



**RESEARCH ARTICLE**

**Synthesis, Identification and Antimicrobial Activity of Some Novel Quinazolinone  
Derivatives and its Metal Complexes**

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**ABSTRACT**

In the present study O, N, O-donating ligand was prepared from the condensation of 2-aminobenzohydrazide and o-vanillin. The chemical structures were confirmed by Mass, ESI Mass, IR, <sup>1</sup>H NMR, <sup>13</sup>C NMR spectroscopy and Elemental analysis. Metal complex of this ligand is neither air- nor moisture-sensitive. The compounds were tested antimicrobial activity against the four bacterial and four fungal strains. The metal complexes display effective inhibitory action than ligand against test organisms.

**KEYWORDS**

Dihydroquinazolinone, Schiff Base, Metal Complexes, Antimicrobial Activity

**INTRODUCTION**

The Schiff bases are the most widely used ligands due to their straightforward synthesis, significant versatility and good solubility in common solvents. They have played an important role in the development of coordination chemistry and it forms stable complexes with different metals.<sup>1</sup> Over the recent decades, studies on the quinazolines are frequently used in a medicinal chemistry. Quinazolines have various remarkable biological and pharmaceutical activities, which are due to the presence of the pyrimidine nucleus. Quinazolinone is an exhilarating pattern as regards its pharmacological importance. Quinazolines display extensive application like antimicrobial<sup>2</sup>, anticonvulsant<sup>3</sup>, anticancer<sup>4</sup>, anti-inflammatory - analgesic<sup>5</sup>, antihypertensive.<sup>6</sup> As per literature survey that the presence of substituted aromatic ring at position 3 as well as

substituent like methyl and phenyl groups at position 2 is necessary requirement for its medicinal properties.<sup>7</sup>

Our ligand possesses three coordinating sites: oxygen of the phenolic -OH, oxygen of the carbonyl function, nitrogen of the benzyl amino group. The ligand may act work as monodentate, bidentate, tridentate. In general Schiff bases and presence of pharmacophores like -NO<sub>2</sub>, -Br,-OH, and -Cl are reported to possess anti-microbial activities.<sup>8,9</sup>

**MATERIAL AND METHODS**

Thin layer chromatography using silica gel G (E. Merck) plates was used to access the reactions and purity of the synthesized compounds. IR spectra were recorded on Shimadzu IR Affinity-1S fourier transform infrared spectrophotometer. Mass spectra were determined by GCMS-QP2010 mass spectrometer, <sup>1</sup>H NMR spectra were determined by Bruker spectrometer (400 MHz) using TMS (internal standard). Elemental data was recorded on Carlo Erba EA 1108 elemental analyzer.

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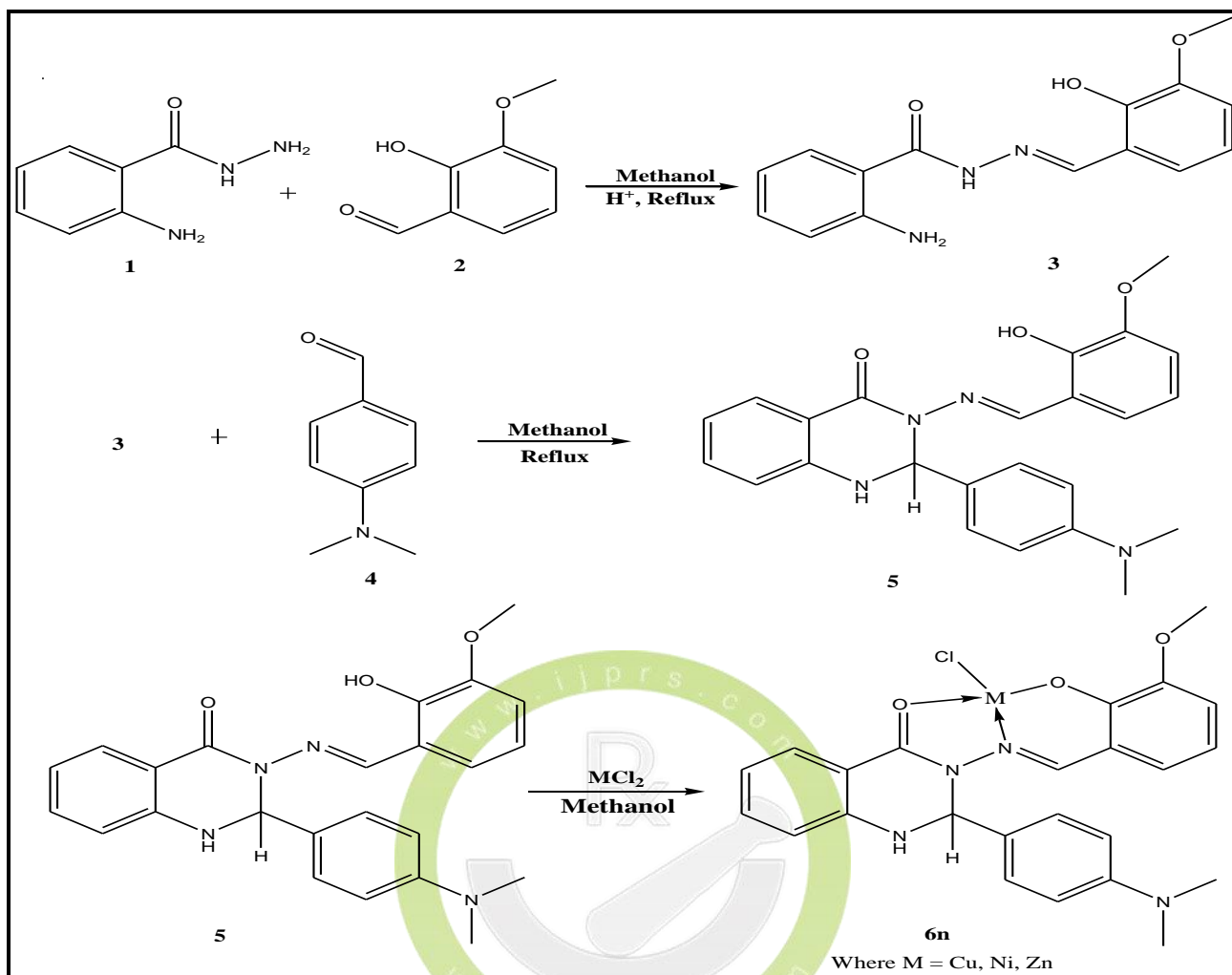


Figure: 1 Reaction Scheme for the Synthesis of Ligand and Metal Complexes

### General Procedure for the Synthesis of Ligand:

To the solution of 2-amino benzohydrazide 1 (0.01 mole) in methanol, o-vanillin 2 was added in the presence of glacial acetic acid to form N'-(2-hydroxy-3-methoxybenzylidene)-2-aminobenzohydrazide 3.

The reaction mixture was heated to 60-65 °C for 2 h. This N'-(2-hydroxy-3-methoxybenzylidene)-2-aminobenzohydrazide 3 was further refluxed with 4-(dimethylamino) benzaldehyde 4 in methanol to give final product 2-[4-(dimethylamino)phenyl]-3-[(E)-(2-hydroxy-3-methoxyphenyl)methylidene]amino]-1,2,3,4-tetraquinazolin-4-one 5. The reaction was monitored by TLC using hexane:ethylacetate (3:7). After the completion of the reaction, the mixture was poured into crushed ice.

It was filtered and the separated solid product was dried under reduced pressure. The ligand was off-white in colour; percentage yield of product was of 81 % with melting point 163°C MS (m/z): 416.47 (M); <sup>1</sup>H-NMR (DMSO-d<sub>6</sub>): δ ppm 3.80 (s, 3H, OMe); 7.33 (m, 1H, Ar-H); 7.75, (d, 2H, J = 8.7 Hz, Ar-H); 7.53, (d, 1H, J = 1.6 Hz, Ar-H); 7.58 (m, 2H, Ar-H); 7.55 (s, 1H, HC=N); 5.67 (s, br, 1H, OH); 6.98 (s, 1H, NH); <sup>13</sup>C-NMR (DMSO-d<sub>6</sub>): δ ppm 56.79 (O-CH<sub>3</sub>); 116.35, 119.49, 123.24, 120.65, 148.21, 148.61, 152.14, 156.24, 114.19, 126.89, 122.35, 135.12, 119.03, 148.19, 127.80, 128.38, 112.11, 152.83, 112.11, 128.30, (Ph); 152.14 (HC=N).

### General Procedure for the Synthesis of Metal Complex:

The Copper, Nickel, Zinc metal complexes were prepared by mixing calculated quantity of ligand

in ethanol and an aqueous solution of the equivalent metal chlorides in 1 : 1 molar ratio. The reaction mixture was refluxed on oil bath for 4-5 hrs. The completion of the reaction was monitored by TLC. Once the reaction was completed, the solvent was evaporated approximately 50%, from hot solution. Then the residue was cooled to room temperature. The solid complex formed and filtered out then washed with hot water and methanol. It was dried in vacuum desiccator over anhydrous CaCl<sub>2</sub>.

## RESULTS AND DISCUSSION

The IR spectral bands of the ligand and its metal complexes are presented in Table 1.

A strong band at 3309 cm<sup>-1</sup> in the IR spectrum of ligand was assigned to ν(NH) while a broad band around 2887 cm<sup>-1</sup> was due to hydrogen-bonded ν(OH) stretching.

The hydrogenon NH was involved in the intermolecular hydrogen bonding with carbonyl oxygen of another molecule. This band in all the complexes shifted to a higher frequency due to the breakdown of the intermolecular hydrogen bonding after complexation. ν(C=O), ν(C=N) and ν(C–O) stretchings were observed at 1649, 1612 and 1365 cm<sup>-1</sup> respectively. On complexation the stretching frequencies corresponding to carbonyl and imine groups decreased by 30–50 and 17–22 cm<sup>-1</sup>, respectively, indicating the involvement of carbonyl oxygen and azomethine nitrogen in the coordination. Absence of ν(OH) in all the complexes is indicative of its participation in the coordination of phenolic oxygen via deprotonation. Increase in the stretching frequency of ν(C–O) in all the complexes is suggestive of the same. Thus the title compound behaves as a monobasic tridentate ONO ligand.

Table 1: IR Bands of Ligand and its Metal Complexes

Compound	ν(NH)	ν(OH) phenolic	ν(C=O)	ν(C=N)	ν(C–O)
MJM-L	3309	2887	1649	1612	1365
MJM-C <sub>1</sub>	3322	n.o.	1605	1585	1375
MJM-C <sub>2</sub>	3355	n.o.	1605	1585	1338
MJM-C <sub>3</sub>	3264	n.o.	1618	1593	1370

Table 2: Elemental Analysis of the Ligand and its Metal complexes

Compound	Empirical formula	C	H	N	M	Cl
MJM-L	C <sub>24</sub> H <sub>24</sub> N <sub>4</sub> O <sub>3</sub>	69.18 (69.21)	5.85 (5.81)	13.35 (13.45)	-	-
MJM-C <sub>1</sub>	[Cu(C <sub>24</sub> H <sub>23</sub> N <sub>4</sub> O <sub>3</sub> )Cl]	55.90 (56.03)	3.52 (4.51)	10.40 (10.89)	12.70 (12.35)	6.35 (6.89)
MJM-C <sub>2</sub>	[Zn(C <sub>24</sub> H <sub>23</sub> N <sub>4</sub> O <sub>3</sub> )Cl]	55.22 (55.83)	4.12 (4.49)	6.44 (6.87)	11.50 (10.85)	10.15 (9.30)
MJM-C <sub>3</sub>	[Ni(C <sub>24</sub> H <sub>23</sub> N <sub>4</sub> O <sub>3</sub> )Cl]	56.80 (56.56)	4.30 (4.55)	5.10 (6.96)	11.56 (10.99)	11.08 (11.52)

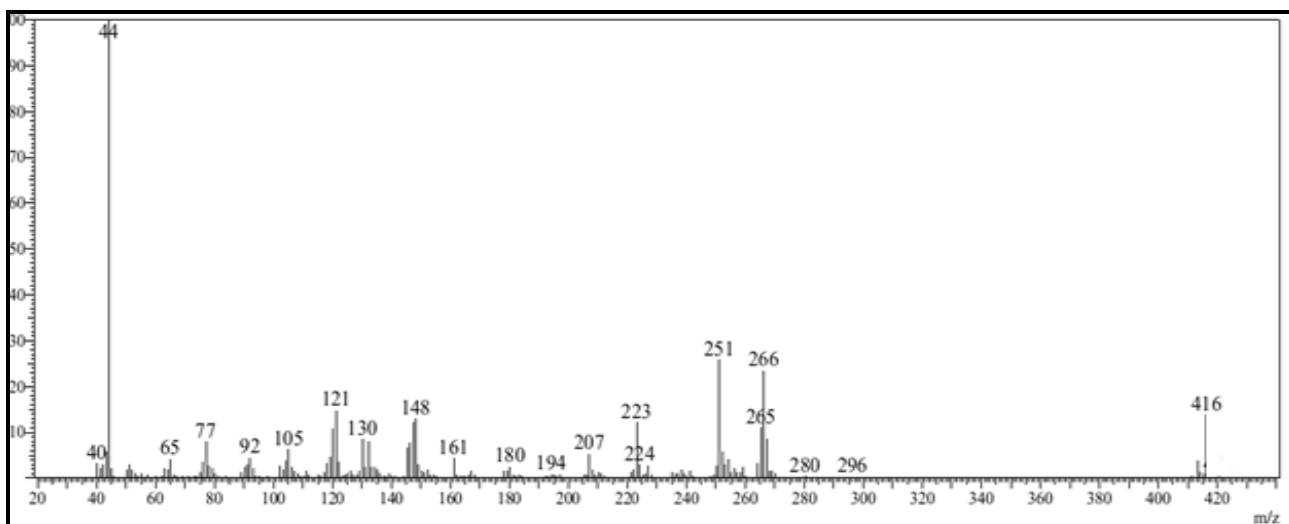


Figure 2: Mass Spectrum of Ligand

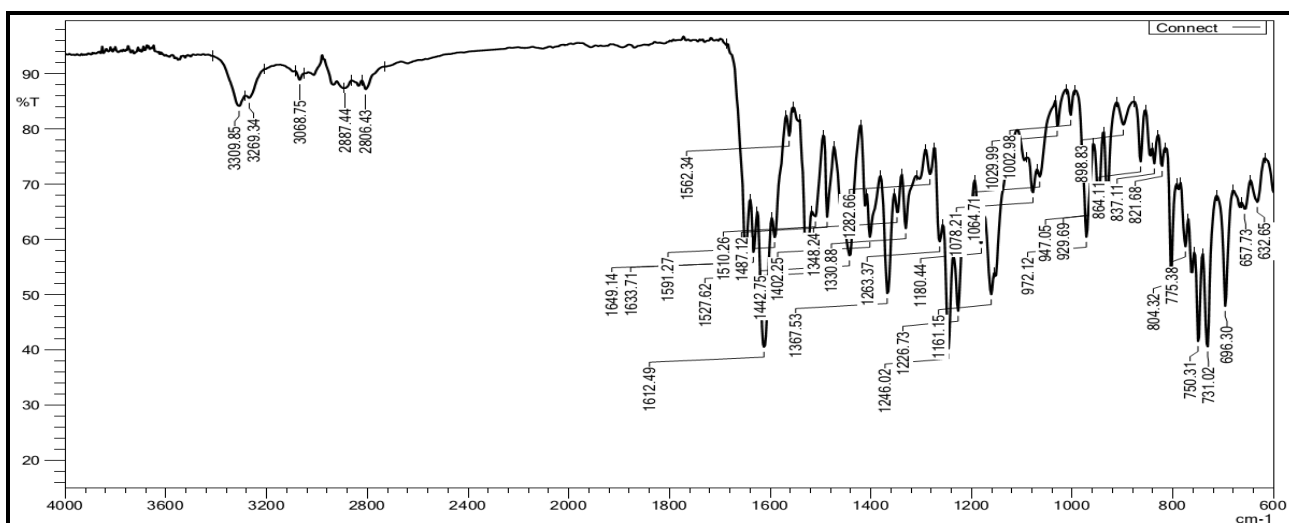


Figure 3: IR Spectrum of Ligand

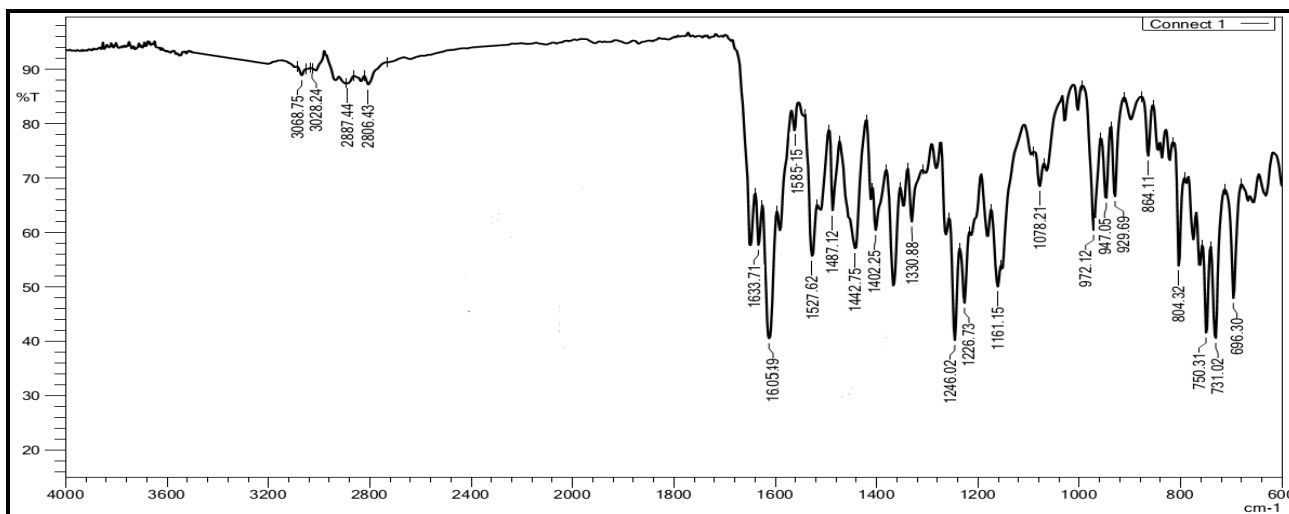


Figure 4: IR Spectrum of Complex MJM C<sub>1</sub>

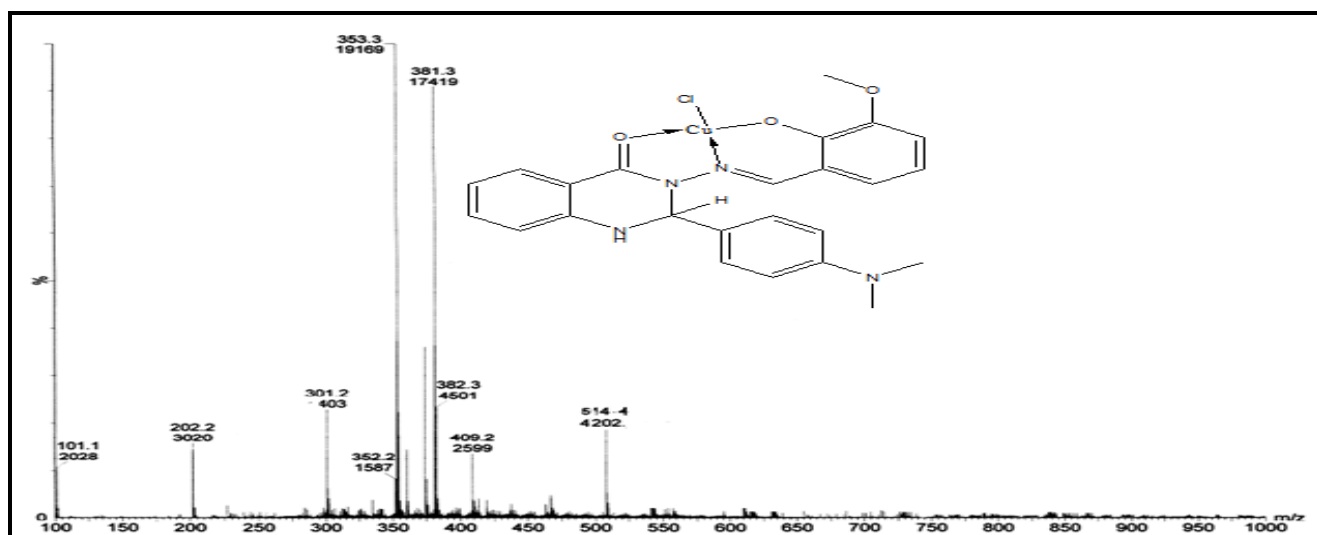

 Figure 5: ESI Mass of Complex MJM C<sub>1</sub>

 Table 3: Minimum inhibitory concentrations (MIC) (in  $\mu\text{g/ml}$ ) of compounds by using macrodilution method

Compound	Minimum inhibitory concentration values (in $\mu\text{g/ml}$ )							
	Antibacterial activity				Antifungal activity			
	E. coli	S. aureus	R. solanacearum	X. vesicatoria	A. niger	A. flavus	F. oxysporum	A. solani
MJM-L	128	128	64	128	128	64	128	128
MJM-C <sub>1</sub>	64	128	64	128	64	64	128	128
MJM-C <sub>2</sub>	64	64	32	64	64	32	64	64
MJM-C <sub>3</sub>	128	128	64	64	128	64	128	128
Chloramphenicol	8	8	8	2	-	-	-	-
Terbinafin	-	-	-	-	8	2	2	2

Disk-agar diffusion method was used for the antimicrobial activity testing of ligand and its metal complexes. Chloramphenicol and Terbinafin were used as standard drugs for antibacterial and antifungal assay. They were dissolved in Dimethyl Formamide at a concentration 0.25 mg/ml. The minimum inhibitory concentration was recorded for all compounds synthesized (Table 3).

Table 4 shows that the ligand and metal complexes exhibited moderate antimicrobial activity. The results displays that all three complexes show better activity than ligand against same microorganisms.

The efficiency of complex depends on the impermeability of the cell membrane of various microorganisms. This is due to chelation which facilitated the complex to cross membrane of cell as Tweedy's chelation theory.<sup>10,11</sup> Complex MJM-C<sub>1</sub> and MJM-C<sub>2</sub> showed more activity than ligand against the tested microbe stains. Complex MJM-C<sub>2</sub> display higher activity against three bacteria E. coli, S. aureus, R. solanacearum and three fungi A. niger, A. flavus and A. solani. Complex MJM-C<sub>3</sub> exhibited moderate activity than ligand against two bacteria R. solanacearum, X. vesicatoria and two fungi A. flavus, F. oxysporum.

Table 4: Antimicrobial activity of ligand and its corresponding metal complexes

Compound	Zone of inhibition (in mm) <sup>a</sup>							
	Antibacterial activity				Antifungal activity			
	E. coli	S. aureus	R. solanacearum	X. vesicatoria	A. niger	A. flavus	F. oxysporum	A. solani
MJM-L	17	13	10	12	09	11	12	10
MJM-C <sub>1</sub>	15	18	18	17	11	12	14	09
MJM-C <sub>2</sub>	21	22	19	15	13	13	14	11
MJM-C <sub>3</sub>	20	18	16	14	12	11	10	10
Chloramphenicol	34	35	32	29	-	-	-	-
Terbinafin	-	-	-	-	22	24	29	25

<sup>a</sup> Average of three replicates.

Where *E. coli* = *Escherichia coli*, *S. aureus* = *Staphylococcus aureus*, *R. solanacearum* = *Ralstonia solanacearum*, *X. vesicatoria* = *Xanthomonas campestris* sp. *vesicatoria*, *A. niger* = *Aspergillus niger*, *A. flavus* = *Aspergillus flavus*, *F. oxysporum* = *Fusarium oxysporum*, *A. solani* = *Alternaria solani*.

## CONCLUSION

The title compound was prepared in two simple steps as out-lined in the Figure 1. In the first step 2-aminobenzoylhydrazide was condensed with o-vanillin to get hydrazine product. It was then reacted with 4-(dimethylamino) benzaldehyde in the second step to get 2-[4-dimethylamino phenyl]-3-[(E)-(2-hydroxy-3-methoxyphenyl) methlidene] amino]-1, 2, 3, 4-tetraquinazolin-4-one in 81% yield. The ligand was well characterized by Mass, IR, <sup>1</sup>H NMR, <sup>13</sup>C NMR and ESI Mass spectral studies. The metal complexes were prepared using respective metal chlorides (Cu, Ni, Zn) with the ligand in 1:1 molar ratio. The analytical data of ligand and its complexes are compiled in Table 2 and 3. All the complexes were non-hygroscopic and stable at room temperature. The antimicrobial studies of metal complexes display moderate activity against bacterial and fungi strain as compare to ligand (Table 3 and 4).

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