

## Synthesis, Characterization and Microbial Evaluation of Heterocyclic Azo Dye Ligand Complexes of Some Transition Metal(II) Ions

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Received: 6 November 2018;

Accepted: 26 December 2018;

Published online: 31 January 2019;

AJC-19277

The synthesis and characterization of cobalt(II), nickel(II), copper(II) and zinc(II) complexes of azo ligand 4-[(5-acetyl-2-aminophenyl)-diazonyl]-1,5-dimethyl-2-phenyl-1*H*-pyrazol-3(2*H*)-one derived from 4-aminoantipyrine and 4-aminoacetophenone are reported. The nature of the compounds have been studied followed by mole ratio and methods of continuous contrast, Beer's law followed during a condensation rate ( $1 \times 10^{-4} - 3 \times 10^{-4}$  M). The analytical data showed that all the complexes are in 1:2 metal-ligand ratio. An octahedral geometry have been suggested for all the compounds and biological studies of all the complexes were evaluated against different types of antimicrobial strains.

**Keywords:** Transition metals, Azo dyes, Microbial studies, Antipyrine derivatives.

### INTRODUCTION

Azo dyes are widely used in the several fields of scientific interest [1,2]. Recently, a sensible growth of interest is found by several researchers in recognition of metal ions azo ligands as complexometric, polarographic and voltammetric studies [3-5]. Complexes of azo compounds have also been extensively studied for their medical and biological applications [6-8]. Azo dyes ligands and their metal chelates are also used for industrial applications, such as dyeing of protein and polyamide fibres, optical memory and photoelectric properties [9-12].

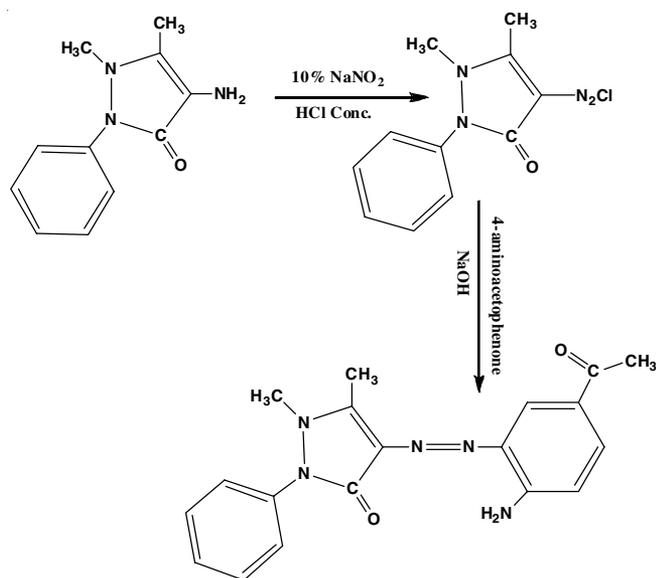
Due to the interesting biological activities, several studies have been reported based on heterocyclic azo dyes as well as metal(II) complexes [2,13]. In this article, synthesis of new azo compound containing biological active compound *i.e.* 4-aminoantipyrine and its transition metal(II) complexes are reported. Moreover, a new azo ligand *viz.* 4-[(5-acetyl-2-aminophenyl)-diazonyl]-1,5-dimethyl-2-phenyl-1*H*-pyrazol-3(2*H*)-one which is derived from 4-aminoantipyrine and 4-aminoacetophenone and its complexes were evaluated for biological studies against different type of antimicrobial strains and also applied as a suitable dye for cotton fibres.

### EXPERIMENTAL

All the chemicals *viz.*  $\text{CoCl}_2 \cdot 6\text{H}_2\text{O}$ ,  $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ ,  $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$ ,  $\text{ZnCl}_2$ , 4-aminoantipyrine, 4-aminoacetophenone were procured from Merck and used as such. Microelemental analysis (CHNSO) have been performed at Dimashq University, Syria, by employing Euro vector EA 3000, single V.3. Single instrument. Conductivity for the compounds resolved in DMSO ( $10^{-3}$  M/L) was recorded at 25 °C utilizing Philips PW-Digital conductimeter. Magnetic features have been achieved through utilizing Auto magnetic susceptibility balance Sherwood Scientific instrument at 25 °C. Atomic absorption has been recorded by employing a Shimadzu A.A-160A Atomic Absorption/Flame Emission Spectrophotometer. <sup>13</sup>C- and <sup>1</sup>H-NMR spectrum have been noted on Bruker-300 MHz Ultra Shield spectrometer at Al-Bayt University utilizing DMSO as solvent and trimethylsilane as reference. UV-visible spectrum have been analyzed using Shimadzu UV-160A Ultra Violet-Visible Spectrophotometer. FTIR analyses was conducted using Shimadzu, FTIR-8400S Fourier transform infrared spectrophotometer at 4000-400  $\text{cm}^{-1}$  using KBr discs.

**Synthesis of ligand:** 4-Aminoantipyrine (0.503 g, 1 mmol) dissolved in a mixture of ethanol (10 mL) and conc.

HCl (2 mL) and then diazotized at 5 °C with 10 % solution of NaNO<sub>2</sub> [14]. Diazotized solution has been added dropwise with constant stirring into a cooled alcoholic solution of 4-aminoacetophenone (0.337 g, 1 mmol). Then 25 mL of NaOH solution (1 M) has been added into a dusky colored mixture and left the solution for precipitation. The precipitated azo ligand has been filtrated, washed several times with dilute ethanolic solution and then dried (**Scheme-I**).



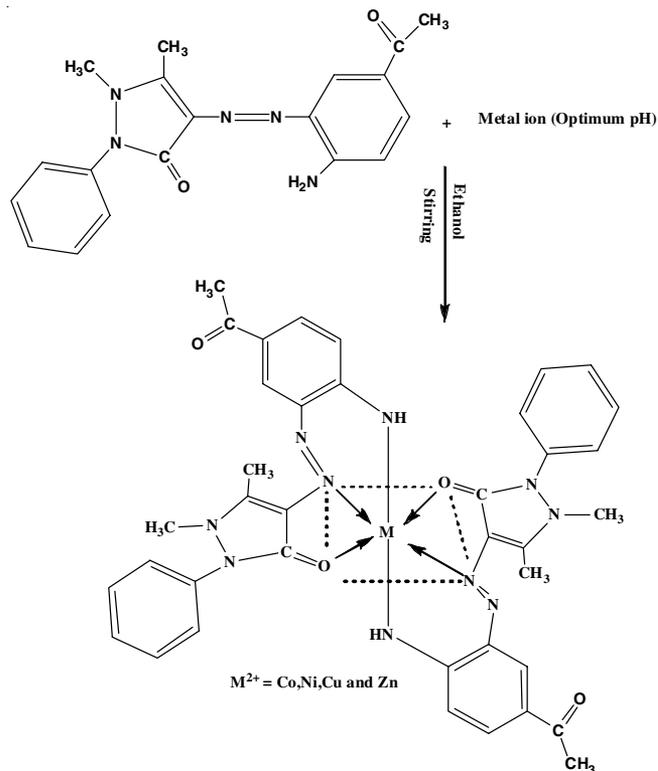
**Scheme-I:** Synthesis to the azo ligand (L)

**Buffer solution:** Dissolved ammonium acetate (0.771 g, 0.01 M) in 1 L of double-deionized water. The pH (5-9) was adjusted using CH<sub>3</sub>COOH or NH<sub>3</sub> solution.

**Standard solution:** Standard solutions of corresponding metal(II) salts have been made by varying concentration of 10<sup>-5</sup>-10<sup>-3</sup> M having pH 5-9.

**Preparation of metal complexes:** Ethanolic solution of ligand (0.349 g, 2 mmol) has been added to the corresponding metal(II) salts with constant stirring at pH solution 5-9. The solution was cooled until dark color precipitate has been obtained, filtered, washed several times with aqueous ethanol and then dried the filtrate at room temperature (**Scheme-II**). The physico-chemical data of the ligand and its metal complexes are listed in Table-1.

**Microbial activities:** The synthesized azo dye ligand and its metal complexes have been screened *in vitro* with their antibacterial and antifungal efficiency using: *Staphylococcus aureus*, *Escherichia Coli*, *Candida albicans* and *Candida tropicalis* by employing the paper disc method. All the compounds have been sterilized at a hot air oven as well as colony for each



**Scheme-II:** Suggested geometry for metal(II) complexes of azo ligand (L)

examined microorganisms having mean subcultured and brooded for about (8 h) before introducing to agar plates. Discs (7 mm diameter) have been soaked for different examine samples (1000 µg/mL) drained and then placed at agar plate by employing sterilized forceps. The plates have been brooded at 37 °C of 48 h and at the end from nursery period, zones of inhibition from different bacteria and fungal have been calculated [15].

## RESULTS AND DISCUSSION

Synthesis of azo ligand 4-[(5-acetyl-2-aminophenyl)-diazenyl]-1,5-dimethyl-2-phenyl-1H-pyrazol-3(2H)-one was achieved by diazotization of 4-aminoantipyrine followed by the condensation of 4-aminoacetophenone in alkaline solution. Synthesized ligand was characterized by spectral studies (<sup>1</sup>H, <sup>13</sup>C NMR, FTIR and UV-vis) and microelemental analysis (CHNO). The physico-chemical data of ligands and its complexes are given in Table-1.

**NMR spectra:** <sup>1</sup>H NMR spectrum of ligand showed multiplet signals at δ 7.389-8.126 ppm assigned to aromatic protons [16]. Signals obtained at δ 3.221 and δ 2.623 ppm are due to δ(N-CH<sub>3</sub>) and δ(CH<sub>3</sub>) of pyrazole, respectively [16], whereas signals at δ 8.537 and δ 2.937 ppm are ascribed due into δ(NH<sub>2</sub>) and δ(CH<sub>3</sub>) of acetyl group. Signals obtained at

TABLE-1  
PHYSICAL PROPERTIES TO THE AZO LIGAND AND THEIR METAL CHELATES

Compounds	Colour	m.p. (°C)	Yield (%)	Elemental analysis (%): Calcd. (Found)				
				M	C	H	N	O
Ligand(L)	Brown	> 300	83	–	65.32 (64.78)	5.44 (4.85)	20.05 (19.91)	9.17 (8.76)
[Co(L) <sub>2</sub> ].H <sub>2</sub> O	Deep brown	204	80	7.63 (7.11)	58.99 (57.93)	4.65 (4.03)	18.11 (17.85)	8.28 (7.84)
[Ni(L) <sub>2</sub> ].H <sub>2</sub> O	Deep brown	228	85	7.51 (6.83)	59.06 (59.01)	4.66 (4.11)	18.13 (17.76)	8.29 (8.06)
[Cu(L) <sub>2</sub> ].H <sub>2</sub> O	Deep brown	179	82	8.22 (7.79)	58.61 (58.04)	4.62 (3.96)	17.99 (16.92)	8.22 (7.76)
[Zn(L) <sub>2</sub> ].H <sub>2</sub> O	Deep brown	235	87	8.34 (7.81)	58.53 (57.91)	4.62 (3.92)	17.77 (16.88)	8.21 (7.98)

$\delta$  4.084 and  $\delta$  2.50 ppm referred to water ( $D_2O$ ) and  $DMSO-d_6$  [17].

$^{13}C$  NMR spectrum of azo ligand shows the signals at  $\delta$  197.307 and  $\delta$  164.183 ppm, which are assigned for (C=O) of acetyl and pyrazole groups. The resonance at  $\delta$  150.367 ppm is due the presence of carbon for amino group. The various signals at  $\delta$  152.427, 134.850, 129.583, 126.266, 124.745, 123.576, 122.731, 119.531, 118.781, 114.729 and 100.881 ppm are due to the carbon atoms of aromatic rings. Resonance at  $\delta$  13.550 and  $\delta$  36.115 ppm are assigned to methyl group in pyrazole group while the signals at  $\delta$  26.735 and  $\delta$  39.500 ppm are due to methyl group of acetyl group and  $DMSO-d_6$  [18,19].

**Metal to ligand ratio:** The optimum concentration for the interaction between the ligand and its metal(II) ions was considered at different pHs, then wavelength ( $\lambda_{max}$ ) have been evaluated. The optimum concentration ( $10^{-5}$  M) of the complexes is found suitable and follows the Lambert-Beer's law with a correlation factor ( $r > 0.9980$ ). The absorption of all the complexes are steady in the presence of buffer solution of  $CH_3COONH_4$  at pH 5-9 (Fig. 1).

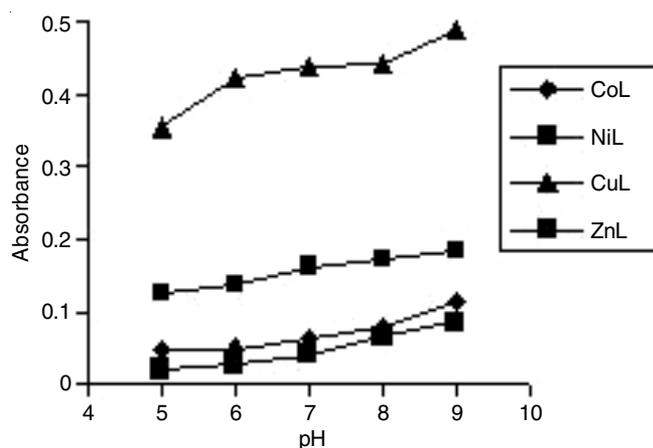
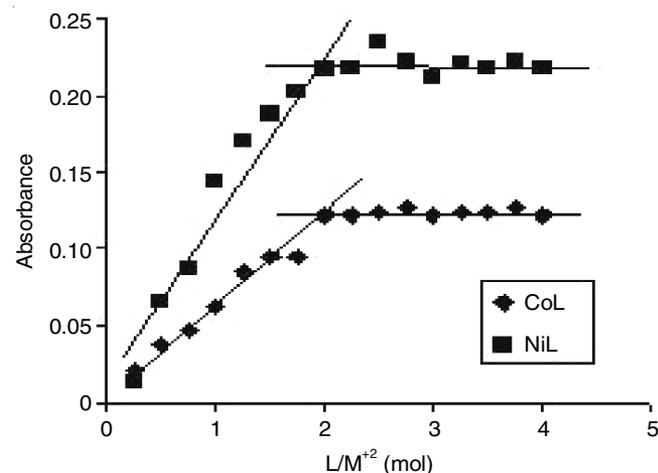


Fig. 1. Effect of pH at absorption ( $\lambda_{max}$ ) of the complexes

The composition of the complexes has been established by mole ratio and job methods (Fig. 2). In both cases, the results revealed a mole ratio [M:L] [1:2] for all the complexes (Table-2). The molar conductivity of azo ligand and its metal(II)



complexes were measured in  $DMSO$  ( $10^{-3}$  M) shows a non-electrolytic nature of the complexes due to its low value [20] (Table-2).

**Determination of stability constant and Gibb's free energy:** Depending on the mole ratio, stability constant (K) of metal to ligand (1:2) can be computed according to the following eqn:

$$K = \frac{1-\alpha}{4\alpha^3 C^3}; \quad \alpha = \frac{A_m - A_s}{A_m}$$

where C = concentration of the complex in solution (mol/L);  $\alpha$  = degree of dissociation,  $A_s$  is the absorption of solution containing a stoichiometric ratio of ligand and metal ion;  $A_m$  is the absorption of the solution containing same volume of metal(II) ions and ligand. High values for stability constant (K) (Table-3) refers to high constancy of the synthesized complexes [21]. Simultaneously, the thermodynamic parameters of Gibb's free energy ( $\Delta G$ ) were also calculated using the following eqn:

$$\Delta G = -RT \ln k$$

where R is the gas constant (8.314 J/mol K), T is the absolute temperature (Kelvin). The negative value of ( $\Delta G$ ) reflects that reaction between azo dye ligand (L) and metal ions is spontaneous (Table-3).

**Effect of time:** Time effect have been studied for colour complex solution under optimum conditions (pH, concentration and wavelength). It was found that the reaction was completed in 5 min at 25 °C and continue to be stable for about 90 min, which showed that the ligand is strongly coordinated with metal salts.

**Electronic absorption spectra:** UV-visible spectra of the synthesized azo ligand (L) and its metal(II) complexes in aqueous ethanol solution ( $10^{-3}$  M) have been studied and the results are given in Table-2. The electronic absorption of azo ligand shows two bands at 298 and 432 nm which is attributed to mild energy ( $\pi-\pi^*$ ) and ( $n-\pi^*$ ) transition, respectively [22]. The Co(II) complex exhibits two peaks at 254 and 442 nm attributed to ligand field and charge transfer, while the bands at 572, 858 and 978 nm were assigned to transition  ${}^4T_{1g}(F) \rightarrow {}^4T_{1g}(P)$ ,  ${}^4T_{1g}(F) \rightarrow {}^4A_{2g}$  and  ${}^4T_{1g}(F) \rightarrow {}^4T_{2g}(F)$  respectively, also the magnetic moment value at 5.01 B.M. which is higher than the

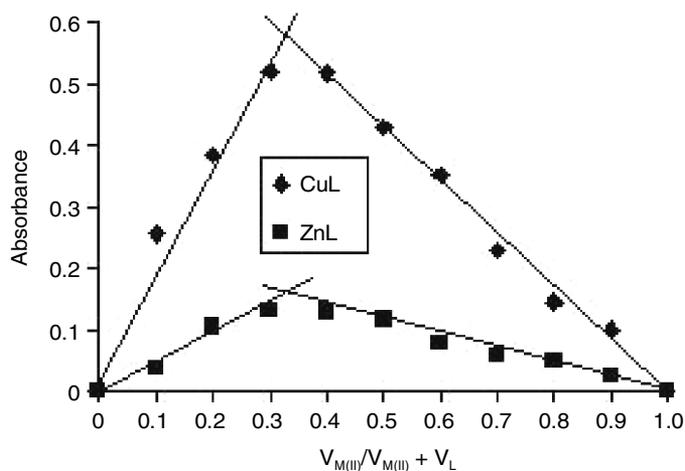


Fig. 2. Mole ratio and Job methods for the solutions of the complexes

TABLE-2  
CONDITIONS OF THE PRODUCED COMPOUNDS AND UV-VISIBLE, MAGNETIC  
SUSCEPTIBILITY AS WELL AS CONDUCTANCE MENSURATIONS DATUM

Compounds	pH	Molar conc. $\times 10^{-4}$	M:L	$\lambda_{\max}$	ABS	$\epsilon_{\max}$	$\Lambda_m$ (S cm <sup>2</sup> mol <sup>-1</sup> )	$\mu_{\text{eff}}$ (B.M)
Ligand(L)	–	–	–	298 432	2.272 1.479	2272 1479	–	–
[Co(L) <sub>2</sub> ].H <sub>2</sub> O	9	2.0	1:2	254 442 572 858 978	0.817 0.368 0.185 0.017 0.095	817 368 185 17 95	14.11	5.10
[Ni(L) <sub>2</sub> ].H <sub>2</sub> O	9	2.5	1:2	240 298 440 592 886 978	1.308 1.361 0.917 0.341 0.020 0.111	1308 1361 917 341 20 111	19.20	2.88
[Cu(L) <sub>2</sub> ].H <sub>2</sub> O	9	3.0	1:2	236 296 560 974	2.155 1.677 0.640 0.137	2155 1677 640 137	16.20	1.74
[Zn(L) <sub>2</sub> ].H <sub>2</sub> O	9	2.5	1:2	294 476	1.571 0.505	1571 505	10.93	Diamag.

TABLE-3  
STABILITY CONSTANT AND GIBBS FREE ENERGY OF THE PREPARED COMPLEXES

Complexes	A <sub>s</sub>	A <sub>m</sub>	$\alpha$	k	ln K	$\Delta G$ (kJ mol <sup>-1</sup> )
[Co(L) <sub>2</sub> ].H <sub>2</sub> O	0.063	0.122	0.483	$28.72 \times 10^6$	17.173	-42.547
[Ni(L) <sub>2</sub> ].H <sub>2</sub> O	0.144	0.218	0.339	$73.44 \times 10^6$	18.111	-44.871
[Cu(L) <sub>2</sub> ].H <sub>2</sub> O	0.325	0.523	0.378	$32.73 \times 10^6$	17.303	-42.869
[Zn(L) <sub>2</sub> ].H <sub>2</sub> O	0.071	0.131	0.458	$22.58 \times 10^6$	16.932	-41.950

calculated spin value [23]. Nickel(II) complex displays three absorption bands at 240, 298 and 440 nm which is attributed to ligand field effect and charge transfer. The electronic bands in the visible region at 592, 886 and 978 nm are assigned to *d-d* transition  ${}^3A_{2g} \rightarrow {}^3T_{1g}(P)$ ,  ${}^3A_{2g} \rightarrow {}^3T_{1g}(F)$  and  ${}^3A_{2g} \rightarrow {}^3T_{2g}(F)$ , respectively. Magnetic moment of this complex was found at 2.88 B.M that has been very near to the octahedral geometry [24].

Similarly, Cu(II) complex shows the bands at 236, 296 and 560 nm which are due to ligand field effect and charge transfer, while band at 974 nm is attributed to *d-d* transition  ${}^2E_g \rightarrow {}^2T_{2g}$  and the magnetic moment from this complex has been found at 1.74 B.M. which is found to be very near to octahedral environment [25]. The spectrum of Zn(II) complex do not display the charge transfer due to its diamagnetic behaviour [26].

**Infrared analysis:** The characteristic IR spectral data of the ligand and its complexes are given in Table-4. The spectrum of ligand (L) exhibited strong bands at 3487 and 3414 cm<sup>-1</sup> which are attributed to the vibration stretching of  $\nu(\text{NH}_2)$ , in all the synthesized complexes which indicates the deprotonation for amino group to coordinated metal ions [27]. Band at 1678 cm<sup>-1</sup> is due to carbonyl  $\nu(\text{C}=\text{O})$  of acetyl group which has no significant change on complexation [28]. The band at 1657 cm<sup>-1</sup> assigned to  $\nu(\text{C}=\text{O})$  vibration in the ligand, which on complexation has been disappeared due to lower frequency implied the coordination for metal(II) ions [29]. The band at

1512 cm<sup>-1</sup> due to azo group is displaced into higher wave-number for all the metal complexes [30]. Similarly, the bands at 1597, 1496, 1454, 1411, 1357, 1307 cm<sup>-1</sup> are due to stretching vibration of  $\nu(\text{C}=\text{C})$  and bending frequency of  $\nu(\text{CH}_3)$  modes [31]. The presence for hydrated water molecule in all the complexes [32] have been observed to broad absorption band around 3525-3414 cm<sup>-1</sup>. The stretching of frequency bands at 497-455 cm<sup>-1</sup> is due to  $\nu(\text{M}-\text{N})$  to  $\nu(\text{M}-\text{O})$  [33,34].

**Microbial activity:** The ligands and its metal complexes have been examined for antibacterial and antifungal activities against *Staphylococcus aureus*, *Esherichia coli*, *Candida albicans* and *Candida tropicalis*. Stock solution ( $10^{-3}$  M) was prepared by dissolving the compounds in DMSO. Table-5 showed that the complexes exhibited better enhanced activity as compared to the ligand. However, among all the complexes, only Zn(II) complex showed the better activity against all the tested organism.

## Conclusion

In this work, a new azo compound 4-[(5-acetyl-2-amino-phenyl)diazanyl]-1,5-dimethyl-2-phenyl-1*H*-pyrazol-3(2*H*)-one derived from 4-aminoantipyrine and 4-aminoacetophenone and its metal(II) complexes are synthesized and characterized by spectral and analytical methods which revealed the octahedral geometry of the complexes. The ligand and its transition metal(II) complexes possess appreciable microbial activities.

TABLE-4  
 MAIN FREQUENCIES TO THE LIGAND AND METAL CHELATES (cm<sup>-1</sup>)

Compounds	(NH <sub>2</sub> ) v(NH)+	v(C=O) acetyl + pyr	v(C=C) + (N=N)	δCH <sub>3</sub> <sub>as,s</sub> + (H <sub>2</sub> O)	v(M-N) + (M-O)
Ligand (L)	3487 sh. 3414 sh. -	1678 s. 1657 sho.	1597 sh. 1512 sho.	1496 s. 1454 sh. 1411 s. 1357 sh. 1307 sh. -	-
[Co(L) <sub>2</sub> ].H <sub>2</sub> O	- 3375 br.	1678 s. 1631 sho.	1597 s. 1519 sho.	1492 sh. 1454 sh. 1408 s. 1357 sh. 1303 sho. 3417 br.	493 w. 474 w.
[Ni(L) <sub>2</sub> ].H <sub>2</sub> O	- 3210 sho.	1678 s. 1647 s.	1597 sh. 1516 sho.	1492 s. 1454 s. 1404 s. 1357 sh. 1307 sho. 3417 br.	489 w. 459 w.
[Cu(L) <sub>2</sub> ].H <sub>2</sub> O	- 3174 br.	1681 s. 1643 sho.	1593 s. 1520 sho.	1492 sh. 1454 s. 1357 sh. 1303 s. 3414 br.	497 w. 455 w.
[Zn(L) <sub>2</sub> ].H <sub>2</sub> O	- 3221 br.	1678 s. 1640 sho.	1597 sh. 1516 s.	1492 sh. 1454 sh. 1408 s. 1357 sh. 1303 sho. 3525 br.	474 w. 462 w.

as = asymmetry, s = symmetry, br = broad, sh = sharp, s = strong, w = weak, sho =shoulder

 TABLE-5  
 DIAMETERS (mm) AT SUPPRESSION FOR MICROBIAL  
 ACTIVITY TO THE AZO LIGAND AND COMPOUNDS

Compounds	<i>Staphylococcus aureus</i>	<i>Esherichia coli</i>	<i>Candida albicans</i>	<i>Candida tropicalis</i>
Ligand (L)	12	12	-	11
[Co(L) <sub>2</sub> ].H <sub>2</sub> O	-	15	-	-
[Ni(L) <sub>2</sub> ].H <sub>2</sub> O	12	13	-	-13
[Cu(L) <sub>2</sub> ].H <sub>2</sub> O	15	14	-	19
[Zn(L) <sub>2</sub> ].H <sub>2</sub> O	20	17	12	24

### CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

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