International Journal of Sciences: Basic and Applied Research (IJSBAR)

ISSN 2307-4531
(Print & Online)

http://gssrr.org/index.php?journal=JournalOfBasicAndApplied

Synthesis, Characterization and Antimicrobial Evaluation of Cr (III) Complexes of 2-Amino -3-(2-hydroxy phenyl) -1-oxazolidin-4-one and 2-Amino -3-(2-hydroxy phenyl) -1-thiozolidin-4-one

Abdisa Gabisa[a], Abebe Tedla[b]*, Abi Tadesse[c], Zewdu Tadesse[d]

[a,b,d]*College of Natural and Computational Sciences, Debre Berhan University 445, Debre Berhan, Ethiopia*

[c]*College of Natural and Computational Sciences, Haramaya University 138, Haramaya, Ethiopia*

[a]*Email: abdisachemist@gmail.com,* [b]*Email: abebetedla@gmail.com,* [c]*Email: abi2003@yahoo.com,*

[d]*Email: ztadesse33@gmail.com*

Abstract

The ligands 2-Imino-3-(2-hydroxyphenyl)-1-oxazolidine-4-one and 2-Imino-3-(2-hydroxy phenyl)-1 thiozolidine-4-one were synthesized by condensation of 2-chloro-N-(2-hydroxyphenyl) acetamide with potassium thiocyanate and potassium cyanate respectively. The chromium metal complexes of the ligands were prepared by refluxing the ligands with hydrated chromium metal salts ($CrCl_3.6H_2O$ and $Cr(NO_3)_3.9H_2O$). Both ligand and metal complexes were characterized using UV-Vis, IR, ^{1}H- and ^{13}C-NMR spectroscopies. Elemental Analysis and conductometric results demonstrated the metal-ligand ratio and non-electrolytic nature of the complexes. IR spectral data revealed that both heterocyclic ligands coordinate through their heterocyclic nitrogen and deprotonated phenolic oxygen to the metal and act as anionic bidentate ligands. Magnetic studies and electronic spectral indicated octahedral geometry of all Cr (III) complexes. The ligands and their complexes were screened in-vitro for their antibacterial and antifungal activities against two bacterial strains, Escheria coli and Staphylococcus aureus and two fungal strains, Aspergilus niger and C.gloeosporioides using agar well diffusion technique. The synthesized complexes were found to be more bioactive than the corresponding free ligands.

Keywords: Antimicrobial screening; Chromium complex; Heterocyclcic ligand; Oxazolidinone; Thiozolidinone.

---

* Corresponding author.

1. Introduction

The rapid emergence of multi-drug resistant microbial pathogens is threatening the commercially available antibiotics, which have been used for decades and saved millions of lives [1-5]. With the existence of this phenomenon, there is growing interest in the discovery of new antibacterial agents [6]. Heterocyclic ligands and their derivatives are one of the most important classes of compounds with wide spectrum of antimicrobial activities that have drawn attention due to their increasing importance in the field of pharmaceuticals [7]. Numerous attempts have been made to synthesize heterocyclic-based molecules in effort to solve problems of pathogenic bacteria and fungi resistance drugs [8]. For instance thiazolidinones, which is a fundamental structure of many synthetic pharmaceuticals, have showed a broad spectrum of biological activities. These molecules with a carbonyl group on the fourth position have been extensively studied in the past owing to their broad range of biological activities. Thiazolidinones substituted at the second position also exhibit unusually high in vitro activities against Mycobacterium tuberculosis, and it is the core building component of penicillin antibiotics [9]. In recent years several new methods have been reported for preparing thiazolidinone derivatives [10]. Heterocyclic compounds with one, two or three coumarin cores contain thiazolidinone moieties and thiazolidinone coumarin derivatives have been proven to have significant biological activities like anticonvulsant [11], cytotoxic [12], antioxidant activity [13], antiviral agents [14], antifungal [15], antibacterial activities [16], and are cyclooxygenase inhibitors [17] as well as anticarcinogenic agent. Reports have recently indicated that substituted thiozolidinone and oxazolidinones inhibit the enzyme, integral component in bacterial peptidoglycan biosynthesis even at low molar level. For instance mercaptoimidazole derivatives have showed bactericidal and fungicidal activities since substitution pattern in oxazole and thiazole derivatives play a crucial role in defining the biological activities [18]. Many other heterocyclic molecules including imidazole, thiazole, carbazole oxazole and benzimidazole etc. have also been found to have antimicrobial activities [19-23].

The search for materials that have novel biological activities has led researcher to transition metal complexes since the activity of ligands can be changed by coordinating with metal ions. The interest in coordination chemistry is increasing continuously with the synthesis and characterization of large number of transition metal complexes with heterocyclic ligands and macrocylic ligands [24-27]. Heterocyclic ligands play important roles in coordination chemistry as they easily form stable complexes with most transition metal ions [28]. Particularly transition metal complexes with nitrogen, oxygen and sulphur containing ligands has drawn more attention since they demonstrated variety of biological activities including antitumor, fungicidal, bactericidal, anti-inflammatory, and antiviral [29].

In the last few years so many studies have been done on the structure, chemical behavior and evaluation of biological activity of several metal complexes to search for substitute drugs that have more strong activity against multi-drug resistant bacteria and fungi than the existing drugs [30]. Many reports have indicated that transition metal complexes possess more powerful antibacterial effect than the corresponding ligands [31, 32]. Chromium is one of the transition metals which exists in wide variety of oxidation states such as +2, +3 and +6 and reacts with many naturally occurring ligands particularly with those that contain N, O and/or S donor atoms to form several isomeric complexes. Despite these results very little is known about the composition and structure of the biologically active forms of chromium [33]. Chromium (III) complexes of macro cyclic ligands

are well known for their biological importance including anti-carcinogenic, antibacterial, and antifungal properties [34] Numerous Chromium (III) complexes have been studied so far. It has been reported that Chromium (III) complexes with O, N and S donor macro cyclic ligands can increase the activity of insulin by binding to a small chromium binding protein [35] though some controversy regarding the exact biochemical forms and the action of Chromium (III) in biological systems. Although a large number of complexes of transition metals with different Schiff's bases of heterocyclic, macrocyclic and other ligands have been studied for their structures and various properties, to the best of our knowledge, there is no any report on the synthesis and properties of complexes of Cr (III) with heterocyclic ligands like 2-Imino-3-(2-hydroxyaryl)-1-oxazolidine-4-one and 2-Imino-3-(2-hydroxyaryl)-1-thiozolidine-4-one. In this article, we present the synthesis, characterization and antimicrobial study of the ligands and their Cr (III) complexes.

2. Materials and Methods

2.1 Reagents and chemicals

All the chemicals used in this study were of analytical grade and used without further purification. Solutions of PDA (potato dextrose agar), Mueller Hinton agar (MHA) were prepared in the laboratory. Solvents employed in synthetic work were used as supplied whereas for spectroscopic and thin layer chromatographic work, HPLC grade solvents were used.

2.2 Characterization techniques

The ^{1}H and ^{13}C NMR spectra of the samples were recorded in $CDCl_3$ on Bruker Ultrashield TM 400 spectrometer using TMS as internal standard. The infrared spectra were recorded on Fourier Transform Infrared (FT-IR) spectrophotometer (prestige- 21) in the range 4000-400 cm^{-1}, in KBr medium. C, H, N elemental analyses were done with a Carlo Erba Model EA1108 analyzer. The melting points of the synthesized compounds were determined in an open glass capillaries using Bibby Sterilin LTD, ST150SA, UK melting point apparatus. Electronic spectral measurements were done using UV/Vis-SP65 SYANO spectrophotometer in 200-800 nm range. Magnetic susceptibility measurements were done using MSB-AUTO, (Sherwood Scientific) magnetic balance. The molar conductivity measurements were carried out using Jenway digital conductivity meter (UK). Antimicrobial evaluation was performed for both the ligands and complexes.

2.3 Synthesis of ligands and complexes

2.3.1 Synthesis of 2-imino-3-(2-hydroxyphenyl)-1- thiazolidin-4-one ligand (L)

The two ligands, 2-imino-3-(2-hydroxyphenyl)-1-thiazolidin-4one (L) and 2-imino-3-(2-hydroxyphenyl) -1-oxazolidin-4-one (L') were synthesized in two steps. The synthesis of the first ligand was carried out as indicated in Scheme 1. To benzene solution of 2-hydroxyaniline (A) (5.45 g, 0.05 mole) in an ice bath was added chloroacetyl chloride (B) (8 mL) slowly with vigorous stirring and a light pink precipitate was formed. The resulting reaction mixture was filtered out, washed with benzene, dried in air and recrystallized from ethanol. Then a mixture of recrystallized 2-hydroxy aryl chloroacetanilide (C) and potassium thiocyanate (1:1

molar ratio) in acetone was refluxed for three hours. The resulting reaction mixture was filtered and the solvent was removed by rotary vapor. The product was washed with excess water and recrystallized from ethanol. Air dried products were collected. Yield: 61 %; ^{1}H NMR (400MHz, DMSO) δ 4.5 (1H), δ 12.7 (1H), δ 6.6-7.9 (4H, m) and δ 4.8 (1H). ^{13}C NMR δ 67 (H_2C), for, δ157.5 (azomethine C), δ (116-129) for aromatic HC, δ 166 (carbonyl C) and δ148 (phenolic group carbon); IR (KBr) ν_{max}/cm^{-1}: 1659(ring C=O), 715d (C-S-C), 1548 (C=N), 3338 and 3410 (N-H), 1329 (C-N-C), 3185 and 3410 (phenolic OH), 1456 and 1597 (benzene C=C), 2983 (benzene C-H) , 750 (ortho-disubstituted); Anal. Calcd for $C_9H_8N_2O_2S$, C, 51.92; H, 5.77; N, 13.46; S, 15.38 %. Found C, 48.66; H, 4.80; N, 12.37; S, 16.10 %.

2.3.2 Synthesis of 2-imino-3-(2-hydroxy phenyl)-1-oxazolidine-4-one (L')

This ligand was synthesized as outlined in Figure 7. A mixture of 2-hydroxy aryl chloroacetanilide and potassium cyanate (1:2 molar ratio) in methanol was refluxed for 2 hrs and the reaction mixture was filtered to remove KCl. Then the solvent was removed by rotary vapor. The resulting product was washed repeatedly with water to ensure complete removal of KCl. The dried product was recrystallized from ethanol. Finally Crystals of product were dried in air. Yield: 69 %; ^{1}H NMR (400MHz, DMSO) δ2.5 (1H), δ4.1(1H), δ(6.7-8.0) (4H, m), δ4.2 (1H). ^{13}C NMR δ34 H2C, δ167 (azomethine C), δ (116-127) for aromatic HC, δ 171 carbonyl C and δ 147.5 (phenolic group carbon); IR (KBr) ν_{max}/cm^{-1}: 1653 (ring C=O), 1106 (C-O-C), 1554 (C=N), 3341 (N-H), 1372 (C-N-C), 3448 (phenolic OH), 1455 and 1600 (benzene C=C), 2983 (benzene C-H), 749 (ortho-disubstituted); Anal. Calcd for $C_9H_8N_2O_3$ C, 51.26; H, 6.25; N, 14.33; S, 0.00 %. Found C, 49.59; H, 5.19; N, 12.72; S, 0.00 %.

2.3.3 Synthesis of Cr (III) complexes

Chromium complexes were prepared using the two synthesized ligands and hydrated chromium metal salts ($CrCl_3.6H_2O$ and Cr $(NO_3)_3.9H_2O$). For the preparation of Cr (III) complexes with the titled ligands the mixture containing equimolar quantities of each metal salts $CrCl_3.6H_2O$ and Cr $(NO_3)_3.9H_2O$ (0.015mol) and each ligands (0.015) in ethanol were refluxed with stirring for about two hours. The reaction mixtures were concentrated on the water bath and cooled to room temperature. The precipitates obtained were filtered out, washed three times with water and ethanol respectively. The resulting products were recrystallized from ethanol and then dried in air.

Chromium complex (Cr1): yield: 59 %; IR (KBr) ν_{max}/cm^{-1}: 1649 (ring C=O), 717d (C-S-C), 1548 (C=N), 3338, 3384 and 3410 (N-H), 1284 (C-N-C), 3186 and 3410 (phenolic OH), 1456 and1595 (benzene C=C), 2978 (benzene C-H) , 749 (ortho-disubstituted), 596 (M-O), 455d (M-N) , 813, 841 and 969 (coordinated water pr, pw, pt)); Anal. Calcd for $[Cr(C_9H_8N_2O_2S)_2Cl(H_2O)]$, C, 41.57; H, 3.08; N, 10.77; S, 12.31; Cr, 10.01 %. Found C, 45.18; H, 4.15; N, 10.31; S, 14.83; Cr, 10.27 %.

Chromium complex (Cr2): yield: 58 %; IR (KBr) ν_{max}/cm^{-1}: 1649 (ring C=O), 705d (C-S-C), 1549 (C=N), 3338 and 3382 (N-H), 1284 (C-N-C), 1457 and1597 (benzene C=C), 2984 (benzene C-H) , 748 (ortho-disubstituted), 597 (M-O), 453d and 541 (M-N),3338, 3382 and 1649 (lattice water) , 831, 901 and 966

(coordinated water pr, pw, pt)); Anal. Calcd for [Cr ($C_9H_8N_2O_2S)_2NO_3(H_2O)$], C, 38.29; H, 3.19; N, 12.41; S, 11.34; Cr, 9.21 %. Found C, 38.80; H, 1.98; N, 11.77; S, 11.70; Cr, 9.54 %.

Chromium complex (Cr3): yield: 55 %; IR (KBr) ν_{max}/cm^{-1}: 1653(ring C=O), 1107(C-O-C), 1553(C=N), 3367(N-H), 1377(C-N-C), 1459 and 1591 (benzene C=C), 749(ortho-disubstituted), 584 (M-O), 477 (M-N); Anal. Calcd for [Cr ($C_9H_8N_2O_{3)3}$]; C, 51.84; H, 3.36; N, 13.44; S, 0.00; Cr, 8.32 %. Found C, 51.90; H, 3.27; N, 7.45; S, 0.00; Cr, 8.26 %.

2.4 Antimicrobial Evaluation

Antimicrobial (antibacterial and antifungal) activities of the ligands and their complexes were investigated *in-vitro* against bacteria and fungi using disc diffusion method. Growth zone of inhibition was measured to determine the antibacterial and antifungal activities of the synthesized ligands and complexes and compared with the commercially available drug *chloramphenicol* (antibacterial) and *bavistin* (antifungal).

2.4.1 Inoculums preparation

The test bacterial strains, *Escherichia coli* (Gram-negative) and *Staphylococcus aurous* (Gram-positive),were transferred from the stock cultures and streaked on Mueller Hinton agar (MHA) plates and incubated for about 24 h. Bacteria were transferred using bacteriological loop to autoclaved MHA that was cooled to about 45^0C in water bath and mixed with gentle swirling the flasks. The medium was then poured to sterile Petri dishes, allowed to solidify and used for the bio-test. For fungi test, mycelia plugs from the stock cultures were transferred to PDA plates and incubated for 6 days. Then spores of the test fungi names were harvested 15 by washing the surface of the colony using 10 ml sterile distilled water and transferred to 50 ml autoclaved PDA cooled to about 35^0C in a water bath. The medium containing spore suspension was poured to sterile plates, allowed to solidify and was used for the paper disc diffusion bioassay.

2.4.2 Antifungal Activity

Paper discs about 3 mm in diameter were cut from Watman-1filter paper with an office paper punch and placed in a beaker covered with aluminium foil and sterilized in an oven at 180^0C for 1 h. Aliquots of 10 µl and 20 µl of the sample solutions of ligands and their complexes were pipetted to the discs. The paper discs impregnated with the sample solutions were then transferred using sterile forceps to PDA seeded with spore suspension of test fungi as described under inoculums preparation above. The petri dishes were incubated at 26^0C for 6 days. All the tests were performed in triplicate. The effectiveness of the samples was evaluated by measuring inhibition zone against the tested organisms.

2.4.3 Antibacterial Activity

Similar procedures were followed for testing antibacterial activities. Paper discs were transferred to Mueller Hinton agar (MHA) plate seeded with bacteria and incubated at 37 ^{0}C for 24h. All the tests were performed in triplicate. Antibacterial activity was evaluated by measuring the zone of inhibition against the tested organisms.

3. Results and Discussion

The reaction of 2-hydroxyaniline and chloroacetyl chloride in an ice bath was afforded 2-hydroxy aryl chloroacetanilide. Subsequently the resulting aryl chloroacetanilide was refluxed with potassium thiocyanate and potassium cyanate to give 2-Imino-3-(2-hydroxyphenyl)-1-oxazolidine-4-one and 2-Imino-3-(2-hydroxy phenyl)-1-thiozolidine-4-one ligands respectively as presented in Figure 6 and 2. The reaction of hydrated chromium metal salts ($CrCl_3.6H_2O$ and $Cr(NO_3)_3.9H_2O$) with these ligands yielded three chromium complexes. All the synthesized ligands and complexes were screened for their antibacterial and antifungals activities.

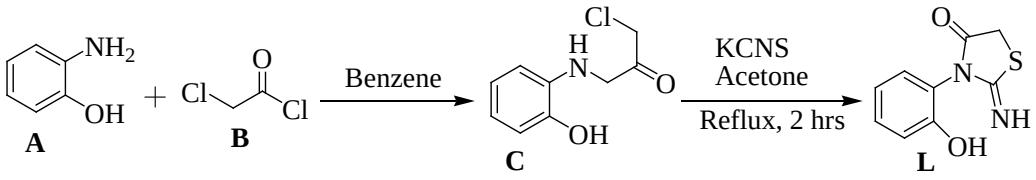

Figure 6: Synthesis of 2-Imino-3-(2-hydroxy phenyl)-1- thiazolidine-4-one

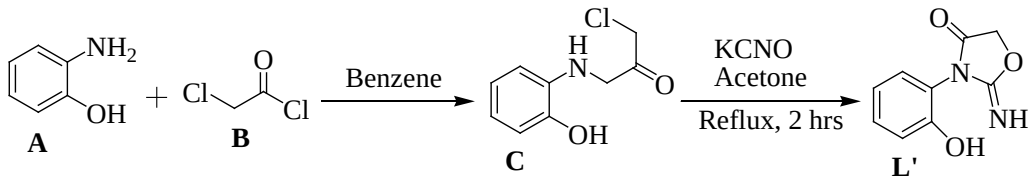

Figure 7: Synthesis of 2-Imino-3-(2-hydroxy phenyl)-1- oxazolidine-4-one

The physical characteristics of all the ligands and complexes are presented in Table 1 and 2. The molecular weights of the synthesized compounds were determined in DMSO solution. The experimental values of the molecular weights of the synthesized compounds are very close to the theoretical values calculated on the basis of bimetallic nature suggesting that all of the complexes are bimetallic complexes. Conductance of all the synthesized chromium complexes in DMSO (10^{-3} M concentration) was measured at room temperature. All the complexes demonstrated molar conductance values ranging from 7.32 to 12.11 $ohm^{-1}cm^2mol^{-1}$ as shown in Table 1, indicating that the non-electrolytic nature of the complexes which is consistent with reported literature [26]. We further performed silver nitrate test to verify the conductometric results of the complexes. No white precipitate was obtained on mixing of each complex with $AgNO_3$ solution in water-ethanol (3:2 v/v). The absence of any ionic chlorine in the complexes is consistent with their non-electrolytic nature of the complexes synthesized. However, the presence of coordinated chlorine in complexes has been tested by decomposing the complexes with concentrated HNO_3 and treating their acidic solutions with aqueous solution of $AgNO_3$. In the case of Cr (III) chloride complexes of thiozolidinone ligands, white precipitate of silver chloride, which is soluble in NH_4OH, was obtained indicating the coordination of chlorine with these metals.

Table 1: Physical properties and analytical data of ligands and their complexes

Compound	MW (found)	Color	Melting Point	MC	Yield (%)
L	208 (204.2)	yellow	120±2	-	61
L'	192 (189.5)	orange	90±1	-	69
Cr1	529.5 (524)	Pale golden	154±1	9.29	59
Cr2	564 (558.3)	Red brown	156±1	12.11	58
Cr3	625 (619.12)	Dark brown	128±1	7.32	55

L: $C_9H_8N_2O_2S$, *thiozolidinone ligand*; L': $C_9H_8N_2O_3$, *oxazolidinone ligand;* Cr1: $[CrL_2Cl(H_2O)]$; Cr2:$[CrL_2NO_3(H_2O)].H_2O$; Cr3: $[CrL'_3]$; MW: *Molecular Weight*; MC: *Molar Conductance*($\Omega^{-1}cm^2\ mol^{-1}$)

The metal contents in the complexes were determined using Atomic Absorption Spectroscopy (AAS). Metal percentage along with analysis data was used to determine metal-ligand ratio in the complexes. For this purpose, 30 mg of each complex was digested completely in concentrated HNO_3 till nearly colourless solution was obtained and analyzed by AAS. The elemental analysis of the ligands and their complexes show that the amount of carbon, hydrogen, nitrogen and sulphur (CHNS) are close to the experimentally determined values as presented in table 2. The experimental percentages of metals in the complexes were calculated using the following equation: $\text{M (\%)} = \frac{\textbf{concentration (ppm) X Volume}}{\textbf{mass of sample taken}} X \frac{100}{1000}$

3.1 Infrared Spectra

FT-IR spectra of complexes were measured to elucidate the binding mode of the ligands with chromium metal ion as compared to the spectra of free ligands (Figure 4 and 5).The characteristic absorption peak at 3410 cm^{-1} in the spectrum of ligand L is due to phenolic *ν* (OH). When the ligand formed complex with chromium metal ion, the peak due to phenolic (OH) was almost disappeared in the resulting complex which indicated the involvement of deprotonated phenolic oxygen in binding with the metal ion. New peak in 527-596 cm^{-1} range appeared corresponding to *ν* (M-O) which confirms coordination of one of the deprotonated phenolic oxygen [36]. After complexation, the band of the ligand at 1548 cm^{-1} due to *ν(*C-N-C) showed substantial decrease, which clearly indicates coordination of pentacyclic ring nitrogen with metal ion. A new band in 455-541 cm^{-1} with doublet structure in complex spectra appeared which further confirms the coordination of pentacyclic ring with nitrogen. Lattice water displays symmetric and asymmetric stretching and bending vibrations at 3338cm-1 and 3382 Cm^{-1} and 1649Cm^{-1} whereas water of coordination peaks appears in 813Cm-1-969Cm^{-1} ranges in the complexes. Doublet peaks in $[CrL_2Cl(H_2O)]$ complex could be due to two closely spaced peaks of ν(Cr-N) and ν (M-Cl). For the complex that contains NO_3 (Figure 2), an additional band at 541Cm^{-1} appeared which might be assigned to ν (Cr-NO_3).

Table 2: Atomic Absorption and Elemental Analysis Data

Cpd	Conc	Abs	Analysis(%), Calcd (found)				Metal (%) Calcd (found)
			C	**H**	**N**	**S**	
L	-	120±2	51.92 (48.66)	5.77 (4.80)	13.46 (12.37)	15.38 (16.10)	-
L'	-	90±1	51.26 (49.59)	6.25 (5.19)	14.33 (12.72)	0.00	-
Cr1	12.09	0.0164	41.57 (45.18)	3.08 (4.15)	10.77 (10.31)	12.31 (14.83)	10.01 (10.27)
Cr2	11.45	0.0157	38.29 (38.80)	3.19 (1.98)	12.41 (11.77)	11.34 (11.70)	9.21 (9.54)
Cr3	10.18	0.0143	51.84 (51.9)	3.36 (3.27)	13.44 (7.45)	0.00	8.32 (8.26)

Similarly the peak at 3448 Cm^{-1} in ligand L' spectrum is attributed to phenolic *v* (OH). This peak has been disappeared in complex spectrum as indicated in figure 2. The absence of *v* (OH) band in the complex spectrum and appearance of new band in 584-585 cm^{-1} range is attributed to *v* (M-O) which indicates the coordination of the deprotonated phenolic group [36]. The band lowering in free ligand L' at 1554cm^{-1} corresponding to pentacyclic ring *v* (C-N-C) on complexation clearly indicates the coordination of the ring nitrogen with metal ion; a new band in 446-447 cm^{-1} with doublet structure in complex spectrum supports the coordination of the ring nitrogen (C-N-C) group of the ligand L'.

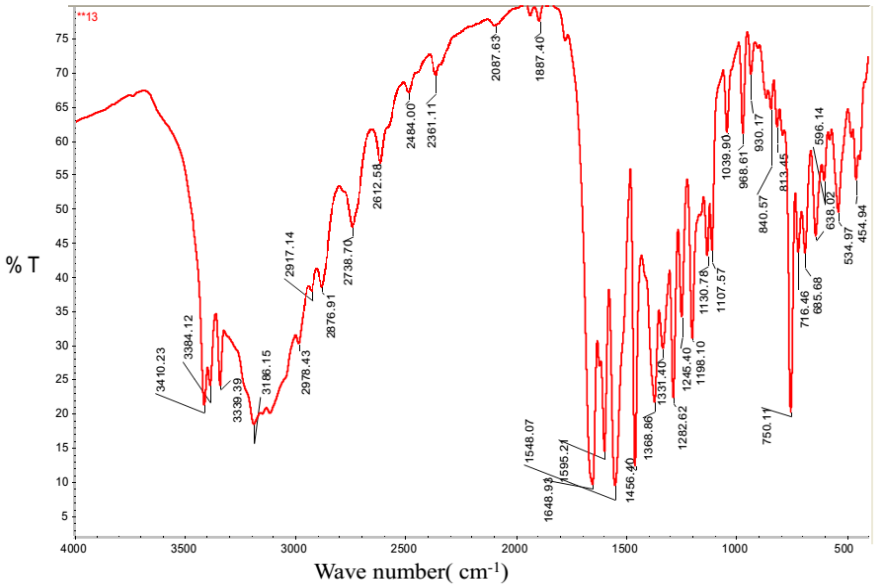

Figure 1: FTIR Spectrum of $[Cr(C_9H_8N_2O_2S)_2Cl(H_2O)]$.

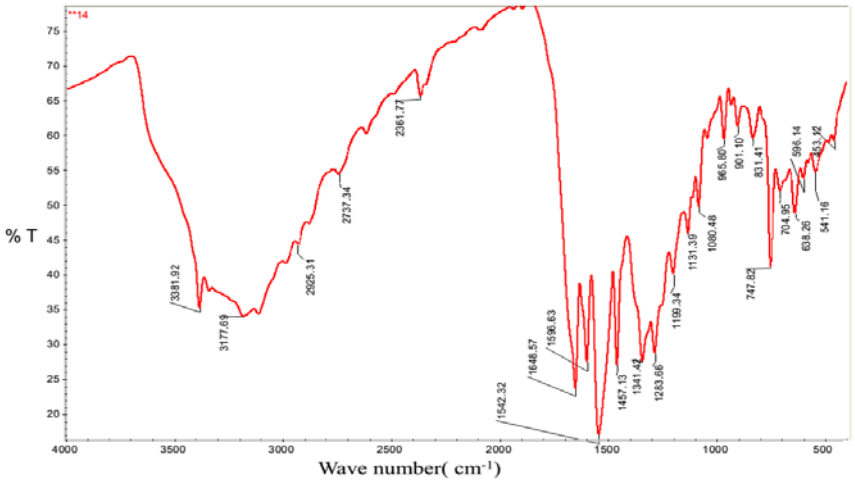

Figure 2: FTIR Spectrum of $[Cr(C_9H_8N_2O_2S)_2NO_3(H_2O)]$

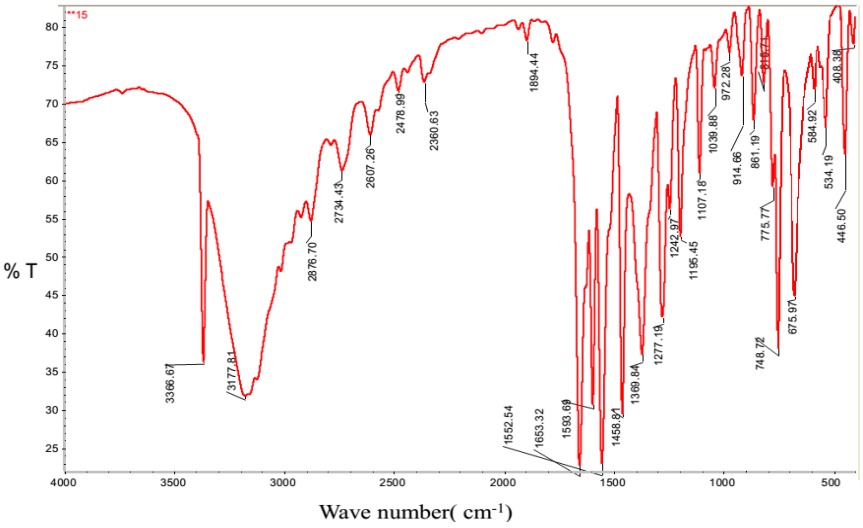

Figure 3: FTIR Spectrum of $[Cr\ (C_9H_8N_2O_3)_3]$

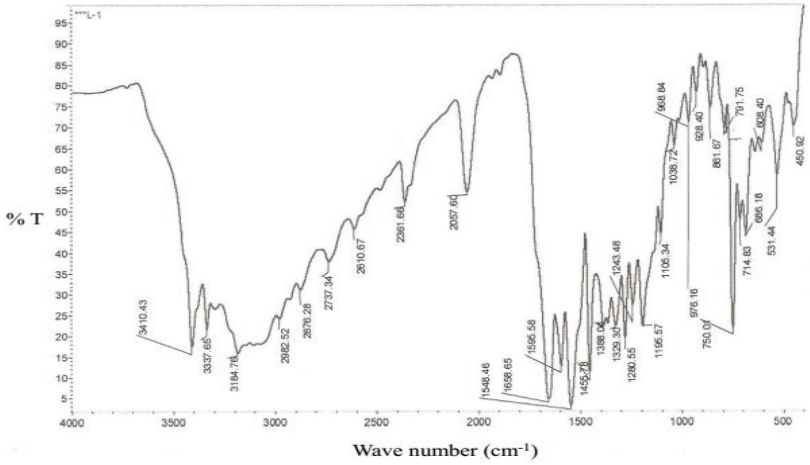

Figure 4: FTIR Spectrum of $C_9H_8N_2O_2S$, thiozolidinone ligand (L)

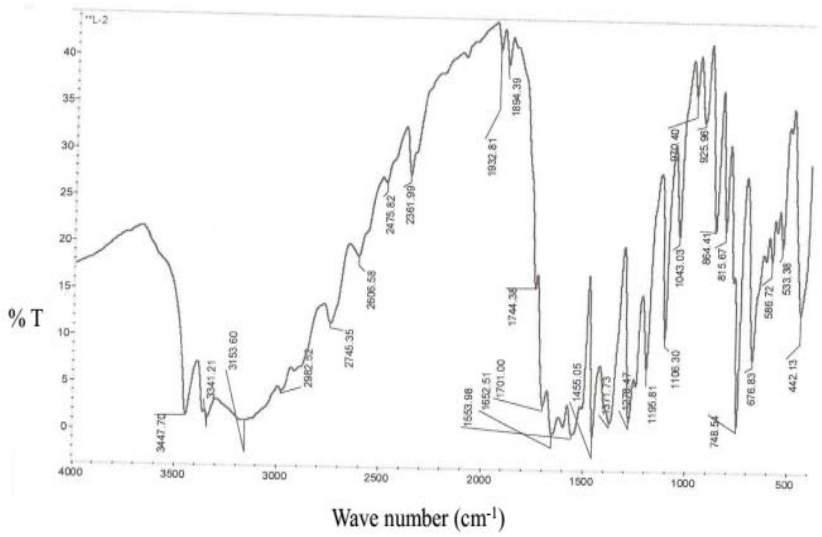

Figure 5: FTIR Spectrum of $C_9H_8N_2O_3$, oxazolidinone ligand (L')

3.2 The Electronic (UV-Vis) Spectra and Magnetic Measurements

Absorption spectra of chromium (III) complexes (Table 3) displayed three /four bands. The first two bands that appeared in 20325- 22727 cm^{-1} and 21739- 25125 cm^{-1} ranges are due to spin allowed $^4A_{2g} \rightarrow {}^4T_{2g}(F)$ ($\nu 1$) , $^4A_{2g} \rightarrow {}^4T_{1g}(F)$ ($\nu 2$) transition respectively, whereas the third band in 28902- 33783 cm^{-1} region corresponds to spin forbidden transition $^2A_g \rightarrow {}^4T_g(P)$ of d^3 octahedral geometry of Cr(III) complexes. A very high energy band in 42735-43103 cm^{-1} range, however, is due to ligand to metal charge transfer. The ligand field parameters were calculated for the complexes as indicated in Table 4. The values of B for the complexes are in the range of 813–909 cm^{-1}, which is low as compared to the free ion value suggesting an interaction between the ligands and chromium (III) ion (presence of covalent character in the complexes). The covalency factor β for the complexes are ranging from 0.792–0.890, which is less than unity indicating the presence of significant amount of covalent bond character between the organic ligands and chromium (III) ion in the complexes. The magnetic moments of the complexes were also measured at room temperature as indicated in Table 4. Magnetic moments of all the complexes were found to be in the range 1.66–1.81. Though they are lower than the lower limit for usual octahedral complexes, they are within the range of reported values for octahedral complexes. The lowering in magnetic moments could be accounted for their binuclear structures involving anti-ferromagnetic interactions [37].

3.4 Antibacterial and Antifungal Activities of Ligands and Complexes

The synthesized ligands and complexes were tested in-vitro against gram-positive, gram-negative bacteria and fungi using paper disc diffusion method. The results obtained from antimicrobial bioassay were expressed in terms of zone of inhibition which was measured in mm as indicated in Table 5. For comparison commercial drugs, chloroamphenicol and Bravistin, were used as reference against bacteria and fungi respectively. Antibacterial activities of ligands (thiozolidinone and oxazolidinone) and their complexes with Chromium (III) were analyzed against gram-positive (*Staphylococcus Aureus)* and gram-negative bacteria *(Escherichia coli).*

Both ligands have shown moderate antibacterial activities as indicated in Table 5 i.e. they inhibited the growth of bacteria to some extent. However the Chromium (III) complexes of oxazolidinone and thiozolidinone demonstrated moderate dose dependent antimicrobial activities against *S.aureus and E.coli* bactria.

Table 3: Electronic spectra and magnetic moment data of the complexes

Cd	Absorption Region (cm^{-1})	Band assignments	Magnetic moments μeff (BM)	Geometry
Cr1	22727	$^4A_{2g}\rightarrow{}^4T_{2g}(F)$	1.68	Octahedral
	24752	$^4A_{2g}\rightarrow{}^4T1g(F)$		
	28902	$^2Ag\rightarrow{}^4Tg(P)$		
	42735	LMCT		
Cr2	22727	$^4A_{2g}\rightarrow{}^4T1g(F)$	1.66	Octahedral
	25125	$^4A_{2g}\rightarrow{}^4T1g(F)$		
	33112	$^2Ag\rightarrow{}^4Tg(P)$		
Cr3	20325	$^4A_{2g}\rightarrow{}^4T_{2g}(F)$	1.81	Octahedral
	21739	$^4A_{2g}\rightarrow{}^4T1g(F)$		
	33783	$^2Ag\rightarrow{}^4Tg(P)$		
	43103	LMCT		

L =$C_9H_8N_2O_2S$; L'=$C_9H_8N_2O_3$ LMCT = Ligand to Metal Charge Transfer

Table 4: Parameters of electronic spectra for chromium complexes

Complexes	Ligands field parameters			
	B	**C**	**10Dq**	**β**
$[CrL_2Cl(H_2O)]$	909	3636	22727	0.890
$[CrL_2NO_3(H_2O)].H_2O$	909	3636	22729	0.885
$[CrL'_3]$	813	3252	20325	0.792

Table 5: Antibacterial activities of synthesized Ligands and their Chromium Complexes

Bacterial stain	Conc. μL	Zone of Inhibition (mm)						
		L	L’	Cr1	Cr2	Cr3	DMSO (Control)	Cpl
E.Coli	10	10	9	15	17	10	-	21
	20	15	21	22	20	16	-	29
S. Aureus	10	13	7	19	21	9	-	23
	20	20	15	21	24	11	-	34

L: *$C_9H_8N_2O_2S$, thiozolidinone ligand*; L’: *$C_9H_8N_2O_3$, oxazolidinone ligand;* Cr1: *$[CrL_2Cl(H_2O)]$;* Cr2*:$[CrL_2NO_3(H_2O)].H_2O$* ; Cr3: *$[CrL'_3]$* ; Cpl: *Chloraphenicol* ; E. Coli: *Escherichia Coli*; S. Aureus: *Staphylococcus Aureus*; Chloramphenicol *is used as Standard for bacteria*

The antifungal activities of all the ligand and chromium metal complexes were evaluated against two fungal cultures *Aspergillus niger* and *C. Gloeosporioides*. As indicated in Table 6 both species of fungi *Aspergillus niger* and *C. Gloeosporioides* are not susceptible to thiozalidinone ligand ($C_9H_8N_2O_2S$) and its chromium complexes ($[CrL_2Cl(H_2O)]$, $[CrL_2NO_3(H_2O)].H_2O$). They did not show any zone of inhibition indicating that they have no any pharmacological potential to control growth of these fungi. But chromium complex of oxazolidinone and the ligand itself demonstrated good antifungal activities against *Aspergillus niger* and *C. Gloeosporioides*. They inhibited they growth of the two fungi. The Chromium (III) complex with oxazolidinone showed a much better activity than the free ligand against *fungi* strain. However in comparison to the standard drug Bravistin, the complex showed comparable and moderate growth inhibition zone for *Aspergillus Niger and C. Gloeosporioides* fungi respectively. The chromium complex of oxazolidinone demonstrated almost similar activities against both *Aspergillus niger* and *C. Gloeosporioides* fungi.

Table 6: Antifungal activities of synthesized Ligands and their Chromium Complexes

Fungal stain	Conc. µL	Zone of Inhibition (mm)						
		L	L’	Cr1	Cr2	Cr3	DMSO (Control)	Bravastin
A. Niger	10	-	4	-	-	15	-	19
	20	-	5	-	-	18	-	24
C.Gloeospori	10	-	3	-	-	16	-	33
oides	20	-	5	-	-	21	-	35

L: $C_9H_8N_2O_2S$, *thiozolidinone ligand*; L’: $C_9H_8N_2O_3$, *oxazolidinone ligand;* Cr1: $[CrL_2Cl(H_2O)]$; Cr2:$[CrL_2NO_3(H_2O)].H_2O$; Cr3: $[CrL'_3]$; A. Niger: *Aspergillus niger*; C. gloeosporioides: *Colletotrichum gloeosporioides*; *Bavistin is used as Standard fungicide*

All synthesized chromium metal complexes have shown more inhibitory activity against bacteria, and fungi as compared to the individual ligands which is consistent with several literatures reported earlier, demonstrating the increase of antifungal and antibacterial activity when of ligands form complexes with metals [38, 39] the activity increase might be accounted to chelation concepts. It is noted that cell permeability of lipid membrane that favors the passage of only lipid soluble materials (lipophilicity) has an important impact to control antimicrobial activity. On chelation the ionic character of the metal decreases and the covalency of the bond between the metal and the ligand increases i. e. there is partial sharing of the positive charge of the metal ion with ligands (donor groups). And there would be delocalization of π-electrons over the whole chelate ring and enhances the lipophilicity of the complex. This increased lipophilicities of complexes allow easy penetration into lipid membranes of organisms and blocks enzymes not to function properly [40].

4. Conclusion

In summary, thiozolidinone- and oxazolidinone-based ligands and their chromium metal complexes were synthesized. The structures of the ligands and complexes were elucidated using spectroscopic techniques (UV-visible, NMR, FT-IR and AAS), molecular weight, molar conductance and magnetic susceptibility measurements. Both the ligands and their complexes were tested for their antifungal and antibacterial activities. FT-IR spectral studies revealed the coordination of heterocyclic nitrogen and deprotonated phenolic oxygen atoms of both ligands to the metal ion. Electronic spectral and magnetic data indicated antiferromagnetic interactions in all the octahedral complexes due to their binuclear structures. Antimicrobial studies have showed that oxazolidinone complexes are effective against both tested bacteria and fungi though their effects are dose dependent. The ligands exhibited lower antifungal and bacterial activities than their corresponding complexes. The complexes in this study were prepared using direct synthesis method, further investigation are recommended using template method of synthesis with other transition metal ions. The Ligands and complexes synthesized should be further exploited for their antimicrobial activities against other pathogens.

Acknowledgment

The authors would like to acknowledge Debre Berhan University and Haramaya University for their financial and material support.

Conflict of Interest

The authors declare that there is no conflict of interest.

References

[1] Z. Golkar, O. Bagazra, D.G. Pace. Bacteriophage therapy: a potential solution for the antibiotic resistance crisis. The Journal of Infection in Developing Countries, 8, 2, 129–136, 2014.

[2] I. M. Gould, A. M. Bal. New antibiotic agents in the pipeline and how they can overcome microbial resistance. Virulence, 4, 2, 185–191, 2013.

[3] G. D. Wright. Something new: revisiting natural products in antibiotic drug discovery. Canadian Journal of Microbiology, 60, 3, 147–154, 2014.

[4] S. Sengupta, M. K. Chattopadhyay, H.P. Grossart. The multifaceted roles of antibiotics and antibiotic resistance in nature. Frontiers in Microbiology, 4, 47, 1-13, 2013.

[5] Centers for Disease Control and Prevention, Office of Infectious Disease Antibiotic resistance threats in the United States, 2013. Apr, 2013. Available at: http://www.cdc.gov/drugresistance/threat-report-2013. Accessed January 11, 2017.

[6] T.D. Tran, T.T.N. Nguyen, T.H. Do, T.N.P. Huynh, C.D. Tran, K. M. Thai. Synthesis and Antibacterial Activity of Some Heterocyclic Chalcone Analogues Alone and in Combination with Antibiotics. Molecules, 17, 6685-6696, 2012.

[7] A. A. Bekhit, O. A. El-Sayed, E. Aboulmagd, J. Y. Park, European Journal of Medicinal Chemistry, 39, 249-255, 2004.

[8] S. L. Badshah, A. Naeem. Bioactive Thiazine and Benzothiazine Derivatives: Green Synthesis Methods and Their Medicinal Importance. Molecules, 21, 1054-1074, 2016.

[9] N. J. Gaikwad, R. N. Tripude. Substituted 4-thiazolidinones as anticonvulsants. Indian Drugs, 31, 593-594, 1994.

[10] M. Cacic, M. Trkovnik, F. Cacic, E. Has-Schon. Synthesis and Antimicrobial Activity of Some Derivatives of (7-Hydroxy-2-oxo-2H-chromen-4-yl)-acetic Acid Hydrazine. Molecules 11, 134-147, 2006.

[11] Amin, K.M., D.E.A. Rahman, Y.A. Al-Eryani. Synthesis and preliminary evaluation of some substituted coumarins as anticonvulsant agents. Bioorganic & Medicinal Chemistry, 16, 5377-5388, 2008.

[12] O. M. Abd El hafez, E. E D. A. Mohamed El Khrisy, F. Badria, A. E. D. Mohamed Fathy. Synthesis and biological investigations of new thiazolidinone and oxadiazoline coumarin derivatives. Archives of Pharmacal Research, 26, 686-696, 2003.

[13] D. L. Maples, R. D. Maples, W. A. Hoffert, T. H. Parsell, A. van Asselt, J. D. Silversides, S. J. Archibald, T. J. Hubin. Synthesis and characterization of the chromium (III) complexes of ethylene cross-bridged cyclam and cycling ligands. Inorganica Chimica Acta 362, 2084–2088, 2009.

[14] R. K. Rawal, R. Tripathi, S.B. Katti, C. Pannecouque, E. De Clercq. Synthesis and evaluation of 2-(2,6-dihalophenyl)-3-pyrimidinyl-1,3-thiazolidin-4-one analogues as anti-HIV agents. Bioorganic & Medicinal Chemistry, 15, 3134–3142, 2007.

[15] K. Omar, A. Geronikaki, P. Zoumpoulakis, C. Camoutsis, M. Soković, A. Ćirić, J. Glamočlija. Novel 4-thiazolidinone derivatives as potential antifungal and antibacterial drugs. Bioorganic & Medicinal Chemistry, 18, 426–432, 2010.

[16] P. Vicini, A. Geronikaki, K. Anastasia, M. Incerti, F. Zani. Synthesis and antimicrobial activity of novel 2-thiazolylimino-5-arylidene-4-thiazolidinones. Bioorganic & Medicinal Chemistry, 14, 3859 - 3864, 2006.

[17] M. G. Vigorita, R. Ottanà, F. Monforte, R. Maccari, M. T. Monforte, A. Trovato, M. F. Taviano, N. Miceli, G. De Luca, S. Alcaro, F. Ortuso. Chiral 3, 3'-(1, 2- ethanediyl)-bis[2-(3,4 dimethoxyphenyl)-4-thiazolidin-ones] with anti-inflammatory activity. Part 11: evaluation of COX-2 selectivity and modeling. Bioorganic & Medicinal Chemistry, 11, 999–1006, 2003.

[18] D. S. Donawade, A.V. Raghu, G. S. Gadaginamath**.** Synthesis and antimicrobial activity of novel linearly fused 5-substituted-7-acetyl-2, 6-dimethyloxazolo-indoles. Indian Journal of Chemistry, 46B, 4, 690-693, 2007.

[19] L. Zhang, X. M. Peng, G. L. Damu, R. X. Geng, C. H. Zhou. Comprehensive review in current developments of imidazole-based medicinal chemistry. Medicinal Research Reviews, 34, 340-437, 2014.

[20] S. F. Cui, Y. Wang, L.V. JingSong, L.V. Damu Guri, C. H. Zhou. Recent advances in application researches of thiazole compounds. Scientia Sinica Chimica. 42, 1105-1131, 2012.

[21] F. F. Zhang, L. L. Gan, C. H. Zhou. Synthesis, antibacterial and antifungal activities of some carbazole derivatives. Bioorganic & Medicinal Chemistry Letters, 20, 1881-1884, 2010.

[22] H. Z. Zhang, C. H. Zhou, R. X. Geng, J. I. Qing-Gang. Recent advances in syntheses of oxazole

compounds. Chinese Journal of Chemistry, 31, 1963-1976, 2011.

[23] S. L. Zhang, L.V. Damu Guri, L. Zhang, R. X. Geng, C. H. Zhou. Synthesis and biological evaluation of novel benzimidazole derivatives and their binding behavior with bovine serum albumin. European Journal of Medicinal Chemistry, 55, 164-175, 2012.

[24] C. Sulekh, T. Monika, A. Swati. Synthesis and characterization of a tetraaza macrocyclic ligand and its cobalt (II), nickel (II) and copper (II) complexes. Journal of the Serbian Chemical Society, 75, 7, 935–941, 2010.

[25] F. A. Abdlseed, M. M. El-Ajaily. Preparation and Spectroscopic Investigation of a Schiff's base Metal Complexes. International Journal of PharmTech Research, 1, 4, 1097-1103, 2009.

[26] A. A. Khandar, S. A. Hosseini-Yazdi, M. Khatamian, P. McArdle, S. A. Zarei. Synthesis, characterization and structure of nickel (II) complexes of a 16-memberd mixed –donor macrocyclic Schiff base ligand, potentially hexadentate, bearing two pendant alcohol functions. Polyhedron, 26, 33-38, 2007.

[27] A. Prakish, B. K. Singh, N. Bhojak, D. Adhikari. Synthesis and Characterization of Bioactive Zn (II) and Cd (II) Complexes with New Schiff Bases Derived from 4-Nitro benzaldehyde and Acetophenone with Ethylenediamine. Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy, 76, 356-362, 2010.

[28] C. Spinu, M. Pleniceanu, C. Tigae. Biologically Active Transition Metal Chelates with a 2-Thiophenecarboxaldehyde-Derived Schiff Base: Synthesis, Characterization, and Antibacterial Properties. Turkish Journal of Chemistry, 32, 487-493, 2008.

[29] A. Chaudhary, A. Phor, R. V. Singh. Potentially biodynamictetraaza macro cycles and their manganese complexes: antiandrogen, antimicrobial and PDI studies. Bioinorganic Chemistry and Applications, 3, 33, 161–177, 2005.

[30] S. Subhasish, D. Dharumadurai, C. Saravanan, T. Noorudin, P. Annamalai. Synthesis, Characterization and Antimicrobial Activity of Cobalt Metal Complex against Drug Resistant Bacterial and Fungal Pathogens. Advances in Biological Research, 4, 4, 224-229, 2010.

[31] R. Kesharwani, P. Singh, Synthesis and Biological Activity of Divalent Metal Chelates of Metronidazole. Asian Journal of Chemistry, 12, 23-26, 2000.

[32] H. Kumar, R. P. Chaudhary. Biological studies of a novel azo based Heterocyclic Schiff base and its transition metal complexes. Der Chemica Sinica, 1, 2, 55-61, 2010.

[33] J. C. Byun, Y. C. Park, J. S. Youn, H. H. Chung, H. L. Nam. Cr (III)-Tetraaza Macro cyclic Complexes Containing Auxiliary Ligands (Part II); Synthesis and Characterization of Cr (III)-Citrato Macro cyclic Complex. Bulletin of the Korean Chemical Society, 26, 4, 243-423, 2005.

[34] C. M. Davis, J. B. Vincent. Elucidating a Biological Role for Chromium at a Molecular Level. Journal of Biological Inorganic Chemistry, 33, 503-510, 2000.

[35] R. Kumar, R. Singh. Chromium (III) Complexes with Different Chromospheres Macrocyclic Ligands: Synthesis and Spectroscopic Studies. Turkish Journal of Chemistry, 30, 77-87, 2006.

[36] A. Reiss, S. Florea, T. Caproiu, N. Stanic. Synthesis, characterization, and antibacterial activity of some transition metals with the Schiff base N-(2-furanylmethylene)-3 aminodibenzofuran. Turkish Journal of Chemistry, 33, 775 – 783, 2009.

[37] J. Lewis, F. E. Mabbs, H. Weigold. The magnetic properties of some manganese (II) Schiff-base complexes and the oxidation products of N, N′-ethylenebis(salicylaldiminato)manganese(II). Journal of Chemical Society A, 1699-1703, 1968

[38] S. Chandra, D. Jain, A. K. Sharma and P. Sharma. Coordination Modes of a Schiff Base Pentadentate Derivative of 4-Aminoantipyrine with Cobalt (II), Nickel (II) and Copper (II) Metal Ions: Synthesis, Spectroscopic and Antimicrobial Studies. Molecules, 14, 1, 174–190, 2009

[39] S. S. Konstantinovic, B. C. Radovanovic, Z. Cakic, V. Vasic. Synthesis and characterization of Co(II), Ni(II), Cu(II) and Zn(II) complexes with 3-salicylidenehydrazono-2-indolinone. Journal of the Serbian Chemical Society, 68, 641-647, 2003.

[40] N. C. Zaneta, L. Xu , Z. Hu , Y. Tomita , P. Li , P. P. Roller , R. Wang , X. Fang , R. Guo , M. Zhang , M. E. Lippman , D. Yang, S. Wang. Discovery of Embelin as a Cell-Permeable, Small-Molecular Weight Inhibitor of XIAP through Structure-Based Computational Screening of a Traditional Herbal Medicine Three-Dimensional Structure Database Journal of Medicinal Chemistry, 47, 10, 2430–2440, 2004.