

## ARTICLE

**Synthesis, Characterization and Antibacterial Study of Some 3d-Metal Complexes of Paracetamol and 1,10- Phenanthroline****Yasmin M.S. Jamil, Mohammed K. Al-Qadasy, Fathi M. Al-Azab and Maher A. Al-Maqtari\****Sana'a University, Faculty of Sciences, Chemistry Department, Yemen.**Received on: 22<sup>nd</sup> Nov. 2017;**Accepted on: 20<sup>th</sup> Feb. 2018*

**Abstract:** Novel complexes of Co(II), Ni(II) and Cu(II) with paracetamol and 1,10-phenanthroline have been synthesized and characterized using infrared spectroscopy, mass spectrometry, electronic absorbance, melting point and conductivity measurements. The two ligands have been found to act as bidentate chelating agents. Paracetamol coordinates through the carbonyl group and nitrogen atom of amide group, while 1,10-phenanthroline coordinates through the two nitrogen atoms. Based on magnetic moment and electronic spectral studies, an octahedral geometry has been assigned for the complexes. Antibacterial screening of the complexes against some gram positive and negative bacteria was tested.

**Keywords:** 1,10-phenanthroline, paracetamol, UV, Thermal analysis, Antibacterial Activity.

**Introduction**

Metals and metal complexes have played a key role in the development of modern chemotherapy<sup>[1]</sup>. For example, complexation of non-steroidal anti-inflammatory drugs to copper overcomes some of the gastric side effects of these drugs<sup>[2]</sup>. A number of drugs and potential pharmaceutical agents also contain metal-binding or metal-recognition sites, which can bind or interact with metal ions and potentially influence their bioactivities and might also cause damages on their target biomolecules<sup>[3]</sup>.

1,10-phenanthroline is one of the most popular bidentate N,N-chelating agents, widely used in the development of coordination chemistry of heterocyclic nitrogen donor ligands<sup>[4]</sup>. Its rigidity makes it an entropically better chelating molecule than 2,2'-bipyridine and it has been exploited to make a variety of simple geometrically diverse complexes<sup>[5]</sup>. Complexes containing 1,10-phenanthroline display exciting photochemical and photo-physical properties and are used as fluorescent sensors for the selective detection of cations<sup>[6]</sup>, anions<sup>[7]</sup> and oxygen<sup>[8]</sup>.

Paracetamol, also known as acetaminophen, is a medication used to treat pain and fever. It is typically used against mild to moderate pain<sup>[9]</sup>. Literature survey failed to reveal any previous work or research regarding the complexation of paracetamol and 1,10-phenanthroline with transition metals. On the other hand, complexes of Co(II), Ni(II) and Fe(III) with aspirin and paracetamol have been synthesized and characterized using infrared, electronic and <sup>1</sup>HNMR spectral, melting point and conductivity measurements<sup>[10]</sup>. Spectrophotometric and pH-metric studies of the aqueous binary and mixed ligand complexes of Pb(II), Cd(II) and Cu(II) were carried out with ascorbic acid and paracetamol<sup>[11]</sup>. The interaction of Mn(II), Co(II), Ni(II), Cu(II) and Zn(II) metal ions with ibuprofen (IBP) and paracetamol (PC) has been studied by pH-metric technique at 0.1 M ionic strength at 302 ± 0.5 K in aqueous medium<sup>[12]</sup>. Complexes of mixed drug paracetamol and sulfamethoxazole with Mn(II), Fe(II), Co(II), Ni(II), Cu(II) and Zn(II) were synthesized at room temperature and characterized by magnetic susceptibility, melting point, percentage of

metal, conductivity measurements, infrared and electronic spectroscopy. The synthesized complexes have proven their potentials as broad-spectrum antimicrobial agents<sup>[13]</sup>.

However, it is of interest to study the synthesis and characterization, thermal behavior and biological screening of Co(II), Ni(II) and Cu(II) complexes of these mixed ligands. The processes of thermal degradation of nickel complexes have been investigated by thermo-analytical methods (TG, DTG). The Coats-Redfern integral method has been used to determine the associated kinetic parameters with the successive steps in the decomposition sequence. 1,10-phenanthroline is biologically active, so its complexes have become of interest to be studied biologically and their activities compared against four species of bacteria.

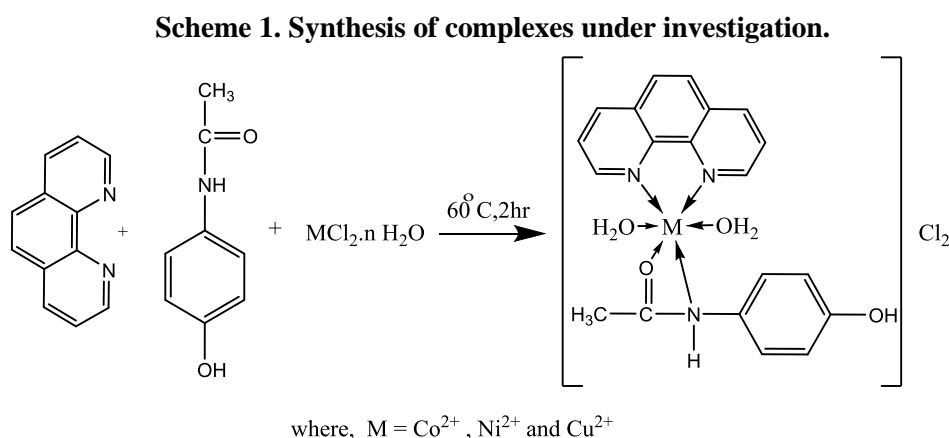
## Materials and Methods

All chemicals, solvents, metal chlorides (cobalt chloride hexahydrate, nickel chloride hexahydrate and copper chloride dihydrate) and 1,10-phenanthroline were commercially (BDH) available and used without further purification. A pure sample of paracetamol was obtained from

Shaphaco Pharmaceutical Company in Sana'a-Yemen. Bacterial strains were used for the study (*Bacillus subtilis* (ATCC 6633), bacteria *Escherichia coli* (ATCC 11303), (*S. aureus* ATCC 29737), (*P. aeruginosa* ATCC 25619). All the tested strains were reference strains and were obtained from the Department of Biology, Division of Microbiology, College of Science and Department of Food Sciences and Technology Sana'a university.

## Synthesis of the Drug Metal Complexes

Generally, the solid complexes were prepared by adding an ethanolic solution of hydrated metal chlorides to an ethanolic solution of mixed ligands of paracetamol and 1,10-phenanthroline in a 1:1:1 mole ratio. The mixture of each was refluxed on hot plate at 60 °C with constant stirring for 2 hours until the colored precipitates were formed. The precipitated solids were filtered off, washed with absolute ethanol, then with DMF and air-dried<sup>[14]</sup>. The proposed stoichiometric equation for the synthesized complexes could be represented as shown in Scheme 1.



## Instrumentation

The IR spectra of the complexes were collected in transmission mode (KBr discs) in the range of 400–4000  $\text{cm}^{-1}$  on a Jasco FT-IR-140 spectrometer at Sana'a University. The electronic absorption spectra were measured in DMSO at a concentration of  $1 \times 10^{-3}$  M in the range of 200–800 nm on a Specord 200 UV-Vis spectrophotometer at Sana'a University.

Carbon, hydrogen and nitrogen analyses of the complexes have been carried out using a Vario EL Fab. CHNS Nr. 11042023 at the

Central Laboratory, Faculty of Science, Cairo University, Egypt. Chloride was determined gravimetrically by silver nitrate<sup>[15]</sup>. The amount of coordinated and uncoordinated water was determined gravimetrically using the weight loss method<sup>[15]</sup> as well as by thermal analysis methods. The metal content was measured using a Perkin-Elmer 2380 flame atomic absorption spectrophotometer at the central lab of the Ministry of Oil, Sana'a-Yemen.

The molar conductance of  $10^{-3}$  M solutions of the ligands and their metal complexes in DMSO was measured using a Jenway conductivity meter, model 4510. All measurements were taken at room temperature on freshly prepared solutions. A Stuart scientific electrothermal melting point apparatus was used to measure the melting points of the metal complexes.

Thin layer Chromatography TLC was carried out on Silica Gel GF254 plates (m-kieselgel G., 0.2 mm thickness) with a 3:1 v/v ethylacetate/petroleum ether solution as eluent mobile at room temperature. The plates were scanned under a 254 nm ultraviolet light<sup>[16]</sup>.

The mass susceptibility (Xg) of the solid complexes was measured at room temperature by the Gouy's method using a magnetic susceptibility balance from Johnson Metthey and Sherwood at Cairo University, Central Lab<sup>[17]</sup>.

Differential Thermal Analysis (DTA) and Thermogravimetric Analysis (TGA) experiments were conducted using a Shimadzu DTA-50 and a Shimadzu TGA-50H thermal analyzers, respectively, at the Micro Analytical Center, Cairo University, Cairo-Egypt. All experiments were performed using a single use top loading platinum sample pan under nitrogen atmosphere at a flow rate of 30 ml/min and a  $10^{\circ}\text{C}/\text{min}$  heating rate in the temperature range of  $20\text{--}800^{\circ}\text{C}$ .

### Biological Screening

The ligands and their metal complexes were tested for their antibacterial activity against four species of bacteria (*Staphylococcus aureus*, *Bacillus*, *Escherichia coli*, *Pseudomonas aeruginosa*),

using the filter paper disc method<sup>[18]</sup>. The screened compounds were dissolved individually in DMSO to prepare a solution of 1000  $\mu\text{g}/\text{ml}$  for each of investigated compounds. Filter paper discs (Whatman No.1 filter paper, 5 mm diameter) were saturated with the solution of these compounds. The discs were placed on the surface of solidified Mollar Henton agar dishes seeded by the tested bacteria. The diameters of inhibition zones (mm) were measured at the end of an incubation period of 24 h at  $37^{\circ}\text{C}$ . Discs saturated with DMSO are used as solvent control. Gentamicin 120 $\mu\text{g}/\text{ml}$  was used as a reference substance for these bacteria<sup>[19]</sup>.

## Results and Discussion

### Synthesis of the Complexes

Metal complexes of 1,10-phenanthroline and paracetamol were prepared using Co(II), Ni(II) and Cu(II). The resulting complexes were discussed and synthesized. The elemental analysis shows that Co(II), Ni(II) and Cu(II) formed complexes with 1,10-phenanthroline and paracetamol in 1:1:1 (metal:1,10-phenanthroline:paracetamol) molar ratio. The synthesized complexes were dark blue, light green and dark green in color, possess high melting points and give one spot in TLC. These complexes were insoluble in water, ethanol, methanol, acetone,  $\text{CCl}_4$ ,  $\text{CHCl}_3$  and DMF, but all of them are soluble in DMSO. From the spectroscopic measurements (infrared, UV-Vis), effective magnetic moment and elemental analysis data, the formula structures are suggested. The conductivity, elemental analysis data and compositions of the complexes are given in Table 1.

**Table 1: Elemental analysis and molar conductance of the complexes.**

Complex (Molecular formula)	F. Wt	$\Lambda_m$ $\Omega^{-1}\text{cm}^2\text{mol}^{-1}$	Element Analysis, Found (Calculated)%				
			C	H	N	M	Cl
[Co(phen)(PC).2H <sub>2</sub> O]Cl <sub>2</sub> (C <sub>20</sub> H <sub>21</sub> Cl <sub>2</sub> N <sub>3</sub> CoO <sub>4</sub> )	497.24	121	48.10 (48.31)	3.99 (4.26)	8.61 (8.45)	11.52 (11.85)	14.25 (14.26)
[Ni(phen)(PC).2H <sub>2</sub> O]Cl <sub>2</sub> (C <sub>20</sub> H <sub>21</sub> Cl <sub>2</sub> N <sub>3</sub> NiO <sub>4</sub> )	497.00	144	48.41 (48.33)	4.21 (4.25)	8.25 (8.45)	12.01 (11.80)	14.40 (14.26)
[Cu(phen)(PC).2H <sub>2</sub> O]Cl <sub>2</sub> (C <sub>20</sub> H <sub>21</sub> Cl <sub>2</sub> N <sub>3</sub> CuO <sub>4</sub> )	501.85	135	47.77 (47.86)	3.99 (4.21)	8.50 (8.37)	12.55 (12.66)	14.00 (14.12)

### Molar Conductance

The molar conductance values of the synthetic complexes obtained in DMSO as a solvent at room temperature are listed in Table 1. The results showed that the Co (II), Ni(II) and Cu(II) complexes with 1,10-phenanthroline and paracetamol have a molar conductance of 121, 144 and 135  $\Omega^{-1} \text{ mol}^{-1} \text{ cm}^2$ , respectively. It is obvious from this data that these chelates are ionic in nature and of the type 1:2 electrolytes<sup>[20]</sup>.

### Infrared Spectra

In the investigated complexes, paracetamol behaves as neutral bidentate molecule, through the oxygen atom of the carbonyl group and the nitrogen atom of the amide group (O and N donor atoms). The metal ion is thus coordinated to two ligands, 1,10-phenanthroline molecule and paracetamol molecule. The assignments of IR bands are summarized in Table 2. A broad band in the range of 3549-3154  $\text{cm}^{-1}$  for all complexes is attributed to  $\nu(\text{NH})$  in paracetamol as well as  $\nu(\text{OH})$  of the phenolic group in addition to the stretch vibration in water. Coordinated water is identified by the appearance of  $p_r$  (rocking) and  $p_w$  (wagging) at 880 and 520  $\text{cm}^{-1}$ , respectively<sup>[21]</sup>.

The strong absorption band at 1625  $\text{cm}^{-1}$  in the spectrum of free paracetamol has been assigned to the C=O stretching<sup>[22]</sup>. This band has been shifted in the spectra of the complexes that by 18-36  $\text{cm}^{-1}$ , confirming complexation to the Metal ion<sup>[23]</sup>. Further evidence for complexation is provided by a slight shift in the frequency of the in-plane bending band of the carbonyl group of paracetamol at 840–830  $\text{cm}^{-1}$ , accompanied by the disappearance of the in-plane bending bands of CNH as well as the appearance and disappearance of the stretching band and the out-of-plane wagging band of NH in the amide group<sup>[24]</sup>. The absorption band at 3325  $\text{cm}^{-1}$  of free paracetamol has been assigned to N-H stretching vibrations<sup>[22]</sup>. This band has been shifted in the spectra of the metal complexes due to coordination by 20-42  $\text{cm}^{-1}$ <sup>[25]</sup>. Based on the above observations, it was concluded that the coordination mode proceeds *via* the participation of the carbonyl-O and NH atoms of the amide group. Also, the Co(II), Ni(II) and Cu(II) complexes have a trans-configuration as indicated by the observation of only one band for each of the M-O and M-N vibrations at 672-645 and 463-439  $\text{cm}^{-1}$ , respectively<sup>[26]</sup>.

1,10-phenanthroline behaves as neutral bidentate molecule. The strong band appearing at 1134  $\text{cm}^{-1}$  is assigned to benzene and pyridine ring stretching vibrations in the free 1,10-phenanthroline<sup>[27]</sup>. This band shows a slight shift by 16-33  $\text{cm}^{-1}$  (Table 2) and a shift of  $\nu(\text{C}=\text{N})$  of 1,10-phenanthroline from 1588  $\text{cm}^{-1}$  to lower frequency in the complexes due to the coordination of the nitrogen atoms to the metal<sup>[28,29]</sup>.

### Mass Spectra

The mass spectra of Co and Ni complexes with 1,10-phenanthroline and paracetamol exhibited molecular ion peaks at  $m/e$  497.31, and 496.90, respectively, which are similar to those calculated. The mass spectrum of  $[\text{Cu}(1,10\text{-phen})(\text{paracetamol})_2\text{H}_2\text{O}]\text{Cl}_2$  complex showed the molecular ion peak at  $m/e$  501.96, which is coincident with the formula weight  $m/e$  465.68 after releasing the coordinated two water molecules from the complex due to temperature elevation throughout the measurement process, supporting thus the identity of the structure.

### Magnetic and Electronic Spectral Studies

The Co(II) complex (Figure 1) exhibited two bands at 18518 and 16000  $\text{cm}^{-1}$ , which were consistent with octahedral geometry and were assigned to  ${}^4T_{1g} \rightarrow {}^4T_{1g}(P)$  ( $\nu_3$ ) and  ${}^4T_{1g} \rightarrow {}^4A_{2g}$  ( $\nu_2$ ) transitions, respectively<sup>[30]</sup>. An observed moment of 4.77 B.M. is supportive of octahedral geometry, since moments in the range 4.7-5.2 B.M. were reported for octahedral Co(II) complexes<sup>[31]</sup>. Furthermore, the Ni(II) complex (Figure 2) showed an absorption band at 16393  $\text{cm}^{-1}$  typical of octahedral geometry, assigned to the  ${}^3A_{2g} \rightarrow {}^3T_{1g}(P)$  ( $\nu_3$ ) transition<sup>[30]</sup>. An observed moment of 3.09 B.M. supports this conclusion, since moments in the range 2.9-3.3 B.M. were reported<sup>[31]</sup>. The Cu(II) (Figure 3) had an absorption band at 13333  $\text{cm}^{-1}$  assigned to  ${}^2E_g \rightarrow {}^2T_{2g}$ . The broadness of the band could be attributed to the overlapping of several bands as a result of strong Jahn-Teller distortion expected in a  $d^9$  ion<sup>[32]</sup>. The magnetic moment values of these complexes (1.68 B.M.) were found to be within the range reported for the  $d^9$ -system containing one unpaired electron<sup>[33]</sup>. The results are shown in Table 3. The Co and Ni complexes show broad and intense absorption bands at 690 and 775 nm, respectively. This absorption is ascribed to the spin-allowed metal-to-ligand charge transfer transitions (MLCT)<sup>[34]</sup>.

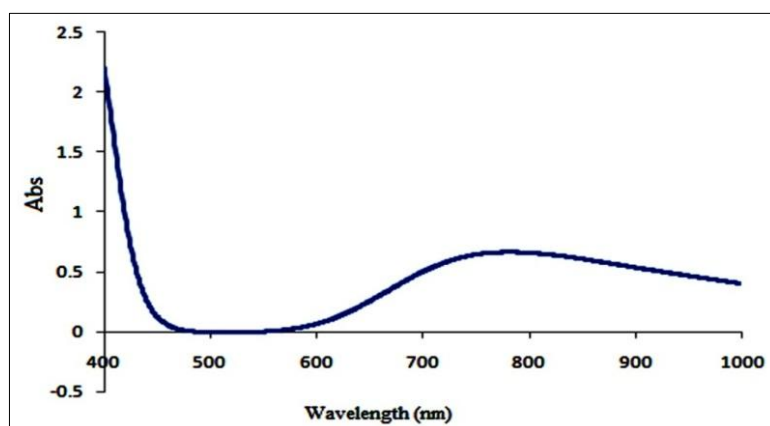
Table 2. Significant IR spectral bands ( $\text{cm}^{-1}$ ) of 1,10-phenanthroline, paracetamol ligands and their complexes.

1,10-phenanthroline	paracetamol	[Co(phen)(PC).2H <sub>2</sub> O] ]Cl <sub>2</sub>	[Ni((phen)(PC).2H <sub>2</sub> O) ]Cl <sub>2</sub>	[Cu(phen)(PC).2H <sub>2</sub> O O]Cl <sub>2</sub>	Assignment
-	3325 <sup>s</sup>	3545 <sup>w</sup>	3567 <sup>w</sup>	3548 <sup>w</sup>	v(NH)
-	3162 <sup>br</sup>	3433 <sup>br</sup>	3376 <sup>br</sup>	3434 <sup>br</sup>	v(OH) and H <sub>2</sub> O
1134 <sup>s</sup>	-	1150 <sup>m</sup>	1161 <sup>m</sup>	1167 <sup>m</sup>	Benzene ring + pyridine ring stretch
3010 <sup>m</sup>	3002 <sup>w</sup>	3018 <sup>w</sup>	3009 <sup>w</sup>	3008 <sup>w</sup>	v CH-arom.
-	2878 <sup>w</sup>	2880 <sup>w</sup>	2880 <sup>w</sup>	2875 <sup>w</sup>	v CH-aliph.
-	1165 <sup>m</sup>	1150 <sup>m</sup>	1148 <sup>m</sup>	1143 <sup>m</sup>	v(C-N)
-	1625 <sup>s</sup>	1661 <sup>m</sup>	1643 <sup>m</sup>	1655 <sup>m</sup>	v(C=O)
1588 <sup>s</sup>	-	1534 <sup>m</sup>	1561 <sup>m</sup>	1545 <sup>m</sup>	v(C=N)
-	-	645 <sup>w</sup>	651 <sup>w</sup>	672 <sup>w</sup>	v(M-O)
-	-	439 <sup>w</sup>	451 <sup>w</sup>	463 <sup>w</sup>	v(M-N)

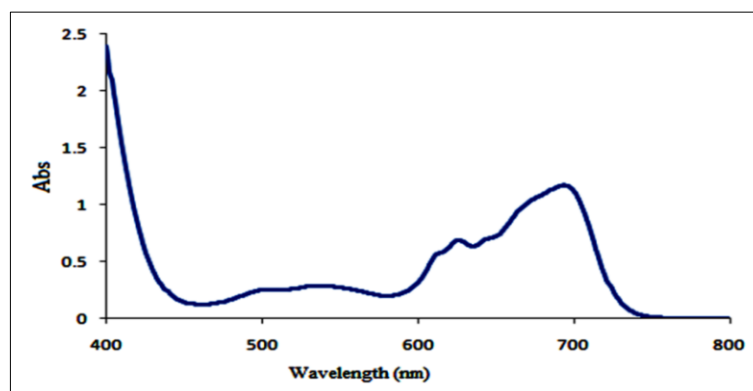
s = strong, m = medium, br = broad, w = weak.

**Table 3. Magnetic moment and electronic spectral data for the 1,10-phenanthroline, paracetamol complexes.**

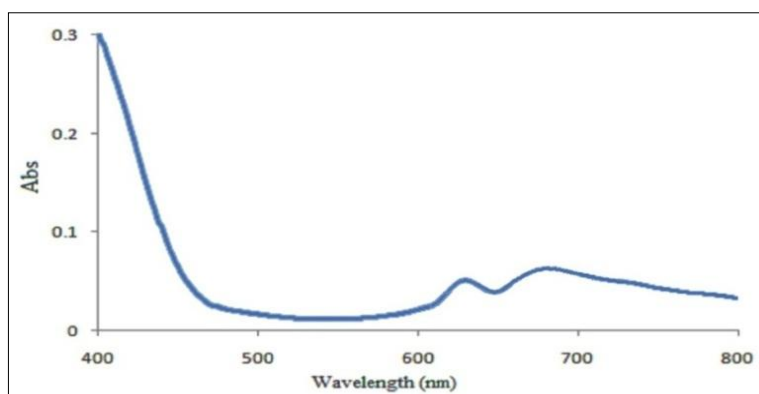
Complex	$\mu_{\text{eff}}$ (B.M.)	d-d transition band ( $\text{cm}^{-1}$ )	Assignments	Supposed structure
[Co(phen)(PC).2H <sub>2</sub> O]Cl <sub>2</sub>	4.77	18518 16000	${}^4T_{1g} \rightarrow {}^4T_{1g}(P)$ ${}^4T_{1g} \rightarrow {}^4A_{2g}$	Octahedral
[Ni(phen)(PC).2H <sub>2</sub> O]Cl <sub>2</sub>	3.09	16393	${}^3A_{2g} \rightarrow {}^3T_{1g}$	Octahedral
[Cu(phen)(PC).2H <sub>2</sub> O]Cl <sub>2</sub>	1.68	13333	${}^2E_g \rightarrow {}^2T_{2g}$	Distorted Octahedral



**Figure 1. UV-visible spectrum of [Co(phen)(PC).2H<sub>2</sub>O]Cl<sub>2</sub> complex.**



**Figure 2. UV-visible spectrum of [Ni(phen)(PC).2H<sub>2</sub>O]Cl<sub>2</sub> complex.**



**Figure 3. UV-visible spectrum of [Cu(phen)(PC).2H<sub>2</sub>O]Cl<sub>2</sub> complex.**

## Thermal Analysis

### Kinetic and Thermodynamic Parameters

The kinetic and thermodynamic parameters were determined by non-isothermal methods. The non-isothermal kinetic analysis for the thermal decomposition of all ligands and complexes in this work was carried out by the application of the Coats-Redfern method<sup>[35]</sup>. The kinetic parameters were evaluated for all stages (Table 4). Kinetic studies were applied for the decomposition stages that occur within a temperature range, resulting in a TG curve providing enough data to be collected. The kinetic parameters ( $T_i$ ,  $T_f$ ,  $\Delta m$ ,  $E_a$  and  $n$ ) were calculated according to the Coats-Redfern method<sup>[36]</sup>, with assistance of the Horowitz-Metzger method<sup>[37]</sup>, as shown in Table 5.

The thermal degradation of [Ni(phen)(PC).2H<sub>2</sub>O]Cl<sub>2</sub> (Figure 4a) reveals three decomposition stages at 25-288, 288-484 and 484-639 °C. The elimination of two coordinated water molecules occurs endothermically with a

sharp peak corresponding to the first step (cal. 7.25%, found 7.20%) with  $T_{DTG}$  and  $T_{dta}$  at 152°C and 157°C, respectively. The activation energy calculated is 40 kJ.mol<sup>-1</sup> (Table 5). It is found that the release of the coordinated water molecules fairly agrees with the literature<sup>[3]</sup>. The removal of 0.5 Cl (Cal. 3.57%, found 3.60%) takes place in the second step with  $T_{DTG}$  at 439 °C and exothermic  $T_{dta}$  (Figure 4b) at 437 °C with an activation energy of 149 kJ.mol<sup>-1</sup>. The third step which appears as a big broad peak corresponds to the loss of 1.5 chloride atoms and C<sub>18.5</sub>H<sub>17</sub>N<sub>3</sub>O fragment (Cal. 70.53%, found 70.57%) with  $T_{DTG}$  (579°C) and broad exothermic  $T_{dta}$  (582°C) peak with an activation energy of 230 kJ.mol<sup>-1</sup>. The values (-162.7, 119.1 and 128.9 J.K<sup>-1</sup>.mol<sup>-1</sup>), (36.4, 143.1 and 222.9 kJ.mol<sup>-1</sup>) and (105.5, 58.3 and 113.1 kJ.mol<sup>-1</sup>) are their entropy, enthalpy and free energy of activation, respectively. The ill-defined residue at the end of the decomposition reaction is NiO and 1.5 C (Cal. 18.65%, found 18.63%).

**Table 4. Characteristic parameters of thermal decomposition (10°C min<sup>-1</sup>) for Ni(II) complex with 1,10-phenanthroline and paracetamol.**

Comp.	Step	TGA			DTA			Reaction
		$\Delta m$ % Found (calc.)	$T_i$ /C°	$T_f$ /C°	$T_{DTG}$	$T_{dta}$	Heat	
[Ni(phen)(PC).2H <sub>2</sub> O]Cl <sub>2</sub>	1	7.20 (7.25)	25	288	152	157	endo	-2 H <sub>2</sub> O
	2	3.60 (3.57)	288	484	439	437	exo	-0.5 Cl
	3	70.57 (70.53)	484	639	579	582	exo	-[1.5Cl + C <sub>18.5</sub> H <sub>17</sub> N <sub>3</sub> O]
Final residue (NiO + 1.5C): 18.63% (18.65)								

endo = endothermic peak, exo = exothermic peak

**Table 5. Kinetic and thermodynamic parameters of the thermal decomposition of Ni(II) complex with 1,10-phenanthroline and paracetamol.**

Comp.	Step	r	n	$Z$ s <sup>-1</sup>	$T_{max}$ K	$E_a$ kJ.mol <sup>-1</sup>	$\Delta S^*$ J.K <sup>-1</sup> .mol <sup>-1</sup>	$\Delta H^*$ kJ.mol <sup>-1</sup>	$\Delta G^*$ kJ.mol <sup>-1</sup>
[Ni(phen)(PC).2H <sub>2</sub> O]Cl <sub>2</sub>	1	0.9869	1.1	2.8x10 <sup>4</sup>	425	40	-162.7	36.4	105.5
	2	0.9900	1.8	3.7x10 <sup>23</sup>	712	149	119.1	143.1	58.3
	3	0.9986	2.1	3.3x10 <sup>6</sup>	852	230	128.9	222.9	113.1

r = correlation coefficient of the linear plot, n=order of reaction, Z = pre-exponential factor.

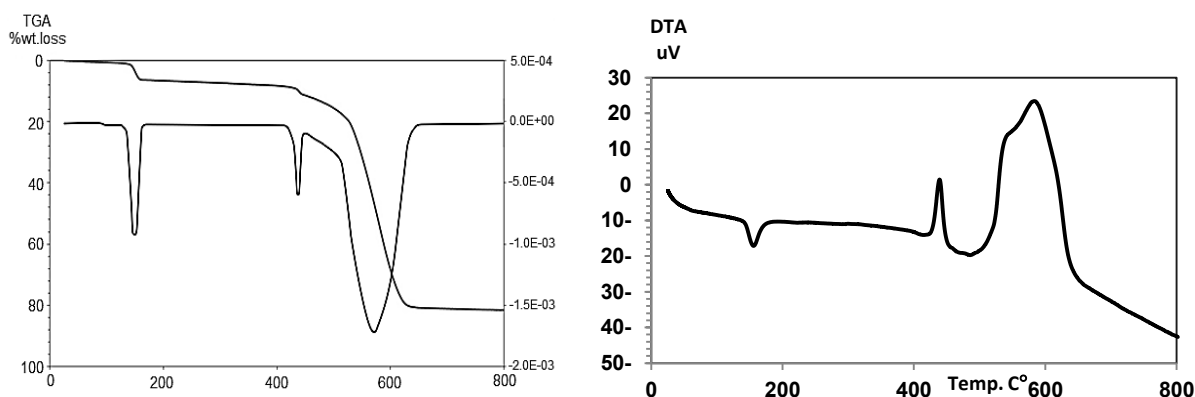


Figure 4: (a) TG and DTG, and (b) DTA thermograms of  $[\text{Ni}(\text{phen})(\text{PC}).2\text{H}_2\text{O}]\text{Cl}_2$  complex.

### Antimicrobial Studies

*In vitro* biocidal activity results of 1,10-phenanthroline and paracetamol-free ligands as well as their metal complexes clearly show that the compounds have antibacterial activity against the tested organisms in the presence of standard gentamicin as antibacterial agent. The results of highest-to-lowest effect are summarized in Table 6.

Lowest activity of drugs was attributed to a probable lipophilic nature, which made permeation through lipid bacteria membrane impossible<sup>[38]</sup>. Generally, the metal(II) complexes were mostly more effective than the metal-free drugs due to chelation, which increases lipophilic character, favoring its permeation through lipid layers of the bacterial membrane as documented<sup>[39]</sup>.

In general, because metal can undergo ligand exchanges, metal complexes are pro-drugs. Ligand substitution can activate the metal complex toward binding to target molecules. It should be recognized that a metal is not just a metal, where the metal ion plus its ligand determine the biological activity<sup>[40]</sup>. In our paper, paracetamol has not given positive results with the tested bacteria. 1,10-phenanthroline ligand has a slightly more antibiotic activity than its complexes against the tested microorganisms under identical experimental conditions. The best activity of 1,10-phenanthroline was attributed to its ability to form hydrogen bond with the cellular content of the bacteria, thereby causing the death of the organism<sup>[41]</sup>. The complex of  $[\text{Cu}(\text{phen})(\text{PC}).2\text{H}_2\text{O}]\text{Cl}_2$  showed highest activity against selected strains of microorganisms due to the presence of copper(II), which is found in living organisms and is an essential cofactor in a number of

enzymes. it is also involved in the function of several proteins and physiological processes, such as cell metabolism, mitochondrial respiration, antioxidation processes and synthesis of some active compounds<sup>[42,43]</sup>. Additionally, copper as a redox-active metal may form stable complexes with chelate ligands containing donor atoms, such as nitrogen, sulfur or oxygen<sup>[43]</sup>. Other complexities are almost non-existent, but what makes the result of the activity very light is the presence of nitrogen and oxygen. It is known that chelation tends to make ligands act as more powerful and potent bactericidal agents<sup>[44]</sup>. The complexes show minor activity against selected strains of microorganisms. It has been suggested that ligands with nitrogen and oxygen donor system inhibit enzyme activity. Coordination reduces the polarity of the metal ion mainly because of the partial sharing of its positive charge with the donor groups within the chelating system<sup>[45-47]</sup>.



**Table 6. Effect of the ligands and their complexes on the growth of bacteria (zone of inhibition in mm).**

Compound (1000 µg/ml)	Bacteria			
	gram-positive		gram-negative	
	<i>Staphylococcus aureus</i>	<i>Bacillus</i>	<i>Pseudomonas Aeruginosa</i>	<i>Escherichia coli</i>
1,10-phenanthroline	++	+++	++	++
paracetamol	-	-	-	-
[Co(phen)(PC).2H <sub>2</sub> O]Cl <sub>2</sub>	-	+++	+	++
[Ni(phen)(PC).2H <sub>2</sub> O]Cl <sub>2</sub>	-	+	-	-
[Cu(phen)(PC).2H <sub>2</sub> O]Cl <sub>2</sub>	++	++	++	++
Gentamicin 120 µg/ml	++	+	++	+

(-) No zone of inhibition was observed.

Moderately sensitive, (+) Inhibition zone of 2-5.

Sensitive, (++) Inhibition zone of 6-10.

Highly sensitive, (+++) Inhibition zone of 11-15.

## Conclusions

In this study, we report the synthesis, characterization and antimicrobial studies of Co(II), Ni(II) and Cu(II) complexes of 1,10-phenanthroline (L<sub>1</sub>) and paracetamol (L<sub>2</sub>). The complexes are formulated as [M L<sub>1</sub> L<sub>2</sub>.2H<sub>2</sub>O]Cl<sub>2</sub>. They are six coordinated complexes. The complexes were characterized by elemental analysis, mass, electronic and IR spectroscopy.

Spectroscopic analyses confirmed the paracetamol coordination through the carbonyl group and nitrogen atom of amide group. Also 1,10-phenanthroline was proposed to be a bidentate ligand and coordinated through N atoms. In the thermal study, kinetic and thermodynamic parameters were estimated from the DTG curves. The antibacterial screening of complexes showed varied activities.

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