Research Article

Synthesis, Characterization and *In vitro* Antibacterial Evaluation of Oxadiazole Derivatives

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Abstract

This research paper reports on findings of novel oxadiazole derivatives. Such compounds were prepared and their complexation was performed by treating them with metal salts of Mn (II), Co (II) and Ni (II). The synthesized derivatives were characterized by elemental analysis, IR and electronic spectral studies and magnetic moment studies. Their structures were further confirmed by ^{1}H NMR spectra. The magnetic behaviour and spectroscopic investigation of complexes indicates mononuclear octahedral structures for complexes. All the derivatives were screened for antibacterial activity against *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Bacillus subtilis*, *Klebsiella pneumonia* and *Escherichia coli*. They showed noticeable antibacterial activity.

***Key Words*:** Oxadiazole; Metal complex; Antibacterial activity

Introduction

To find new compounds and explore its applications for the welfare of human beings is a very common but a prominent characteristic of chemists. Lots of compounds are exclusively studied for such a purpose and oxadiazole is also one of such compounds. As the name itself indicates, oxadiazoles are five membered ring compounds. Besides, two carbon atoms, one oxygen and two nitrogen atoms are ring making atoms in these compounds. These compounds have captured notice due to their diverse pharmacological activities. Various research papers have reported their insecticidal (Zheng et al., 2003), anticonvulsant (Zarghi et al., 2005), fungicidal (Yang et al., 2001), antitubeculosis (Oruc et al., 2004), antimicrobial (Maslat et al., 2002) and anti-inflammatory -analgesic (Mymoona et al., 2009) activities. Mesomorphic properties of metallomesogens derivatives of oxadiazoles were reported (Parra et al., 2003). Transition metal complexes of oxadiazoles were also studied (Ibraheem et al., 2010). Antibacterial activities of some metal chelates of oxadiazole derivatives were reported (Ibrahim et al., 2010; Alsafee, 2014). Review of this literature indicates that complex compounds of oxadiazole possess diverse properties.

Materials and Methods

Experimental

All the chemicals used were of AR (Analytical Reagent) grade and used as such without further purification.

General method for synthesis of compounds (1-a to 1-c)

General method for the synthesis of compounds 5-substituted-3-{[(8-hydroxyquinolin-5-yl) amino] methyl}-1, 3, 4-oxadiazole-2 (3*H*)-thione (1) is shown in Figure 1.

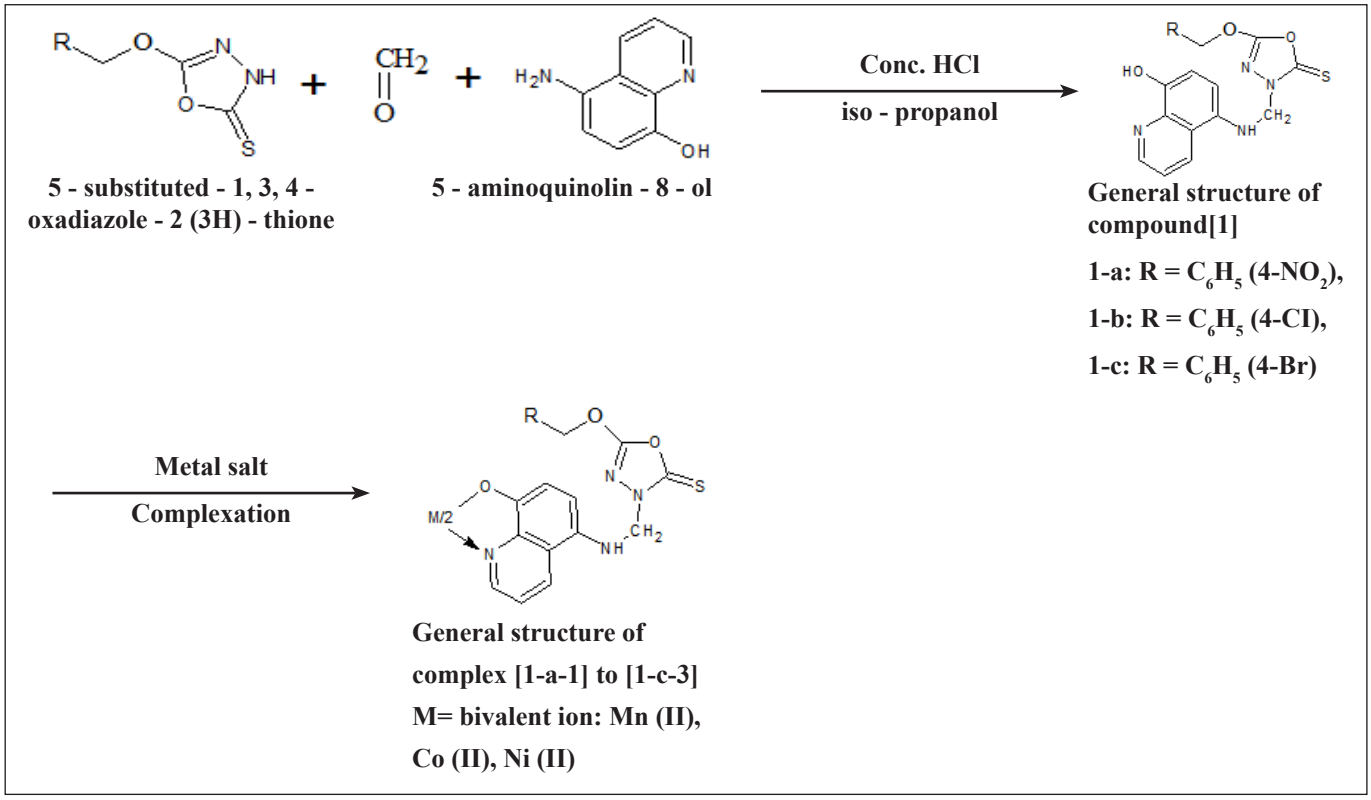

Figure 1 General method of preparation for compounds and complexes.

5- Substituted 1, 3, 4-oxadiazole-2 (3*H*)-thione (0.01 mole), 5-amino-8-quinolinol (0.01 mole) and methanal (0.03 mole) were added to iso-propanol (50 ml). Concentrated hydrochloric acid (2-3 ml) was also added to the reaction mixture. It was heated on the steam bath up to 10-11 h. The purity of compounds was checked by Thin Layer Chromatography (TLC) using silica Gel-G in the solvent system of n-hexane and ethyl acetate (v/v = 1:3). The spots were observed by exposure to iodine vapour or UV light. Iso-propanol was distilled out. Water was added to extract the product into the aqueous layer. The aqueous layer was made alkaline by addition of 10% aqueous solution of sodium hydroxide (NaOH). Methylene dichloride (60 ml) was added to the resultant mixture. Organic layer which was separated, dried over anhydrous sodium sulphate (Na_2SO_4) and distilled out atmospherically. In this way, the product 5-substituted-3-{[(8-hydroxyquinolin-5-yl) amino] methyl}-1, 3, 4-oxadiazole-2 (3*H*) -thione (1) was synthesized.

Following the above procedure, three oxadiazole compounds: **1-a**: 3-{[(8-hydroxyquinolin-5-yl) amino] methyl}-5-[(4-nitrobenzyl) oxy]-1, 3, 4-oxadiazole-2 (3*H*)-thione, **1-b**: 5-[(4-chlorobenzyl) oxy]-3-{[(8-hydroxyquinolin-5-yl) amino]methyl}-1, 3, 4-oxadiazole-2 (3*H*)-thione, and **1-c**: 5-[(4-bromobenzyl) oxy]-3-{[(8-hydroxyquinolin-5-yl) amino] methyl}-1, 3, 4-oxadiazole-2 (3*H*)-thione were prepared. The melting points of all these compounds were taken in open capillary glass tubes and are uncorrected. The % of yield and melting points of such compounds are as below:

1-a: % of yield: 59, Melting Point: 194 °C [M. F.: $C_{19}H_{15}N_5O_5S$]

1-b: % of yield: 75, Melting Point: 178 °C [M. F.: $C_{19}H_{15}ClN_4O_3S$]

1-c: % of yield: 83, Melting Point: 167 °C [M. F.: $C_{19}H_{15}BrN_4O_3S$]

Characterization of compounds (1-a to 1-c)

The elemental analysis was performed using Thermo Finnigan Flash EA 1112 analyzer. It is shown in Table-1. The analyses supports the predicted structure of compounds (1-a to 1-c) (Figure1).

Table 1 Elemental analysis of compounds.

Compound	%C		%H		%N		%S	
	Found	Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.
1-a	53.66	53.64	3.54	3.55	16.46	16.46	7.47	7.54
1-b	55.03	55.01	3.65	3.64	13.55	13.51	7.71	7.73
1-c	49.60	49.68	3.23	3.30	12.18	12.20	6.93	6.98

Calcd.: Calculated.

Spectral properties

IR spectra of compounds were recorded on Jasco FTIR spectrophotometer with KBR discs technique. ^{1}H NMR spectra were recorded on a Joel-GSX 400 at 400MHz instrument using DMSO-d_6 as a solvent. NMR chemical shifts were recorded in δ value and TMS was used as an internal standard. Mass spectra were obtained on a Joel D-300 spectrometer.

The noteworthy spectral properties of compounds were as below:

1-a: IR: 3690 (-OH), 3100, 1615, 1498 (Aromatic), 1638, 1557, 1474 (hydroxyquinoline), 3455 (-NH-), 2872, 2765, 1470 (-CH_2-) cm^{-1}, ^{1}H NMR: δ =11.25 (*s*, -NH-), 6.80-7.95 (m, quinoline), 6.10 (*s*,-OH), 3.40 (*s*, -CH_2). Mass (m/z): M^+: 425.20 (Found), 425.08 (Calcd.)

1-b: IR: 3585 (-OH), 3045, 1590, 1492 (Aromatic), 1654, 1520, 1466 (hydroxyquinoline), 3365 (-NH-), 2911, 2856, 1444 (-CH_2-) cm^{-1}, ^{1}H NMR: δ =11.10 (*s*,-NH-), 7.15-8.14 (m, quinoline), 6.03 (*s*, phenolic-OH), 3.28 (*s*,-CH_2-). Mass (m/z): M^+: 458.35 (Found), 458.00 (Calcd.)

1-c: IR: 3710 (-OH), 3070, 1480, 1370 (Aromatic), 1660, 1548, 1461 (hydroxyquinoline), 3405 (-NH-), 2920, 2873, 1450 (-CH_2-) cm^{-1}, ^{1}H NMR: δ =11.05 (*s*,-NH-), 6.90-7.62 (*m*, quinoline), 6.20 (*s*, phenolic-OH), 3.34 (*s*,-CH_2-). Mass (m/z): M^+: 414.24 (Found), 414.06 (Calcd.)

Preparation of complexes (1-a-1 to 1-c-3)

For the synthesis of complexes of compounds (1-a to 1-c), compound (1-a/1-b/1-c) (0.001 mole) was dissolved in 90 ml of methanoic acid and 2-3 ml of distilled water (solution-1).

Preparation of Mn (II) complex

A solution of Manganese chloride hexahydrate (0.0005 mole) was prepared in 100 ml distilled water and solution-1 was slowly added into it. The pH of the solution was kept 5.6-5.7. The resultant product separated as a solid mass was digested on a water bath at 70 °C for 2-3 h. The product was filtered, washed with water-ethanol mixture (v/v=1:1) and dried.

Preparation of Co (II) complex

A solution of Cobalt nitrate hexahydrate (0.0005 mole) was prepared in 100 ml distilled water and solution-1 was slowly added into it. The pH of the solution was kept 6.1-6.2. The resultant product obtained as a solid mass was digested on a water bath at 70 °C for 2-3 h. The product was filtered, washed with water-ethanol mixture (v/v=1:1) and dried.

Preparation of Ni (II) complex

A solution of Nickel nitrate hexahydrate (0.0005 mole) was prepared in 100 ml distilled water. Solution-1 was gradually added into it maintaining the pH of the solution 6.0-6.1. The product separated as a solid mass was digested on a water bath at 70 °C for 2-3 h. The product was filtered, washed with water-ethanol mixture (v/v=1:1) and dried.

Characterization of complexes

Table 2 Molecular formula, molecular weight, melting point and yield of metal complexes.

Complex	Molecular formula	Molecular weight	Melting point	Yield %
1-a-1	$C_{38}H_{28}N_{10}O_{10}S_2Mn$ (II)·$2H_2O$	939.39	251	78
1-a-2	$C_{38}H_{28}N_{10}O_{10}S_2Co$ (II)·$2H_2O$	943.78	183	59
1-a-3	$C_{38}H_{28}N_{10}O_{10}S_2Ni$ (II)·$2H_2O$	943.54	202	70
1-b-1	$C_{38}H_{28}Cl_2N_8O_6S_2Mn$ (II)·$2H_2O$	918.68	238	61
1-b-2	$C_{38}H_{28}Cl_2N_8O_6S_2Co$ (II)·$2H_2O$	922.68	210	80
1-b-3	$C_{38}H_{28}Cl_2N_8O_6S_2Ni$ (II)·$2H_2O$	922.44	226	84
1-c-1	$C_{38}H_{28}Br_2N_8O_6S_2Mn$ (II)·$2H_2O$	1011.34	193	60
1-c-2	$C_{38}H_{28}Br_2N_8O_6S_2Co$ (II)·$2H_2O$	1011.58	159	57
1-c-3	$C_{38}H_{28}Br_2N_8O_6S_2Ni$ (II)·$2H_2O$	1007.58	168	73

The elemental analysis of all the complexes was performed using Thermo Finnigan Flash EA 1112 analyzer and a Perkin-Elmer 2400 analyzer. The elemental analysis data are given in Table 3. This analysis confirms the proposed structures of the complexes. General structure of complexes is given in Figure 1.

The metal content (Mn (II), Co (II) and Ni (II)) of all the complexes was found by standard methods described in the literature (Vogel, 2004). The study indicates that stoichiometry of metal-ligand (M-L) in the complexes is 1: 2.

The molar conductivity of solution (1×10-3M) of complex in N, N-Dimethylmethanamide (DMF) was determined by Systronics model-305 direct reading conductivity meter. The values of molar conductivities are shown in Table 4.

Table 3 Elemental analysis: % of metal, C, H, N and S elements of complexes

Complex	Elemental analysis									
	% Metal		%C		%H		%N		%S	
	Found	Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.
1-a-1	5.89	5.85	48.94	48.98	3.04	3.00	14.90	14.91	6.64	6.83
1-a-2	6.23	6.24	48.77	48.75	3.05	2.99	14.87	14.84	6.71	6.80
1-a-3	6.30	6.22	48.66	48.76	3.01	2.99	14.91	14.85	6.90	6.98
1-b-1	5.95	5.98	49.97	50.08	3.06	2.99	12.10	12.20	6.99	6.98
1-b-2	6.46	6.39	49.81	49.86	3.05	3.06	12.18	12.20	6.98	6.95
1-b-3	6.31	6.36	49.79	49.88	3.03	3.06	12.24	12.15	7.02	6.95
1-c-1	5.40	5.43	45.42	45.49	2.90	2.80	11.11	11.08	6.35	6.34
1-c-2	5.85	5.83	45.43	45.49	2.74	2.79	11.02	11.08	6.30	6.34
1-c-3	5.74	5.83	45.61	45.66	2.19	2.80	11.13	11.12	6.28	6.37

Calcd.: Calculated.

Table 4 Values of magnetic moment and conductivity of complexes.

Complex	χ_g	χ_m	Observed magnetic moment μ_{eff} (BM)	Calculated magnetic moment μ_{eff} (BM)	Molar conductivity (Mhos cm^2 mol^{-1})
1-a-1	14.9	0.0158	5.88	5.92	6.22
1-a-2	7.1	0.0075	3.90	3.87	22.04
1-a-3	3.49	0.0037	2.84	2.83	10.16
1-b-1	15.06	0.0163	5.94	5.92	8.01
1-b-2	7.52	0.0082	3.88	3.87	21.86
1-b-3	3.6	0.0039	2.87	2.83	9.36
1-c-1	15.34	0.0152	5.98	5.92	8.82
1-c-2	6.88	0.0068	3.92	3.87	24.05
1-c-3	3.79	0.0038	2.75	2.83	10.04

Magnetic susceptibility (χ) was determined using a Gouy magnetic balance at room temperature (300 K). Mercury (II) tetrathio cyanatocobaltate (II) was used as a standard and diamagnetic corrections were made with Pascal's constants. The effective magnetic moment was determined by the following equation:

$$\mu_{eff} = 2.84\sqrt{(\chi_M \cdot T)}$$

Here, T is the absolute temperature.

The theoretical value of the magnetic moment was calculated with the following equation:

$$\mu_{eff} = \sqrt{(n(n+2))\ BM}$$

Here, n is a number of unpaired electrons.

The values of magnetic susceptibility and magnetic moment are given in Table 4. The reflectance spectra were recorded on a Beckman DU spectrophotometer using Magnesium oxide (MgO) as a reference. The data of characteristic absorption bands is given in Table 5.

The important FTIR spectral features of complexes are as below:

1-a-1: 3600 (-OH), 3355 (-NH), 2951 (-OCH_2), 2856, 1426 (-CH_2-), 1612, 1557, 1492, 1400 (quinoline) cm^{-1}

1-a-2: 3615 (-OH), 3340 (-NH), 2934 (-OCH_2), 2866, 1418 (-CH_2-), 1600, 1559, 1511, 1397 (quinoline) cm^{-1}

1-a-3: 3632 (-OH), 3369 (-NH), 2940 (-OCH_2), 2860, 1430 (-CH_2-), 1621, 1565, 1505, 1410 (quinoline) cm^{-1}

1-b-1: 3610 (-OH), 3330 (-NH), 2956 (-OCH_2), 2870, 1420 (-CH_2-), 1615, 1568, 1512, 1427 (quinoline) cm^{-1}

1-b-2: 3585 (-OH), 3365 (-NH), 2948 (-OCH_2), 2854, 1430 (-CH_2-), 1605, 1572, 1498, 1400 (quinoline) cm^{-1}

1-b-3: 3540 (-OH), 3333 (-NH), 2940 (-OCH_2), 2862, 1435 (-CH_2-), 1614, 1562, 1490, 1430 (quinoline) cm^{-1}

1-c-1: 3590 (-OH), 3380 (-NH), 2952 (-OCH_2), 2867, 1440 (-CH_2-), 1599, 1559, 1515, 1420 (quinoline) cm^{-1}

1-c-2: 3612 (-OH), 3325 (-NH), 2948 (-OCH_2), 2870, 1437(-CH_2-), 1611, 1550, 1503, 1419 (quinoline) cm^{-1}

1-c-3: 3620 (-OH), 3330 (-NH), 2955 (-OCH_2), 2874, 1428 (-CH_2-), 1612, 1560, 1510, 1424 (quinoline) cm^{-1}

Table 5 Electronic spectral data of complexes

Complex	Absorption band cm^{-1}	Transition
1-a-1	23400	$^6A_{1g} \rightarrow {}^4A_{1g}({}^4E_g)$
	17999	$^6A_{1g} \rightarrow {}^4T_{2g}({}^4G)$
	16346	$^6A_{1g} \rightarrow {}^4T_{1g}({}^4G)$
1-a-2	22900	$^4T_{1g}(F) \rightarrow {}^4T_{2g}(P)$
	19103	$^4T_{1g}(F) \rightarrow {}^4A_{2g}$
	8850	$^4T_{1g}(F) \rightarrow {}^4T_{2g}(F)$
1-a-3	22610	$^3A_{2g} \rightarrow {}^3T_{1g}(P)$
	12990	$^3A_{2g} \rightarrow {}^3T_{1g}(F)$
1-b-1	24011	$^6A_{1g} \rightarrow {}^4A_{1g}({}^4E_g)$
	18480	$^6A_{1g} \rightarrow {}^4T_{2g}({}^4G)$
	15970	$^6A_{1g} \rightarrow {}^4T_{1g}({}^4G)$
1-b-2	23940	$^4T_{1g}(F) \rightarrow {}^4T_{2g}(P)$
	18137	$^4T_{1g}(F) \rightarrow {}^4A_{2g}$
	8706	$^4T_{1g}(F) \rightarrow {}^4T_{2g}(F)$
1-b-3	22201	$^3A_{2g} \rightarrow {}^3T_{1g}(P)$
	15814	$^3A_2g \rightarrow {}^3T_{1g}(F)$
1-c-1	24021	$^6A_{1g} \rightarrow {}^4A_{1g}({}^4E_g)$
	18008	$^6A_{1g} \rightarrow {}^4T_{2g}({}^4G)$
	15427	$^6A_{1g} \rightarrow {}^4T_{1g}({}^4G)$
1-c-2	24087	$^4T_{1g}(F) \rightarrow {}^4T_{2g}(P)$
	19815	$^4T_{1g}(F) \rightarrow {}^4A_{2g}$
	8594	$^4T_{1g}(F) \rightarrow {}^4T_{2g}(F)$
1-c-3	21969	$^3A_{2g} \rightarrow {}^3T_{1g}(P)$
	14016	$^3A_{2g} \rightarrow {}^3T_{1g}(F)$

***In vitro* antibacterial activity**

Oxadiazole derivatives were screened for their antimicrobial activity using cup plate method against *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Bacillus subtilis*, *Klebsiella pneumonia* and *Escherichia coli* using DMF as a solvent (Barry, 1986; Xia et al., 2001; Jones et al., 1984). Nutrient agar was used as a culture medium. The Nutrient agar was prepared by dissolving Agar (20 g), Peptone (10 g), Beef extract (0.5 g) and Sodium chloride (0.5 g) in distilled water (1000 ml) and pH adjusted to 6.8, autoclaved at 151/inch^2 pressure for 20 min. The solution of Chloramphenicol (100 µg/ml) was prepared in DMF and used as a standard drug. DMF was used as a solvent control. The *in vitro* antibacterial activity was carried out against 24 h old cultures of bacteria. The concentration of complexes tested was 100 µg/ml. Laminar airflow bench was swapped with 70 % alcohol and a UV lamp was switched on. After 30 min, the UV lamp was switched off. All the reagents media, inoculums and glassware were placed in laminar airflow bench to maintain aseptic condition. After the inoculums had dried, cups of diameter 6 mm were made in the agar plate with a sterile cork borer. The test solutions were added to these cups with a micropipette and the plates were then incubated at 37 °C for 24 h. The diameter of the inhibition after 24 h was measured as the zone of inhibition in millimeters. The results were corrected for DMF. The results of antibacterial studies are shown in Table 6 and Table 7.

Table 6 Antibacterial activity of compounds.

Compound	Zone of inhibition (mm)				
	Pseudomonas aeruginosa	*Staphylococcus aureus*	*Bacillus subtilis*	*Klebsiella pneumoniae*	*Escherichia coli*
Chloramphenicol	19	21	19	17	26
1-a	16	15	13	6	13
1-b	13	14	13	5	09
1-c	09	10	08	8	15

Table 7 Antibacterial activity of complexes.

Complex	Zone of inhibition (mm)				
	Pseudomonas aeruginosa	*Staphylococcus aureus*	*Bacillus subtilis*	*Klebsiella pneumoniae*	*Escherichia coli*
1-a-1	11	9	8	10	14
1-a-2	8	12	10	8	7
1-a-3	9	13	13	6	13
1-b-1	12	14	12	9	8
1-b-2	14	11	10	7	9
1-b-3	10	12	9	6	12
1-c-1	9	10	9	9	8
1-c-2	13	8	8	9	11
1-c-3	15	11	12	8	15

Results and Discussion

The Mn (II), Co (II) and Ni (II) complexes are non-electrolytes as indicated by their molar conductivity values 6.22 to 24.05 Mhos cm^2 mol^{-1}.

The electronic spectra of Mn (II) complexes demonstrate three bands in the every region of 23400-24021, 17999-18480 and 15427-16346 cm^{-1} which can be due to $^6_{A1g} \rightarrow {}^4A_{1g}$ (^4E_g), $^6A_{1g} \rightarrow {}^4T_{2g}$ (^4G) and $^6A_{1g} \rightarrow {}^4T_{1g}$ (^4G) electronic transitions respectively. It indicates octahedral geometry of Mn (II) complexes. These complexes exhibit magnetic moment (μ_{eff}) from 5.88 to 5.98 BM. It is also supporting octahedral geometry of these complexes (Rahmouni et al., 1999).

Co (II) complexes reveal two bands in the every region of 22900-24087, 18137-19815 and 8599-8850 cm^{-1} which can be assigned to $^4T_{1g}$ (F) $\rightarrow$ $^4T_{2g}$ (P), $^4T_{1g}$ (F) $\rightarrow$ $^4A_{2g}$ and $^4T_{1g}$ (F) $\rightarrow$ $^4T_{2g}$ (F) respectively suggesting octahedral structure around Co (II) ion. These complexes exhibit magnetic moment (μ_{eff}) from 3.88-3.92 BM. It indicates octahedral geometry of these complexes.

The electronic spectra of Ni (II) complexes exhibit two bands in the every region of 21699-22610 and 12990-15814 cm^{-1} which can be attributed to $^3A_{2g} \rightarrow {}^3T_{1g}$(P) and $^3A_{2g} \rightarrow {}^3T_{1g}$ (F) transitions respectively for octahedral configuration

around central nickel ion. These complexes exhibit magnetic moment from 2.75 - 2.87 BM. It indicates octahedral geometry of these complexes.

Here, compound 1-a showed highest antibacterial activity against *P. aeruginosa*, *S. aureus* and *B.subtilis*. Compound 1-c showed highest activity against *K. pneumonia* and *E. coli*.

Highest inhibition of bacteria was noted for complex 1-c-3 against *P. aeruginosa*. Complexe 1-b-1 exhibited highest inhibition against *S. aureus*. Complex 1-a-3 showed maximum inhibition for *B. subtilis*. Complexes 1-a-1 showed highest inhibition against *K. pneumoniae* while complex: 1-c-3 was very effective against *E. coli*.

Conclusion

According to the reaction route shown in Figure 1, the compounds (1-a to 1-c) and its complexes (1-a-1 to 1-c-3) were synthesized in satisfactory amount. Spectral studies went well with the expected structures shown in Figure 1. Considering the stoichiometry, electronic and magnetic data obtained, octahedral geometry can be assigned to all the complexes prepared. All the compounds tested show reasonable antibacterial activity against species like *P. aeruginosa*, *S. aureus*, *B. subtilis*, *K. pneumoniae* and *E. coli*. The noticeable antimicrobial activity of the compounds may be resulting from the presence of the oxadiazole ring systems and the metal chelation. Thus, prepared molecules displayed decent antibacterial activity against selected species of bacteria which makes them valuable molecules for these kinds of applications.

References

Alsafee, B. A. H. (2014) Preparation and characterisation of some transition metal complexes of new 4-[(5- ethyl-1, 3, 4-oxadiazol-2-yl) sulfanyl] aniline. *The Swedish Journal of Scientific Research* 1(6): 11-23.

Barry, A. L. (1986) Ed. Lorian, V., *Procedure for testing antimicrobial agent in agar media: theoretical considerations: antibiotics in laboratory medicine,* 2nd ed., Williams & Wilkins, Baltimore.

Ibraheem, H., Adel, H., Ahmed , A., Salih, N., Salimon, J., Graisa, A., Farina, Y. and Yousif, E. (2010) Synthesis, characterization and antimicrobial activity of some metal ions with 2-thioacetic-5-phenyl-1, 3, 4- oxadiazole. *Journal of Al-Nahrain University* 13(1): 43-47.

Jones, R. N., Barry, A. L., Gaven, T. L. and Washington, J. A. (1984) *Manual of clinical microbiology*, 4th ed., American society for microbiology, Washington DC.

Maslat., A, O., Abussaud, M., Tashtoush, H. and Talib, M, AL. (2002) Synthesis, antibacterial, antifungal and genotoxic activity of Bis-1, 3, 4-oxadiazole derivatives. *Polish Journal of Pharmacology* 54: 55-59.

Mymoona, A., Husain, A. and Azad, B. (2009) Aroyl propionic acid based 2, 5-disubstituted-1, 3, 4-oxadiazoles: synthesis and their anti-inflammatory and analgesic activities. *European Journal of Medicinal Chemistry* 44: 2372-2378.

Oruc, E., Rollas, S., Kandemirli, F., Shvets, N. and Dimoglo, A. (2004) 1, 3, 4-thiadiazole derivatives. synthesis, structure elucidation, and structure - antituberculosis activity relationship investigation. *Journal of Medicinal Chemistry* 47: 6760-6767.

Parra, M., Hernández, S. and Alderete, J. (2003) Metallomesogens derived from chelating schiffs bases containing 1, 3, 4-oxadiazole and 1, 3, 4-thiadiazole: synthesis, characterization and study of mesomorphic properties. *Journal of the Chilean Chemical Society* 48(1): 57-60.

Rahmouni, N., T. Djebbar, S., Chenah, N. and Benali-Baitich, O. (1999) Synthesis, characterization and electrochemical behaviour of some manganese and copper complexes with tetradentate schiff base ligands. *Synthesis and Reactivity in Inorganic and Metal-Organic Chemistry* 29(6): 979-994.

Vogel, A. I. (2004) Revised by Jeffery, G. H., Bassett, J., Mendham, J. and Denney, R. C, *Textbook of Quantitative Chemical Analysis*, 6th ed., Pearson, New Delhi.

Xia, Y., Yang, Z. Y., Hour, M. J., Kuo, S. C., Xia, P., Bastow, K. F., Nakanishi, Y., Nampoothiri, P., Hackl, T., Hamel, E. and Lee, H. K. (2001) Antitumor agents. Part 204: Synthesis and biological evaluation of substituted 2-arylquinazolinones. *Bioorganic and Medicinal Chemistry Letters* 11 (9): 1193-1196.

Yang, G. F., Liu, Z. M. and Qing, X. H. (2001) Synthesis of 5, 7-dimethyl-2- (5-substituted-1, 3, 4-oxadiazole-2-yl) -methylenethio-1, 2, 4-triazolo[1,5-a] pyrimidines as potential fungicides, *Chinese Chemical Letters* 12 (10): 877-880.

Zarghi, A., Tabatabai, S. A and Faizi Ahadian, A. (2005) Synthesis and anticonvulsant activity of new 2 substituted benzyloxyphenyl-1, 3, 4-oxadiazoles. *Bioorganic Letters* 15: 1863-1865.

Zheng, X., Li, Z., Wang, Y., Chen, W., Huang, Q., Liu, C. and Song, G. (2003) Synthesis and insecticidal activities of novel 2, 5-disubstituted 1, 3, 4-oxadiazoles. *Journal of Fluorine Chemistry* 123: 163-169.