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Research Article

SYNTHESIS AND ANTI-MICROBIAL ACTIVITY OF SOME SUBSTITUTED BIS[2-((E)-2-(4-BENZYLIDENEAMINO)THIAZOL-4-YL)-4-METHYLPHENOL] METAL COMPLEXES

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ABSTRACT

During the past two decades, considerable attention has been paid to the chemistry of the metal complexes of Schiff bases containing nitrogen and other donors [1,2]. This may be attributed to their stability and applications in many fields such as catalysis, biocidal activity, *etc*. Reaction of heteroaromatic 2-amino-4-arylthiazoles with metal (II) acetate resulted substituted Bis[2-((E)-2-(4-benzylideneamino)thiazol-4-yl)-4-methylphenol] metal complexes (**2a-x)** moiety in a one step process. 2-amino-4-arylthiazoles derivatives were prepared by initial treatment of substituted acetophenone with thiourea and iodine, followed by basification with ammonium hydroxide. The representative Schiff base ligand and its metal complex have been characterized by UV-Visible, IR, ^{1}H NMR spectrum. The synthesized metal complexes were tested in vitro to their antibacterial activity against bacteria *E.Coli, S.Aureus, P.Areuginoso, K.Pneumoniae* and fungi *C.Albicans* and *S.Cerevisiae.* Some of these metal complexes exhibited pronounced antimicrobial activity.

Keywords: 2-amino-4-arylthiazoles, Acetophenone, Antimicrobial activity.

INTRODUCTION

Thiazole is a parent structure for an important class of nitrogen and sulphur-containing heterocycles, in particular, Schiff base of thiazole derivatives, which are widely encountered in rhodopsin, which is found in the mammalian eye. These thiazoles exhibit a variety of biological activity e.g., antimicrobial, antihistaminic, antiviral and find application as active principle in a number of pharmaceutical preparations including, e.g., Vitamin B1 (thiamine), penicillin, and carboxylase [3]. The chemistry of 2-amino-4-phenylthiazole Schiff base derivatives has been much investigated [4]. However, data on reaction of substituted 2-amino-4-phenylthiazole Schiff base with metal acetate are very scarce. Schiff bases are used in analytical chemistry as ligands for determination of various transition metals. They are also convenient synthons for preparation of various heterocycles, as well as for cyclization of terpenes S. E. Sadigova et al. [5] examine the reaction of 2-amino-4-arylthiazoles with aromatic aldehydes. They carry out reaction of 2-(2-hydroxybenzylideneamino)-4-phenylthiazole with copper, zinc, manganese, cobalt, and nickel acetates to synthesize new coordination compounds.

During the past two decades, considerable attention has been paid to the chemistry of the metal complexes of Schiff bases containing nitrogen and other donors [6,7]. This may be attributed to their stability and applications in many fields such as catalysis, biocidal activity, *etc*.

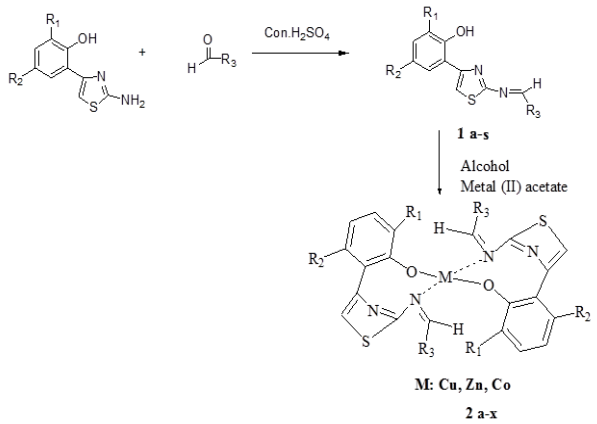
Schiff bases with first row transition metal complexes such as copper, nickel, cobalt, etc shows diverse biological activity such as they exhibit fungicidal, bactericidal, antiviral and antitubercular activity [8-14]. The drugs of copper (II) complexes have been the subject of a large number of research studies [15,16], may be due to the biological role of Cu(II) and its synergetic activity with the drug [17]. There of copper (II) complexes have been evaluated against several pathogenic fungai and bacteria [18-20]. Here we have synthesized Schiff base and there metal complexes by the reaction of substituted 2-((E)-2-(benzylideneamino) thiazol-4-yl)phenol with metal acetate (Scheme).

MATERIALS AND METHODS

Synthesis of amino thiazole

Iodine (0.1mole) was added to a mixture of (0.1mole) 1-(2-hydroxy-5-methylphenyl)ethanone and (0.3mole) of thiourea. The mixture was heated on a water bath in a closed vessel for 24 h, diluted with water, and heated again until it became almost homogeneous. The small amount of elemental sulfur was filtered off, the filtrate was cooled and made alkaline by adding aqueous ammonia, and precipitate was filtered off and recrystallized from ethanol and acetic acid (70:30). Yield (85%), mp 205^{0}C; IR (KBr): ν_{max}cm^{-1} 1635 (C=N); 3375, 3290 (NH_2), 3450 (-OH) cm^{-1}; ^{1}H NMR δ: 3.7-3.9 (2H, NH_2), 2.50(3H, CH_3), 6.92-7.25 (3H, CH, Ar-H), 10.23 (1H, Ar-OH). Elemental analysis: Found, %: C 58.09; H 4.62; N 13.48; S 15.31. (**$C_{10}H_{10}N_2OS$**). Calculated, %: C, 58.23; H, 4.89; N, 13.58; S, 15.55.All 2-amino-4-phenyl thiazole were synthesized in a similar way.

SCHEME



Synthesis of multisubstituted Schiff base ligands

General synthesis of (E)-2-(2-(4-methoxy-benzylideneamino) thiazol-4-yl)-4-methylphenol (1a)

(E)-2-(2-(4-methoxybenzylideneamino)thiazol-4-yl)-4-methylphenol was synthesized by the reaction between 2-(2-aminothiazol-4-yl)-4-methylphenol (0.0048mole) and anisaldehyde (0.0048mole) in the presence of conc.H_2SO_4 (2-3 drop) in ethanolic medium gives the desired product. The yield was 87%. M.P.: 147^{0}C. IR (KBr): ν_{max}cm^{-1} 3608, 3100, 2210, 1962, 1502, 680cm^{-1}. ^{1}H-NMR : δ 2.57 (s, 3H, Ar-CH_3), 3.76 (s, 3H, Ar-OCH_3), 6.68-6.70 (d, 1H, J=8.04Hz), 6.90-6.91 (d, 1H, J=8.03Hz), 7.39-7.41 (t, 2H), 7.42-7.42 (t, 2H), 7.43 (s, 1H, thiazole), 7.82 (s, 1H), 8.21 (s, 1H, N=CH), 9.15 (s, 1H, Ar-OH). All multisubstituted Schiff base were synthesized in a similar way, physical characterization data depicted in **table 1**.

Table 1: Synthesis of substituted (E)-N-benzyllidene-4-phenylthiazol-2-amines (1 a-h)

Schiff Base 1 a-h	R^1	R^2	R^3	R^4	R^5	Yield (%)	M.P. (^{0}C)
1a	OH	H	H	CH_3	4-OCH_3-Ar	86	147
1b	OH	I	H	CH_3	4-$N(CH_3)_2$-Ar	89	172
1c	OH	Br	H	CH_3	4-$N(CH_3)_2$-Ar	89	197
1d	OH	Br	H	CH_3	4-OCH_3-Ar	90	162
1e	OH	Br	H	CH_3	4Cl-Ar	87	163
1f	OH	Br	H	Cl	4-OCH_3-Ar	88	192
1g	OH	H	H	Cl	4-Cl-Ar	86	180
1h	OH	Br	H	Cl	3-NO_2-Ar	84	243

Table 2: Synthesis of substituted Bis[2-((E)-2-(4-benzylideneamino)thiazol-4-yl)-4-methylphenol] metal complexes (2 a-x)

Entry	R_1	R_2	R_3	m.p. (^{0}C)	Empirical Formula/ Yield (%)	Calcd (%) (Found) C	H	N
2a	H	CH_3	4-OCH_3-Ar	237	$C_{36}H_{30}Cu$	60.87	4.26	7.89
					$N_4O_4S_2$/86	(60.91)	(4.31)	(7.90)
2b	I	CH_3	4-$N(CH_3)_2$-Ar	242	$C_{37}H_{31}Cu$	45.66	3.21	8.64
					$I_2N_6O_2S_2$/89	(45.70)	(3.20)	(8.65)
2c	Br	CH_3	4-$N(CH_3)_2$-Ar	257	$C_{38}H_{34}Br_2$	51.04	3.83	9.40 (9.42)
					$CuN_6O_2S_2$/89	(51.10)	(3.86)	
2d	Br	CH_3	4-OCH_3-Ar	232	$C_{36}H_{28}Br_2$	49.81	3.25	6.45
					$CuN_4O_4S_2$/90	(49.86)	(3.28)	(6.52)
2e	Br	CH_3	4-Cl-Ar	233	$C_{34}H_{22}Br_2Cl_2$	46.57	2.53	6.39
					$CuN_4O_2S_2$/87	(46.60)	(2.57)	(6.43)
2f	Br	Cl	4-OCH_3-Ar	262	$C_{34}H_{22}Br_2Cl_2$	44.93	2.44	6.16
					$CuN_4O_4S_2$/88	(44.98)	(2.45)	(6.20)
2g	H	Cl	4-Cl-Ar	240	$C_{32}H_{18}Cl_4$	50.57	2.39	7.37
					$CuN_4O_2S_2$/86	(50.62)	(2.40)	(7.42)
2h	Br	Cl	3-NO_2-Ar	243	$C_{32}H_{16}Br_2Cl_2$	40.94	1.72	8.95
					$CuN_6O_6S_2$/84	(40.92)	(1.75)	(8.97)
2i	H	CH_3	4-OCH_3-Ar	243	$C_{36}H_{30}$	60.87	4.26	7.89
					$ZnN_4O_4S_2$/68	(60.90)	(4.28)	(7.85)
2j	I	CH_3	4-$N(CH_3)_2$-Ar	261	$C_{37}H_{31}$	45.66	3.21	8.64
					$ZnI_2N_6O_2S_2$/86	(45.62)	(3.22)	(8.69)
2k	Br	CH_3	4-$N(CH_3)_2$-Ar	>300	$C_{38}H_{34}Br_2$	51.04	3.83	9.40
					$ZnN_6O_2S_2$/73	(51.09)	(3.89)	(9.46)
2l	Br	CH_3	4-OCH_3-Ar	278	$C_{36}H_{28}Br_2$	49.81	3.25	6.45
					$ZnN_4O_4S_2$/75	(49.86)	(3.28)	(6.48)
2m	Br	CH_3	4-Cl-Ar	293	$C_{34}H_{22}Br_2Cl_2$	46.57	2.53	6.39
					$ZnN_4O_2S_2$/76	(46.62)	(2.56)	(6.42)
2n	Br	Cl	4-OCH_3-Ar	276	$C_{34}H_{22}Br_2Cl_2$	44.93	2.44	6.16
					$ZnN_4O_4S_2$/78	(44.95)	(2.46)	(6.19)
2o	H	Cl	4-Cl-Ar	267	$C_{32}H_{18}Cl_4$	50.57	2.39	7.37
					$ZnN_4O_2S_2$/89	(50.60)	(2.43)	(7.41)
2p	Br	Cl	3-NO_2-Ar	245	$C_{32}H_{16}Br_2Cl_2$	40.94	1.72	8.95
					$ZnN_6O_6S_2$/77	(40.97)	(1.75)	(8.94)
2q	H	CH_3	4-OCH_3-Ar	263	$C_{36}H_{30}Co$	60.87	4.26	7.89
					$N_4O_4S_2$/59	(60.88)	(4.29)	(7.90)
2r	I	CH_3	4-$N(CH_3)_2$-Ar	263	$C_{37}H_{31}Co$	45.66	3.21	8.64
					$I_2N_6O_2S_2$/78	(45.68)	(3.25)	(8.67)
2s	Br	CH_3	4-$N(CH_3)_2$-Ar	264	$C_{38}H_{34}Br_2$	51.04	3.83	9.40 (9.43)
					$CoN_6O_2S_2$/66	(51.07)	(3.89)	
2t	Br	CH_3	4-OCH_3-Ar	244	$C_{36}H_{28}Br_2CoN_4O_4S_2$/83	49.81	3.25	6.45 (6.48)
						(49.83)	(3.27)	
2u	Br	CH_3	4-Cl-Ar	275	$C_{34}H_{22}Br_2Cl_2$	46.57	2.53	6.39
					$CoN_4O_2S_2$/87	(46.60)	(2.55)	(6,40)
2v	Br	Cl	4-OCH_3-Ar	256	$C_{34}H_{22}Br_2Cl_2$	44.93	2.44	6.16
					$CoN_4O_4S_2$/76	(44.96)	(2.46)	(6.20)
2w	H	Cl	4-Cl-Ar	276	$C_{32}H_{18}Cl_4$	50.57	2.39	7.37
					$CoN_4O_2S_2$/81	(50.61)	(2.45)	(7.40)
2x	Br	Cl	3-NO_2-Ar	243	$C_{32}H_{16}Br_2Cl_2$	40.94	1.72	8.95
					$CoN_6O_6S_2$/73	(40.96)	(1.75)	(8.97)

Analytical methods and physical measurements

Melting points were determined by open capillary method and are uncorrected. All solvents were distilled prior to use TLC was performed on silica gel G. The UV-Visible spectra was observed on UV-1700 Shimadzu. The ^{1}H NMR spectra were recorded on a Brucker AC 400 (MHz) from solutions in DMSO-d_6 using TMS as internal reference. The IR spectra of the samples were recorded on a

Perkin-Elmer 1800 spectrophotometer in the 4000–400 cm^{-1} range using KBr pellets and mass spectra were measured with a GC-MS (70ev).

RESULTS AND DISCUSSION

The reaction between metal acetate with the Schiff base of thiazole has been carried out in 1:2 molar ratios resulting in the isolation of metal complex as a solid material. These are monomeric and possess sharp melting points. They are soluble in methanol, chloroform, DMSO and DMF.

UV-Vis spectra.

The electronic absorption spectral bands of the complexes (Cu, Co and Zn) were recorded over the range 200-800 nm in DMSO and their λmax values together with tentative assignments [19]. The spectral profiles below 350 nm are similar and are ligand centered transitions (intraligand (IL) π-π* and n-π*) of benzene and non-bonding electrons present on the nitrogen of the azomethine group in the Schiff base complexes [22]. Cu(II) complexes shows d-π* Metal-Ligand Charge Transfer (MLCT) transitions in the region 400-448 nm For Co(II) complexes the assigned bands at about 390-448 nm to d-π* Metal-Ligand Charge Transfer (MLCT) transitions The Ni(II) complexes are diamagnetic and the bands around 390-427 nm

IR spectra

The structure of the prepared complexes was refined on the basis of their IR spectra. The IR absorption bands were assigned with account taken of the data given in[23]. Of particular interest was the frequency range 1700-1500 cm^{-1}, where bands belonging to stretching vibrations of C-OH, C=N, and C=C bonds appear. In going from the free ligand to the complexes, the ν(C=C) band does not change its position. The ν(C=N) frequency decreases on the average by 10-15 cm^{-1} on complex formation, and new absorption bands appear at 1245-1250 cm^{-1} due to stretching vibrations of the C-O bond. These data suggest that the ligand coordinates to the central metal ion through the oxygen and nitrogen atoms. The copper(II), nickel(II), and cobalt(II) complexes are colored substances. Therefore, they can be used in photometric determination of the corresponding metals.

^{1}H NMR spectrum

In the ^{1}H NMR spectrum, the broad signals at δ 8-12 ppm are assigned to the protons of the hydroxyl groups. Single protons of -CH=N have chemical shifts at δ 5.8-6.5 ppm and signals around δ 6.8-8.0 ppm are attributed to the protons of aromatic rings.

The title metal complexes (**2a-x**) have been prepared from the corresponding Schiff base on reaction with copper, zinc, and cobalt acetates to synthesize new coordination compounds.

The composition of the resulting complexes was determined by mass, elemental analysis. The molecular ion peak for the ligand (**1a**) was observed at 324 *m/z* which is also supported by the "nitrogen rule", since the compound possesses two nitrogen atoms. For the copper complex (**2a**), the molecular ion peak appeared at 709 *m/z* which confirm the stoichiometry of metal complexes as being of the ML type. Other complexes also supported the mass spectra and elemental analysis data.

Bis[2-((E)-2-(4-methoxybenzylideneamino)thiazol-4-yl)-4-methylphenol]copper (II) 2a.

M.P. : 237^{0}C; IR (KBr): $\nu_{max}cm^{-1}$ 3100, 2990, 1962, 1245, 680cm^{-1}. ^{1}H-NMR : δ 2.77 (s, 3H, Ar-CH_3), 3.76 (s, 3H, Ar-OCH_3), 6.50 (s, 1H), 6.68-6.70 (d, 2H, J=8.04Hz), 6.90-6.91 (d, 2H, J=4.6Hz), 7.39-7.49 (t, 1H), 7.65-7.66 (d, 1H, J=5.2Hz), 7.82 (s, 1H), 9.15 (s, 1H, Ar-OH). ^{13}C NMR : δ 25.1, 66.7, 99.7, 115.5, 118.8, 121.3, 127.4, 132.1134.5, 138.2, 149.3, 154.3, 159.6, 161.8. MS (m/z) : (709.10 M^+).

Bis[2-((E)-2-(4-(dimethylamino)benzylideneamino)thiazol-4-yl)-6-iodo-4-methylphenol]copper (II) 2b.

M.P. : 242^{0}C; IR (KBr): $\nu_{max}cm^{-1}$ 3120, 2999, 1242, 769cm^{-1}. ^{1}H-NMR : δ 2.32 (s, 3H, Ar-CH_3), 2.80 (s, 6H, Ar-$N(CH_3)_2$), 6.58 (s, 1H), 6.68-6.70 (d, 2H, J=8.04Hz), 7.10-7.12 (d, 2H, J=7.96Hz), 7.36-7.38 (d, 1H, J=8.04Hz), 7.65-7.66 (d, 1H, J=3.68Hz), 8.82 (s, 1H, Ar-OH). ^{13}C NMR : δ 25.5, 65.1, 88.6, 102.1, 115.6, 124.2, 128.3, 132.2, 135.5, 140.2, 148.1, 1149.5, 160.1, 162.3. MS (m/z) : (971.93 M^+).

Bis[2-((E)-2-(4-(dimethylamino)benzylideneamino)thiazol-4-yl)-6-bromo-4-methylphenol]copper (II) 2c.

M.P.: 257^{0}C; IR (KBr): $\nu_{max}cm^{-1}$ 3110, 1701, 1390, 1248, 724, 670cm^{-1}. ^{1}H-NMR : δ 2.16 (s, 3H, Ar-CH_3), 4.15 (s, 6H, Ar-$N(CH_3)_2$), 7.20-7.20 (d, 2H, J=2.68Hz), 7.38-7.41 (q, 2H), 7.62 (s, 1H), 7.73-7.77 (d, 1H, J=5.00Hz), 7.85-7.87 (d, 1H, J=9.2Hz), 11.96 (s, 1H, Ar-OH). ^{13}C NMR : δ 26.4, 67.3, 101.2, 115.3, 125.1, 129.5, 131.2, 136.2, 136.9, 138.5, 149.2, 150.5, 153.3, 162.1. MS (m/z) : (892.98 M^+).

Bis[2-((E)-2-(4-methoxybenzylideneamino)thiazol-4-yl)-6-bromo-4-methylphenol]copper (II) 2d.

M.P.: 232^{0}C; IR (KBr): $\nu_{max}cm^{-1}$ 3012, 2991, 1590, 1690, 1245, 735, 680cm^{-1}. ^{1}H-NMR : δ 2.35 (s, 3H, Ar-CH_3), 4.10 (s, 3H, Ar-OCH_3), 7.58-7.59 (d, 2H, J=3.12Hz), 7.63-7.64 (d, 2H), 7.85-7.86 (d, 1H, J=4.64Hz), 8.01-8.04 (d, 1H, J=9.8Hz), 8.27 (s, 1H), 12.21 (s, 1H, Ar-OH). ^{13}C NMR: δ 21.1, 64.1, 99.8, 116.3, 124.3, 128.7, 130.3, 133.5, 138.9, 139.2, 149.8, 152.4, 159.8, 161.2. MS (m/z): (866.92 M^+).

Bis[2-((E)-2-(4-chlorobenzylideneamino)thiazol-4-yl)-6-bromo-4-methylphenol]copper (II) 2e.

M.P.: 233^{0}C; IR (KBr): $\nu_{max}cm^{-1}$ 3105, 1710,1250, 682.1cm^{-1}. ^{1}H-NMR : δ 2.16 (s, 3H, Ar-CH_3), 7.31 (s, 1H), 7.62-7.64 (d, 2H, J=8.36Hz), 7.75-7.76 (d, 2H, J=6.4Hz), 7.87-7.88 (d, 1H, J=2.96Hz), 8.21-8.25 (d, 1H, J=15.52Hz), 12.13 (s, 1H, Ar-OH). ^{13}C NMR : δ 23.7, 65.7, 102.1, 114.2, 124.3, 129.9, 132.7, 134.4, 136.8, 138.5, 144.3, 149.8, 153.0, 162.2. MS (m/z) : (876.82 M^+).

Bis[2-((E)-2-(4-methoxybenzylideneamino)thiazol-4-yl)-6-bromo-4-chlorophenol]copper (II) 2f.

M.P.: 262^{0}C; IR (KBr): $\nu_{max}cm^{-1}$ 1530, 1340, 1238, 721, 675cm^{-1}. ^{1}H-NMR : δ 4.15 (s, 3H, Ar-OCH_3), 7.58-7.59 (d, 2H, J=4.04Hz), 7.61-7.62 (d, 2H, J=1.16Hz), 8.01-8.04 (d, 1H, J=1.92Hz), 8.12-8.15 (d, 1H, J=2.08Hz), 8.27 (s, 1H), 11.50 (s, 1H, Ar-OH). ^{13}C NMR : δ 85.3, 100.2, 114.1, 115.7, 124.2, 127.8, 128.9, 129.6, 131.9, 135.8, 148.2, 153.0, 158.7, 160.4. MS (m/z): (908.81 M^+).

Bis[2-((E)-2-(4-chlorobenzylideneamino)thiazol-4-yl)-4-chlorophenol]copper (II) 2g.

M.P.: 240^{0}C;IR (KBr): $\nu_{max}cm^{-1}$ 1603, 1645, 1246, 1010, 767cm^{-1}. ^{1}H-NMR : δ 6.68-6.70 (d, 2H, J=8.00Hz), 6.89-6.91 (d, 2H, J=8.8Hz), 7.12-7.38 (m, 2H), 7.65-7.66 (d, 1H, J=4.28Hz), 7.98 (s, 1H), 9.01 (s, 1H, Ar-OH). ^{13}C NMR : δ 64.2, 101.2, 118.9, 123.4, 128.4, 129.8, 132.3, 134.8, 144.5, 149.7, 155.6, 163.7; MS (m/z) : (758.89 M^+).

Bis[2-((E)-2-(3-nitrobenzylideneamino)thiazol-4-yl)-6-bromo-4-chlorophenol]copper (II) 2h.

M.P.:243^{0}C; IR (KBr): $\nu_{max}cm^{-1}$ 1640, 1248, 700, 530cm^{-1}. ^{1}H-NMR : δ 6.84-6.85 (d, 1H, J=4.48Hz), 7.16-7.38 (m, 4H), 7.65-7.66 (d, 1H, J=4.28Hz), 7.98 (s, 1H), 9.17 (s, 1H, Ar-OH). ^{13}C NMR : δ 67.2, 103.2, 117.3, 118.1, 124.2, 125.2, 128.2, 130.5, 134.5136.7, 147.6, 149.2, 155.3, 160.1. MS (m/z) : (938.76 M^+).

The other complexes were synthesized in a similar way.

PHARMACOLOGICAL IMPORTANCE

***In Vitro* antibacterial and antifungal activities**

The *in vitro* biological screening effects of the investigated compounds were tested against the bacteria: *Pseudomonous aeruginosa* (ACTT 27853), *Staphylococcus aureus Crown* 1, *Escherichia coli* (ATCC 8739), and *Klebsilla Pneumoniae (FMS 5)* and antifungal activity against *candida albicans (ATCC 1023)* and *Saccharamuces Cerevisiae (WET 136)*. The primary activities were carried out at 50 ug/mL DMSO by well-diffusion method [24] using nutrient agar medium. The inoculated plates were incubated at 35^{0}C for 24 hr in case of bacteria and 48 hr in case of fungus. Cefodizine and Nystatin were used as standard drugs. The zone of inhibition was expressed in mm of compounds (**2a-x**) compared with standard drugs against microbacteria and funguses are mentioned in **table 3**.

Agar Plate Technique Antimicrobial activity

Bioefficacies of the synthesized compounds were checked *in vitro*. The *in vitro* antimicrobial activities of the complexes have been evaluated against several bacteria and fungi by the agar plate technique. The compounds were directly mixed with medium in different concentration control were also run. The antibacterial and antifungal activities of the ligands and their complexes were tested by using well-diffusion method. The antibacterial and antifungal activities of the new compounds against micro bacteria, viz *Escherichia coli, Staphylococcus aureus, Klebsiella pneumoniae*, and *Pseudomonas aeruginosa*, and fungi, viz *Candida albicans*, and *Saccharomyces cerevisiae*, are presented in table 2. Cefodizime and Nystatin are taken as the standard reference antibiotics for antibacterial and antifungal activities. The antibacterial and antifungal activities of standard antibiotics gave 28 and 12 mm inhibition zones for fungi and bacteria, respectively. The results showed that Cu(II), Zn(II), and Co(II) metal complexes exhibits slight active against three bacteria viz. *Escherichia Coli, Staphylococus aureus, Klebsiella Pneumoniae* and both fungi, *Candida albicans*, and *Saccharomyces Cerevisiae* compare with standard antibiotics. All the Cu (II), Zn (II), and Co (II) metal complexes have a greater effect against *Escherichia coli* than the other bacteria in this study and all these metal complexes has no activity against *P.Aeruginoso*. All metal complex exhibits relatively slight activity against fungi viz *Candida albicans* and *Saccharomyces cerevisiae*. But this metal complex exhibits moderate activity according to: Cefodizine and Nystatin antibiotics. The variation in the activity of different metal complexes against different microorganisms depends on either the impermeability of cells of the microbes or differences in ribosomes in microbial cells [25].

Table 3: Zone of inhibition in mm for compounds 2a-x to reference drugs activity against bacteria and Fungus at conc. 50µg/mL in DMSO

Entry	Bacterial inhibition zone (mm)				Fungal inhibition zone (mm)	
	e.coli	*s. aureus*	*p.aeruginoso*	*k.pneumoniae*	*c.albicans*	*s.cerevisiae*
2a	10	0	0	0	0	8
2b	11	0	0	7	0	7
2c	9	7	0	8	7	8
2d	10	8	0	8	0	8
2e	8	0	0	0	0	7
2f	12	0	0	8	0	7
2g	12	7	0	7	0	0
2h	9	0	0	7	8	8
2i	9	0	0	0	7	7
2j	11	8	0	0	7	8
2k	9	8	0	7	7	9
2l	9	0	0	7	8	6
2m	12	0	0	7	7	7
2n	10	7	0	0	0	7
2o	11	0	0	7	7	7
2p	9	0	0	0	8	8
2q	11	0	0	0	7	0
2r	13	0	0	0	0	8
2s	11	0	0	7	0	7
2t	10	7	0	8	7	8
2u	12	8	0	8	0	8
2v	11	8	0	0	7	8
2w	9	8	0	7	7	9
2x	9	0	0	7	8	6
Cef.	28	12	0	12	-	-
Nys.	-	-	-	-	18	20

Cef: Cefodizine, Nys: Nystatin

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