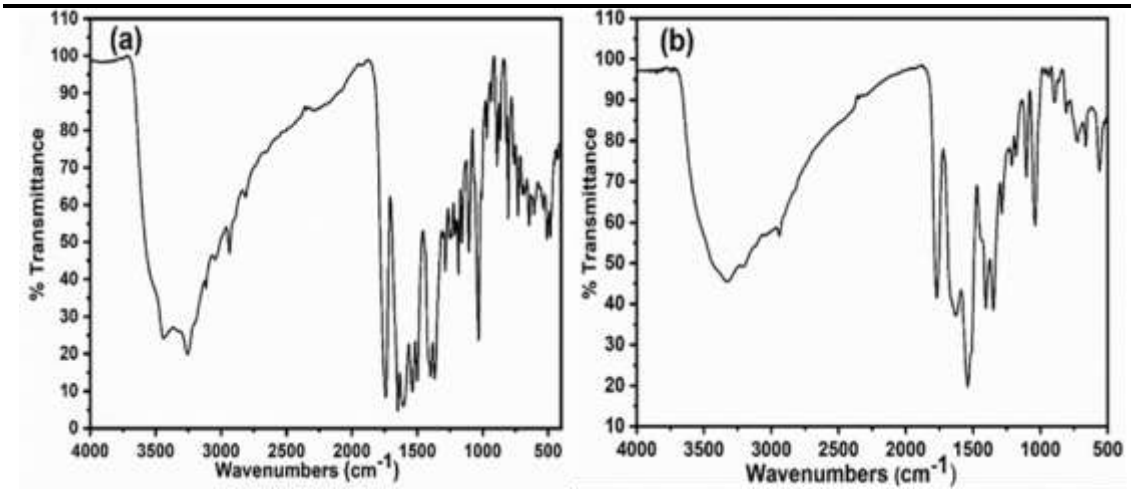

Figure 2: FT-IR spectra of the (a) free Ceftriaxone and (b) $[Cr(ceft)Cl_2(H_2O)_2]H_2O$ complex.

2.1. FT-IR spectra of mixed metal complexes.

The various bands from the FT-IR spectra of mixed metal complexes of ceftriaxone are listed in **Figure 3** and **Table 3Error! Reference source not found.**. All prepared complexes displayed observable bands at 3340-3370 cm^{-1}, indicating coordination of the water molecules. The water molecules are also confirmed by the formation of the metal-oxygen band at 530 cm^{-1} [18]. The lactam band appears at a higher wavenumber (1760-1768 cm^{-1}). The band related to the amid group in all mixed complexes appeared at 1650-1651 cm^{-1}. The non-observable shift in the wavenumbers indicates that the coordination of the ligand and metal ions occurs through the oxygen from the lactam carbonyl group. In all the mixed complexes, the band of the free ceftriaxone at 1610 cm^{-1} for the υ_{COO} (asymm) shifted to higher wavenumbers (1630-1635 cm^{-1}) indicating that the carboxylic group participated in the complexation process. The estimated separation in all mixed complexes is higher than 200 cm^{-1}, confirming a monodentate carboxylate. After coordination with metal ions, the remaining carboxylate bands: γ(COO), ω(COO) and ρ(COO) shifted to higher wavenumbers. The υ_{C-O} in triazolic ring shifted to lower wavenumbers (1401–1407cm^{-1}) indicating its participation in the complexation process [14]. The band at 510 cm^{-1} in binary Cr(III) complex was very small in mixed metal complexes. It is evident that another metal was coordinated in the complex.

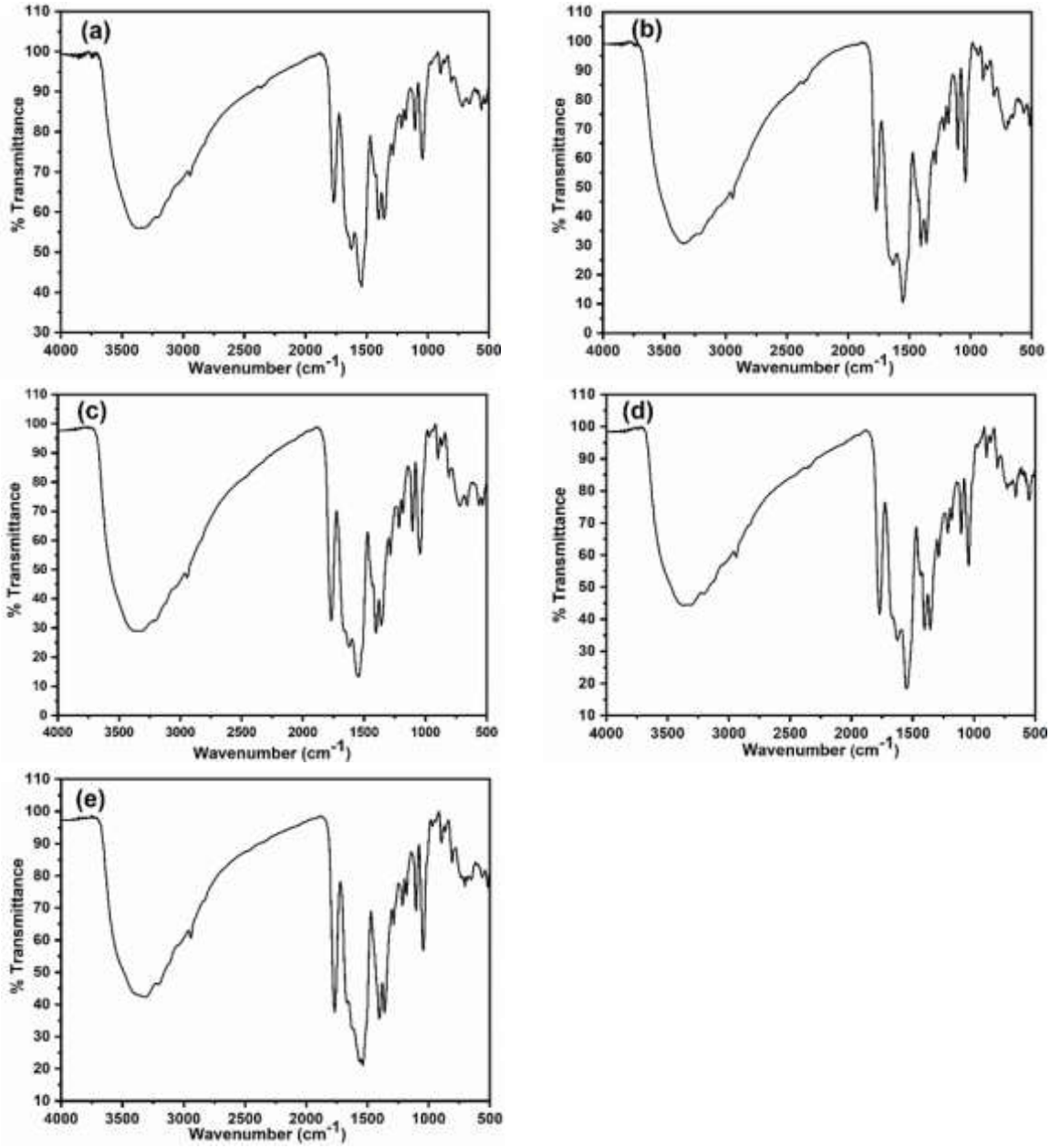

Figure 3. IR spectra for the mixed metal complexes (a) $[CrCo(ceft)_2Cl(H_2O)_3]$, (b)$[CrMn(ceft)_2Cl(H_2O)_3]$, (c)$[CrNi(ceft)_2Cl(H_2O)_3]$, (d)$[CrCu(ceft)_2Cl(H_2O)_3]$and (e) $[CrCd(ceft)_2Cl(H_2O)_3]$.

Table 3: FT-IR spectra of mixed metal complexes.

	Wavenumbers (cm^{-1})				
Assignment	**$[CrCo(ceft)_2Cl(H_2O)_3]$**	**$[CrMn(ceft)_2Cl(H_2O)_3]$**	**$[CrNi(ceft)_2Cl(H_2O)_3]$**	**$[CrCu(ceft)_2Cl(H_2O)_3]$**	**$[CrCd(ceft)_2Cl(H_2O)_3]$**
υ_{O-H} H_2O	3363	3346	3352	3354	3343
υ_{C-H} β-lactam ring	2944	2937	2939	2940	2936
$\upsilon_{C=O}$ β-lactam ring	1768	1762	1760	1766	1765
$\upsilon_{C=O}$ amide	1651	1650	1650	1650	1650
υ_{COO} Asymm	1630	1632	1632	1633	1635
υ_{COO} Symm	1362	1366	1366	1363	1366
υ_{C-O} Triazolic ring	1403	1401	1407	1407	1401
υ_{C-N} β-lactam ring	1217	1219	1218	1218	1217
υ_{C-O} Methoxy group	1106	1108	1099	1105	1101
υ_{C-O} Oxime	1040	1038	1043	1043	1042
γ(COO)	907	911	907	906	912
ω(COO)	671	676	676	675	673
ρ(COO)	580	587	586	582	586

3. Electronic spectra and magnetic moment of the binary Cr(III) complex.

The λ_{max} of the absorption bands recorded as ($1x10^{-3}$M) DMF solutions of Cr (III) binary complex are characterized by three regions presented in **Table 4**. The electronic spectra of the $[Cr(ceft)Cl_2(H_2O)_2]H_2O$ complex displayed 302, 340, and 556 nm. The two bands at lower wavelengths can be attributed to charge transfer (CT) transition, and the higher one for the complex due to the d-d band, indicates an octahedral geometry around Cr(III)ions[21]

The magnetic moment of 3.49 B.M., shown in **Table 4**, supports these findings. Similar to the result anticipated for octahedral structures, this verified the octahedral geometry in the high spin state. The Cr(III) has purely octahedral geometry, according to the complex's μ_{eff} value. The oxygen atoms of lactam carbonyl and carboxylic groups supported the proposed structure, which was based on the bidentate nature of ceftriaxone and the presence of two chloride ions and two water molecules in the inner sphere. [22].

3.1. Electronic spectra and magnetic moment of the mixed metal complexes.

According to **Table 4**, the mixed metal complexes' electronic absorption spectra and μeff values in Bohr magneton units are displayed. The electronic spectrum of the $[CrCo(ceft)_2Cl(H_2O)_3]$ complex displayed three bands at 336, 522, and 672 nm. The CT transition is responsible for the band at the lower wavelength. The other two bands are associated with the d-d transition, which can be attributed to the octahedral spatial configuration surrounding Co(II) ions. [23]. The orbital contribution to the complex's spin is responsible for the greater value of μeff (7.71 B.M) than anticipated.

The electronic spectrum of $[CrMn(ceft)_2Cl(H_2O)_3]$ complex showed three bands at 268, 335 and 476 nm. The two bands at lower wavelength are assigned to CT ($t_{2g} \rightarrow \pi^*$), while the other one (480 nm) is due to CT ($\pi \rightarrow e_g$). The magnetic value (9.73 B.M) indicates the octahedral configuration in a high spin state corresponding to high spin $3d^5$ system Mn(II) and is extra evidence for the octahedral structure [22].

For the $[CrNi(ceft)_2Cl(H_2O)_3]$ complex, three bands at 322, 424, and 630 nm were observed. The first two bands are due to CT transition, and the last band for d-d transition, indicates the octahedral geometry [24]. The higher magnetic value (7.21 B.M) than the expected value is due to the great interactions of Cr(III) and Ni(II) ions.

Also in the $[CrCu(ceft)_2Cl(H_2O)_3]$ complex, three bands at 306, 544, and 700 nm were observed. The band at the lower wavelength is for the CT transition, while the other bands are for d-d transition [25]. As mentioned above, the higher magnetic value (7.5 B.M) than the expected value indicating high spin octahedral configuration due to the strong interactions between Cr(III) and Cu(II) ions [25].

On the other hand, the $[CrCd(ceft)_2Cl(H_2O)_3]$ complex displayed two bands at 322, and 530 nm which were assigned for the CT, and d-d transitions, respectively [26]. The estimated magnetic value (3.3 B.M) is similar to the expected value indicating a high spin octahedral configuration. The oxygen atoms of lactam carbonyl and carboxylic groups supported the proposed structure, which was based on the bidentate nature of ceftriaxone and the presence of two chloride ions and two water molecules in the inner sphere.

Table 4: Electronic absorption and the μ_{eff} values of the binary and mixed complexes.

Complex	λ_{max} (nm)	Assignment	μ_{eff} (B.M) at 298 k
$[Cr(ceft)Cl_2(H_2O)_2]H_2O$	302 340 556	CT transition CT transition d-d transition	3.49
$[CrCo(ceft)_2Cl(H_2O)_3]$	336 522 672	CT transition d-d transition d-d transition	7.71
$[CrMn(ceft)_2Cl(H_2O)_3]$	268 335 476	CT ($t_{2g} \rightarrow \pi^*$) CT ($t_{2g} \rightarrow \pi^*$) CT ($\pi \rightarrow e_g$)	9.73
$[CrNi(ceft)_2Cl(H_2O)_3]$	322 424 630	CT transition CT transition d-d transition	7.21
$[CrCu(ceft)_2Cl(H_2O)_3]$	306 544 700	CT transition d-d transition d-d transition	7.5
$[CrCd(ceft)_2Cl(H_2O)_3]$	322 530	CT transition d-d transition	3.3

4. Thermogravimetric analysis (TGA) of the binary Cr(III) complex

The thermogram of the complex ran up to 800 °C, and the theoretical data agrees with the experimental findings, confirming the proposed composition. The thermal analysis of the complex $[Cr(ceft)Cl_2(H_2O)_2]H_2O$ in **Figure 4a** showed three steps. The first one is due to dehydration process of the two coordinated and one crystalline water molecules, mass loss of 7.4% (Calc. 7.4 %) is observed. The second mass loss of 26.8% (Calc. 26.41%) is caused by the decomposition of the complex structure with a probable loss of gases. The last mass loss of 44.9% is due to the decomposition of the rest of the complex, leaving a residual product of Cr_2O_3 (found 20.9% and calc. 10.4%), the difference between the calculated and found percent could be assigned to the presence carbon residue admixed with Cr_2O_3 [14].

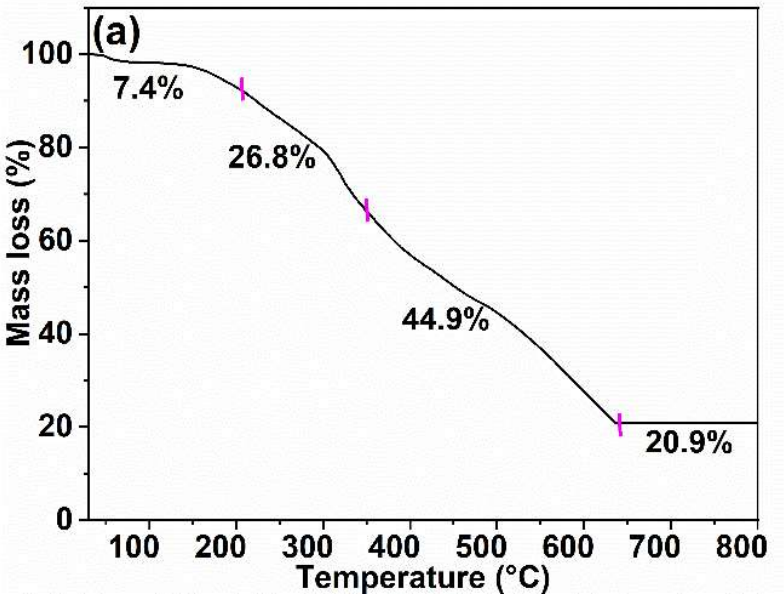

Figure 4a: TGA of $[Cr(ceft)Cl_2(H_2O)_2]H_2O$ complex

5. Transmission electron microscopy (TEM).

The morphological shape and particle size of the $[Cr(ceft)Cl_2(H_2O)_2]H_2O$ complex was examined via transmission electron microscopy. TEM images are displayed in **Figure 5**, in which their particles show uniform spheres. The size distribution curve shows particles of the complex with 0.015-0.055 nm in diameter, and the average diameter of the spheres is ~ 0.03 nm.

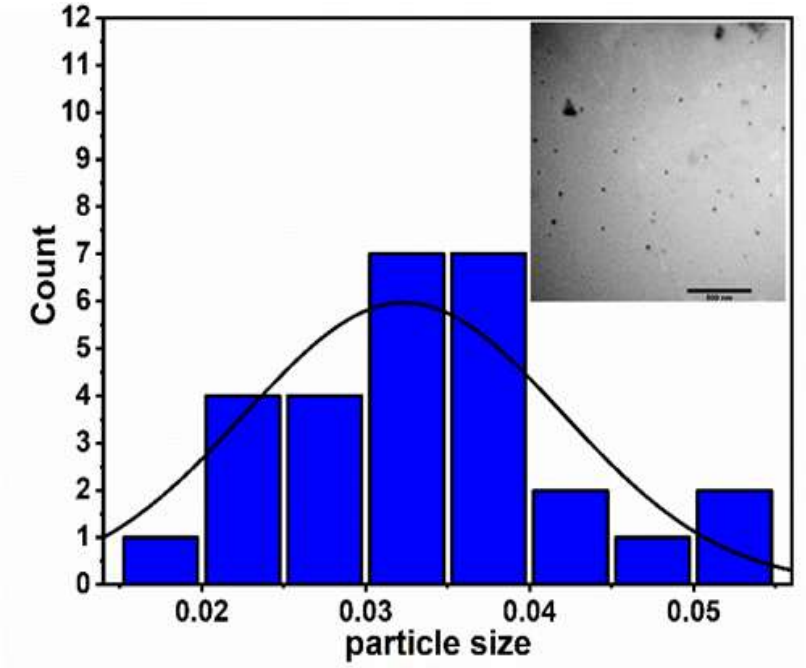

Figure 5: TEM image of $[Cr(ceft)Cl_2(H_2O)_2]$ H_2O complex

Based on the FT-IR, electronic absorption spectra, and μ_{eff} values, the suggested structures of binary Cr(III) and mixed complexes can be represented as in **Figure 6**.

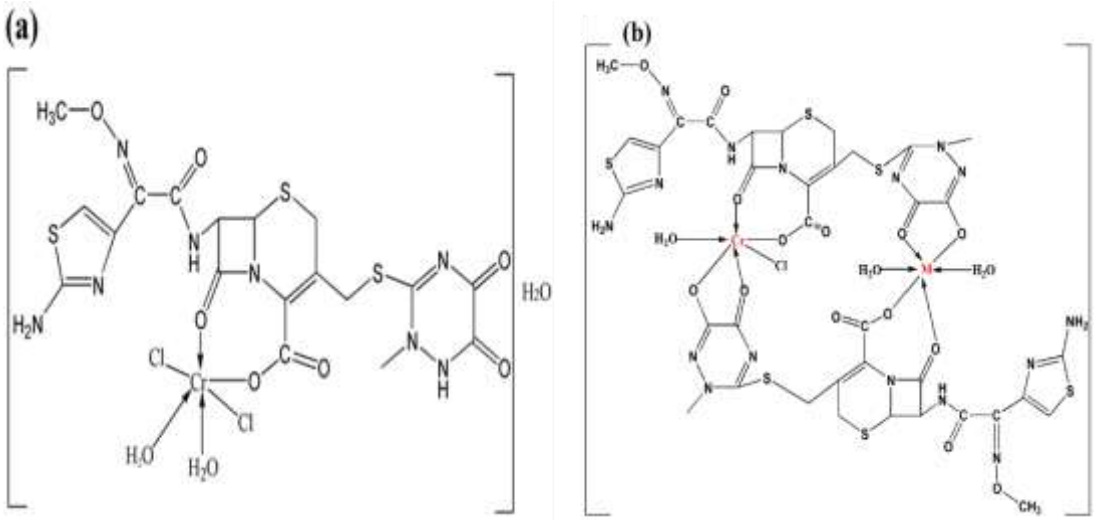

Figure 6: The suggested structure of binary Cr(III) and mixed metal complexes; (a) $[Cr(ceft)Cl_2(H_2O)_2]H_2O$, and (b) $[CrM(ceft)_2Cl(H_2O)_3]$; M is Co(II), Mn(II), Ni(II), Cu(II) or Cd(II).

6. Antibacterial activity

The antibacterial activity of free ligand and metal complexes was studied against various Gram (+ve) bacteria such as *Bacillus cereus, Micrococcus luteus and Staphylococcus aureus, and Gram (-ve) bacteria such as Escherichia coli, Pseudomonas aeruginosa, and Serratia marcescens.* The obtained results are presented as the inhibition zone of the bacterial growth measured in mm and compared to that obtained from chloramphenicol as a reference antibacterial drug and are displayed in **Figure 7**. It can be observed that all complexes show higher activity against *Bacillus cereus* and *Escherichia coli* except $[CrCd(ceft)_2Cl(H_2O)_3]$ which has nearly the same activity compared to ceftriaxone. All complexes show higher activity against *pseudomonas aeruginosa* than the activity of ceftriaxone, moreover, they have lower activity against *Micrococcus luteus, Sarratia marcescens* and *Staphylococcus aureus*. A comparison of the antibacterial activity of prepared complexes with that of ceftriaxone was illustrated in **Figure 7**. Minimal inhibitory concentration values (MIC) of some ceftriaxone complexes $[Cr(ceft)Cl_2(H_2O)_2]H_2O$, $[CrMn(ceft)_2Cl(H_2O)_3]$ and $[CrNi(ceft)_2Cl(H_2O)_3]$ were determined using ceftriaxone as a reference. MIC represents the lowest concentration of an antibacterial agent that will inhibit the growth of a tested organism. The MICs (in µg/ml) for the complexes and the corresponding inhibition zone in mm are shown in **Table 6** and **Figure 8**. From the results, we can see that complex $[CrMn(ceft)_2Cl(H_2O)_3]$ has the highest MIC with an inhibition diameter of 12 mm against the test bacteria, whereas MIC of the complexes against *bacillus cereus, Escherichia coli and Micrococcus luteus* is greater than that of ceftriaxone.

Compound	*Bacillus cereus*	*Micrococcus luteus*	*Staphylococcus aureus*	*Pseudomonas aeruginosa*	*Serratia marcescen*	*Escherichia coli*
(Ceftriaxone antibiotic)	8	23	22	10	18	8
$[Cr(ceft)Cl_2(H_2O)_2]H_2O$	13	15	14	15	14	13
DMF	8	10	10	10	10	8
$[CrCo(ceft)_2Cl(H_2O)_3]$	9	15	18	15	15	9
$[CrMn(ceft)_2Cl(H_2O)_3]$	10	16	15	16	15	10
$[CrNi(ceft)_2Cl(H_2O)_3]$	11	17	18	16	17	14
$[CrCu(ceft)_2Cl(H_2O)_3]$	9	12	16	14	10	10
$[CrCd(ceft)_2Cl(H_2O)_3]$	8	14	14	14	17	8

Table 5: Antibacterial activity of the free ligand and metal complexes

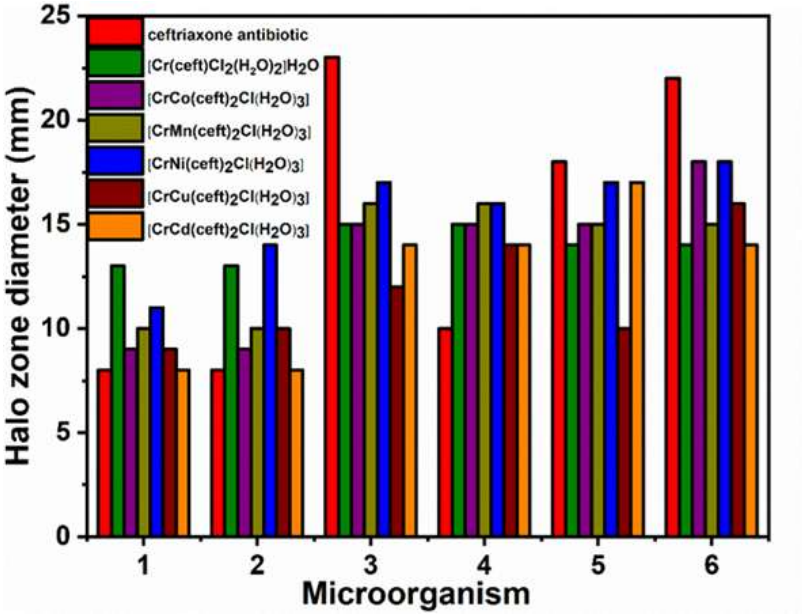

Figure 7: Comparison of antibacterial activity of prepared complexes with that of Ceftriaxone where (1) *Bacillus cereus*, (2) *Escherichia coli*, (3) *Micrococcus luteus*, (4) *pseudomonas aeruginosa*, (5) *Sarratia marcescens* and (6) *Staphylococcus aureus*.

Table 6: Minimum Inhibition Concentrations (MIC) For Some Ceftriaxone Complexes.

	Bacillus cereus	***Micrococcus luteus***	***Staphylococcus aureus***	***Pseudomonas aeruginosa***	***Serratia marcescens***	***Escherichia coli***
Ceftriaxone antibiotic	0	8 (2.5)	7 (20)	0	7 (2.5)	0
$[Cr(ceft)\ Cl_2(H_2O)_2]H_2O$	6 (5)	7 (5)	7 (20)	7 (20)	8 (5)	7 (5)
$[CrMn(ceft)_2\ Cl(H_2O)_3]$	7 (2.5)	7 (2.5)	10 (2.5)	10 (2.5)	10 (2.5)	7 (2.5)
$[CrNi(ceft)_2\ Cl(H_2O)_3]$	7 (20)	7 (2.5)	7 (10)	7 (5)	7 (5)	7 (20)

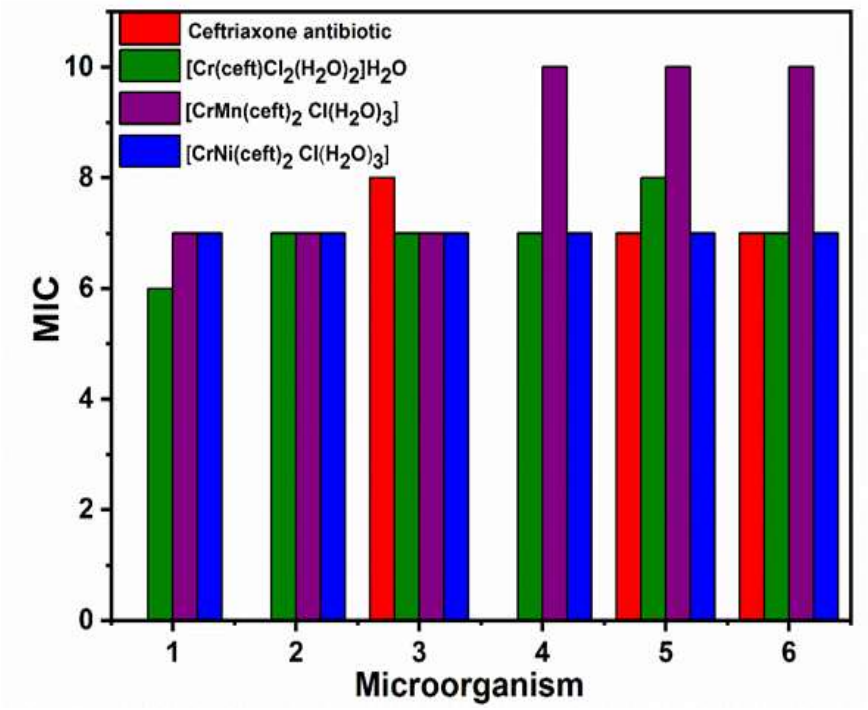

Figure 8: MIC of some prepared complexes with that of Ceftriaxone where (1) *Bacillus cereus*, (2) *Escherichia coli*, (3) *Micrococcus luteus*, (4) *pseudomonas aeruginosa*, (5) *Sarratia marcescens* and (6) *Staphylococcus aureus*.

CONCLUSION

This study aimed to synthesize ceftriaxone complexes by the reaction with Cr(III) to form binary $[Cr(ceft)Cl_2(H_2O)_2]H_2O$ complex and synthesize mixed metal metals with ceftriaxone to form $[CrM(ceft.)_2Cl(H_2O)_3]$ where M is Co(II), Mn(II), Ni(II), Cu(II), and Cd(II)ions . The prepared complexes displayed an octahedral geometry. For antibacterial activity, all complexes were highly effective against *Bacillus cereus* except $[CrCd(ceft)_2Cl(H_2O)_3]$ which has the same effect as ceftriaxone. All complexes were highly effective against *Pseudomonas aeruginosa* compared to ceftriaxone. For *Escherichia coli* all complexes have a higher effect than ceftriaxone except $[CrCd(ceft)_2Cl(H_2O)_3]$ which has the same effect as ceftriaxone. All complexes have higher effects against *Pseudomonas aeruginosa* than ceftriaxone, but all complexes have the lowest effect against *Serratia marcescens*, *Micrococcus luteus* and *Staphylococcus aureus* compared to ceftriaxone.

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