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Metal Pharmacologically Active Agents: Mode of New Tridentate Glycine Amino Acid with Diketone (Benzil) and 4-Aminoantipyrine Complexes

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Abstract

The paper presents the synthesis of complex combinations of Co(II), Ni(II), Cu(II), and Cd(II) with Schiff base obtained by the condensation reaction of 4-aminoantipyrine with benzil (diketone) and glycine amino acid. All complexes via direct reactions of metal ions with ligand in (1:2) molar ratio respectively. These complexes have been characterized via a variety of physiochemical techniques include elemental analyses (CHN), ^{1}H-NMR, (IR), (UV-Vis), molar conductance, magnetic moment measurement, thermal gravimetric analysis (TGA), XRD, and computational chemistry. Infrared spectra; shows that the ligand behaves as a tridentate ligand and is coordinated through N, N, O as a donor atoms sequence towards the metal ions. Consequently, all the complexes showed octahedral shapes. Finally, the synthesized Schiff base and metal complexes were screened for their biological activity against bacterial species,one gram-positive bacteria (*Staphylococcus aureus*), and three gram-negative bacteria *Pseudomonas aereuginosa*, *Escherichia coli,* and *Klebsiella pneumonia*. These compounds show the different activity of inhibition on the growth of the bacteria respectively.

Keywords: Glycine amino acid, Schiff base 4-Amino antipyrine, Metalcomplexes, Benzil, Antibacterial.

1. Introduction

Due to their wide spectrum of biological activities, heterocyclic complexes continues to dominate the area of medicinal chemistry. Antipyrine derivatives and their metal complexes have wide applications in biological activities [1,2] due to, their interesting structural features [3,4]. Subsequently, it is reported that 4-aminoantipyrine Schiff bases and their metal complexes possess numerous biological applications that include antifungal, antibacterial, analgesic, antipyretic and anti-inflammatory [5-9]. Transition metal complexes of pyrazole derivatives have received more attention as beneficial anti-cancer agents [10,11]. On the other side coumarin derivatives, well-known fluorescent molecules, also possess a wide range of biological activities viz. antimicrobial, anti-allergic, anti-inflammatory, antitumor, etc. [12-14]. Coumarin derivatives have been found useful in the treatment of thehuman immune deficiency virus [15,16]. In vitro and in vivo studies have suggested the possible use of coumarins in the treatment of cancer as well [17]. Formation of coordination bond brings extensive changes in biological properties of the ligand and also in metal ions [18]. Worth to mention that chelation can cure many diseases. Very recently we have reported the biological importance of different structural groups including coumarins and their metal complexes [19]. Schiff bases also have antimicrobial activities and functional importance in medicinal chemistry [20]. Spectroscopic ally active metal centres with stable, inert, and non-toxic nature are exceptionally valuable in biological systems [21]. In this work primary amino group of 4-antipyrine is made to react with a benzil and the product condensation with glycine amino acid. Then incorporating an azomethine and carboxylic groups in the molecule which were further reacted with Co(II), Ni(II), Cu(II), and Cd(II) metal ions to form respective metal complexes. These newly synthesized Schiff bases and their metal complexes were characterized by various spectroscopic techniques. Selected newly synthesized compounds have been evaluated for their various biological properties.

Experimental

Materials and Methods

2.1. Chemicals and Instrumentations

All the chemicals were supplied by (BHD, Fluke and Sigma Aldrich). The electro thermal melting point

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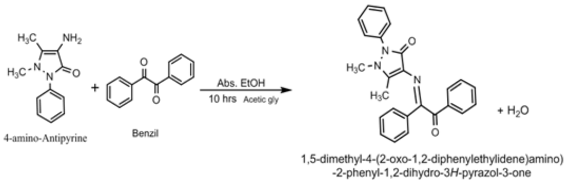
modern 9300 was used to measure the melting point of the ligand and its complexes. Molar electrical was measured in DMF (10^{-3}M) conductivity meter (model 4510–jenway). C, H, and N analysis was carried using PerkinElmer, (USA 2400-II). Electronic spectra was recorded in DMF(10^{-3}M) on Shimadzu spectrophotometer double beam model 1700.FTIR spectra were recorded FTIR spectrophotometer (Shimadzu) with range of wave number 4000-400cm^{-1}. The ^{1}H-NMR spectrometer DMSO-d^6 as a solvent as well as TMS an internal reference standard (Shimadzu) aVance500 MHz. Magnetic susceptibility measurements were carried out on a balance magnetic susceptibility of the complexes is measured by Guoy balance using Hg[Co(NCS)$_4$] as a calibrant at room temperature and diamagnetic correction have been made by Pascal'sconstants by Citizen Balance (at room temperature). Molar susceptibilities were corrected using Pascal constant absorption spectrophotometer (flame and graphite analysis) in the scientific researchcentre. The complexes were studied by thermogravimetry (TG-DSC) in a static air atmosphere, with a sample using a balance recorded on a TGA Mattler-Touledo the XRD powder pattern of the ligand and Co(II) complex it is collected using a Philips X'Pert Pro diffract meter.

2.2. Synthesis of the Schiff base Benzil- 4-aminoantipyrine

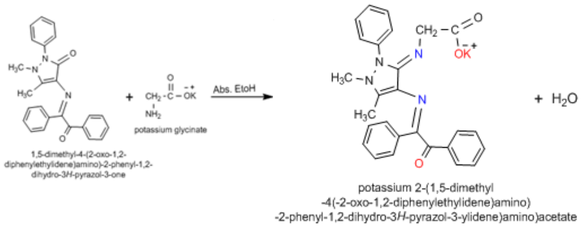
A solution of 4-Aminoantipyrine (0.02 mol) was dissolved in 10ml of ethanol in a beaker and added to a solution of benzil (0.02mol) which was dissolved in50ml of ethanol in a round-bottomed flask. These two mixtures were mixed and reflux with stirring for 10hrs. [22,23]. The mixture was cooled to room temperature and pour into crushed ice. Orange precipitate obtained was isolated upon filtration before it was crystallized using ethanol via slow evaporation technique.



Scheme 1: Synthesis of the Schiff base benzil-4-aminoantipyrine.

2.3. Formulation of new fangled Schiff base Ligand (K$_4$-ABin-Gly)

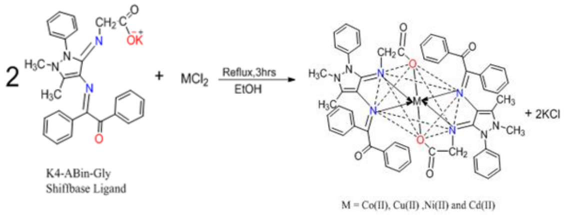
The amino acid glycine (0.01 mol) dissolved in a 1:1 water–ethanol mixture (40 ml) was added to a hot ethanolic solution (30 ml) of KOH (0.01 mol) the resulting potassium glycinate salt solution was stirred to obtain a homogeneous solution [19]. Then to this solution was added drop-wise an ethanolic solutionof1,5-dimethyl-4-(2-oxo-1,2diphenylethylidene)amino)-2-phenyl-1,2-dihydro-3H-pyrazol-3-one (3.21g, 0.01 mol). The resultant mixture was refluxed for 3 hrs. Dark yellow colored plate like crystalline product (K4-ABin-Gly) Schiff base formed was filtered and recrystallized from ethanol [24,25].



Scheme 2: Formulation of new fangled Schiff base ligand (K $_4$-ABin-Gly).

2.4. Synthesis of Co^{II}, Ni^{II}, Cu^{II}, and Cd^{II} complexes

To an alcoholic solution (15 ml) of (1mmol) of $CoCl_2.6H_2O/NiCl_2.6H_2O/CuCl_2.2H_2O/CdCl.6H_2O$ was added an alcoholic solution (25 ml) of Schiff bases (K4-ABin-Gly) (2 mmol) ligand and refluxed on awater bath for 2 hrs. [22,23]. The separated complex was filtered, washedthoroughly with water, ethanol, ether,and finally dried in vacuum overfused $CaCl_2$.



Scheme 3: Synthesis of Co^{II}, Ni ^{II},Cu^{II}, and Cd ^{II} complexes.

2. Results and discussion:

General

Schiff base ligand (K$_4$-ABin-Gly) is a dark yellow crystal, that is partiallysoluble in water and soluble in solvents. Reacting thisligand with the metallic ions has different color crystals. All complexes arereasonably air-stable, insoluble in water, but soluble in most organic solvents such as dimethylsulfoxide, dimethylformamide, chloroform, acetone, methanol, and ethanol.

3.1.Physical Characteristics and Elemental Investigation

The physical characteristics and outcomes taken from C.H.N. investigation and metal substances of the arranged complexes are explained in Table1. All the metal(II) complexes were dissolved in DMF for the molar conductivities measurement at [10^{-3}M] of room temperature. The lower conductance values (7.8–10.6 ohm $^{-1}$ cm^2 mol^{-1}) of the complexes support their non-electrolytic nature (Table3). The investigation data had been acceptable with planned magnetic studies. The molecular procedure of the ligand and its metal complexes had been proposed in relation to these data jointly with those acquired from spectral in addition to the magnetic susceptibility of metal complexes and molar conductivities. Every (1:2) metal to ligand solid complexes have been separated and showing that the complexes have [1:2] metal:ligand stoichiometry of the type [1M:2L] where in (K 4-ABin-Gly) acts as a tridentate ligand.

3.2. IR spectra

The IR spectra provide valuable information regarding the coordinating sites of ligand. The IR spectra of the complexes were compared with that of the free ligand (K_4-ABin-Gly) to determine the changes that might have taken place during the complexation. A comparative study of the IR spectra of ligand and its metal complexes reveals that certain peaks are common and therefore, only important peaks, which have been either shifted or newly appeared are discussed. The spectrum of free Schiff base (K_4-ABin-Gly) ligand, showed a band of the –C=N– group in the region of 1699cm^{-1} (vs.) which was shifted to lower frequencies in the spectra of all the complexes (1645–1647cm^{-1}) indicating the involvement of –C=N– nitrogen in coordination to the metal ion [22,23]. Coordination of the Schiff base to the metal through the nitrogen atom was expected to reduce the electron density in the azomethine link and to lower the $\boldsymbol{\nu}$(C=N) vibration $\boldsymbol{\nu}$asmy (COO^{-}) band of free ligand (K_4-ABin-Gly) observed at 1595cm^{-1} was shifted to lower wave number in the spectra of metal complexes 1581–1591cm^{-1}. The $\boldsymbol{\nu}$smy (COO^{-}) band of free ligand (K_4-ABin-Gly) observed at 1495cm^{-1} was shifted to lower wave number in the spectra of metal complexes 1452–1463cm^{-1}, representing coordination of carboxylic acid group with metal ion through the oxygen atom [26]. Assignment of the proposed coordination sites was further supported by the appearance of medium bands at 505–530 cm^{-1} and 420–440 cm^{-1} which could be attributed to the$\boldsymbol{\nu}$(M–N) and $\boldsymbol{\nu}$(M–O) [24,25] vibrations respectively. The IR spectrum of (K_4-ABin-Gly) ligand and Ni-complex shown in Figures1,2 and Table 2.

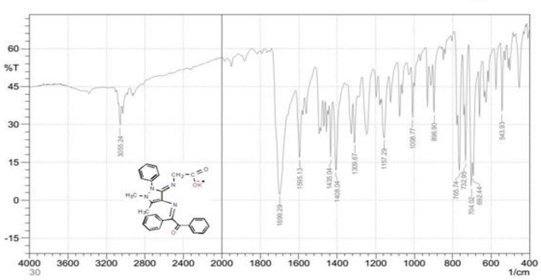


Fig.1: Infrared spectrum of (K_4-ABin-Gly) Ligand.

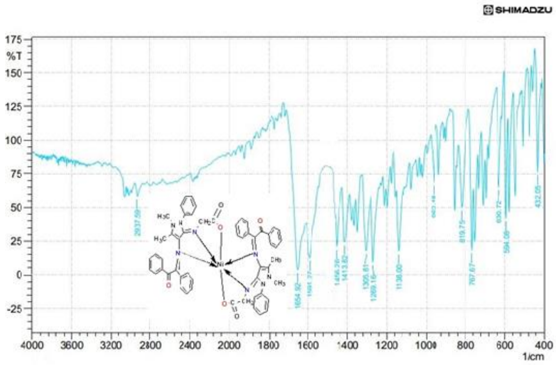
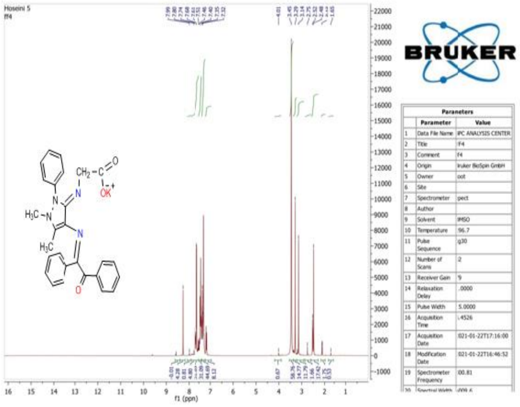


Fig.2: Infrared spectrum of complex [Ni(K_4-ABin-Gly)$_2$].

3.3. ^{1}H-NMR spectra

The spectra of ligand was recorded in (DMSO-d^6) at room temperature using tetramethylsilane (TMS) as internal and spectrum was shown in Figure 3.^{1}H-NMR spectrum of the Schiff base ligand shows a peak at (7.99 – 7.32δ ppm, multiplet 9H) aromatic the ligand ^{1}H-NMR spectrum of (K_4-ABin-Gly) recorded also shows the following signals:(2.12 δppm -CH_3) [22, 23] (3.29δppm -N-CH_3)(2.75δ ppm- 1H singlet - CH-COO-) of glycine group respectively. All the protons were to be in their expected region. The conclusions drawn from these studies offer additional support to the mode of bonding discussed in their IR spectra the number of protons.



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18	Modification Date	021-01-22T16:46:52
19	Spectrometer Frequency	00.81

Fig. 3. ^{1}H-NMR spectrum of(K_4-ABin-Gly) ligand.

3.4. Magnetic measurements

The Co(II) complex has a magnetic moment of 4.62B.M. (Table 3), which is in agreement with the value for high spin octahedral Co(II) complexes [27], the present Ni(II) complex shows a magnetic moment value of 3.08B.M.within the range of 2.9–3.3B.M. [28] suggesting an octahedral environment. The Cu(II) complex shows a magnetic moment value of 2.09B.M., higher than the spin-only value 1.73B.M. expected for one unpaired electron, monomeric and consistent with a distorted octahedral geometry. The Cd(II) complex is diamagnetic and according to the empirical formulae of these complexes, an octahedral geometry [29].

Table 1:Elemental analysis and some physical properties for ligand (K_4-AMetB-Gly) and its chelate.

Compound	**ν** C=N	**ν** C- O	**ν** COO^-asmy.	**ν** COO^-smy.	**ν** M − N	**ν**M − O
(K_4-ABin-Gly)	1699	1157	1595	1435	--	--
[Co (K_4-ABin-Gly)$_2$]	1645	1128	1581	1463	440	507
[Ni (K_4-ABin-Gly)$_2$]	1654	1138	1591	1456	432	530
[Cu (K_4-ABin-Gly)$_2$]	1645	1134	1583	1452	420	501
[Cd (K_4-ABin-Gly)$_2$]	1647	1132	1587	1456	425	505

Table 2: The Infrared (IR) spectrums of ligand and its chelate complexes.

Compounds	Color	M.p. (°C)	Yeild %	Mol. formula (mol. Wt)	Found (calc)%			
					C	H	N	M
K_4-ABin-Gly	Orange	183	83	$C_{27}H_{23}KN_4O_3$ (490.14)	66.11 (66.09)	4.73 (4.75)	11.42 (11.40)	--
[Co (K_4-ABin-Gly)$_2$]	Dark Green	191	71	$C_{54}H_{46}CoN_8O_6$ (961.29)	67.43 (67.41)	4. 82 (4.80)	11.65 (11.69)	6.13 (6.10)
[Ni (K_4-ABin-Gly)$_2$]	Light Green	198	73	$C_{54}H_{46}NiN_8O_6$ (960.29)	67.44 (67.40)	4.82 (4.78)	11.65 (11.69)	6.10 (6.18)
[Cu (K_4-ABin-Gly)$_2$]	Dark brown	201	72	$C_{54}H_{46}CuN_8O_6$ (965.28)	67.10 (67.14)	4.80 (4.77)	11.59 (11.57)	6.67 (6.62)
[Cd (K_4-ABin-Gly)$_2$]	Lemon yellow	171	70	$C_{54}H_{46}CdN_8O_6$ (1016.26)	63.87 (63.89)	4.57 (4.53)	11.04 (11.10)	11.07 (11.02)

Table 3: The electronic spectrums of ligand and its chelate complexes, magnetic susceptibility, and values of molar conductance of complexes.

Compounds	Band position, cm^{-1}	Transition	Ω^{-1} cm^2mol^{-1}	Suggested Geometry	μeff (B.M.)
(K_4-ABin-Gly)	40485 23202	$\pi \rightarrow \pi^*$ $n \rightarrow \pi^*$	--	--	--
[Co (K_4-ABin-Gly) $_2$]	39063 33670 13003 19920	Center ligand Center ligand $^4T_{1}g \rightarrow {}^4A_{2}g(F)$ $^4T_{1}g \rightarrow {}^4T_{1}g(P)$	8.1	Octahedral	4.62
[Ni (K_4-ABin-Gly) $_2$]	11498 14239 21074	$^3A_{2}g \rightarrow {}^3T_{2}g(F)$ $^3A_{2}g \rightarrow {}^3T_{1}g(F)$ $^3A_{2}g \rightarrow {}^3T_{1}g(P)$	10.6	Octahedral	3.03
[Cu (K_4-ABin-Gly) $_2$]	18865	$^2B_{1}g \rightarrow {}^2Eg$	9.0	Octahedral	2.03
[Cd (K_4-ABin-Gly) $_2$]	21008	d $\pi(Cd)^{+2} \rightarrow \pi^*(L)$	7.8	Octahedral	Dia

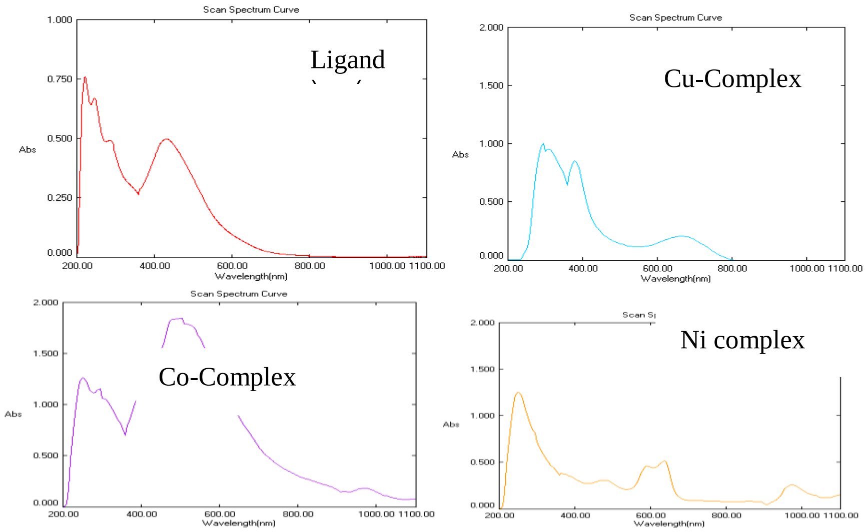


Fig.4. Spectrum U.V – Vis of ligand and its complexes.

3.5. Electronic spectra

The ligand (K_4-ABin-Gly) free donor observable absorption bands at 40485and 23202 cm^{-1} assigned to $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ transitions, respectively. The absorption bands of Co(II), Ni(II), and Cu(II) complexes shifted to higher values and the appearance of novel bands is due to complexation behaviour. The appearance of new bands for Co(II), Ni(II), and Cu(II) complexes which may be assigned to ligand-metal charge transfer [29], spectrums of ligand (K_4-ABin-Gly) and its complexes Co(II), Ni(II), and Cu(II) in DMF [10^{-3}M] have been examined and the spectral details have been depicted in Table 3.

3.6. XRD analysis

Powder XRD patterns of Schiff base [Co (K_4-ABin-Gly) $_2$] complex were recorded in the ranges of 2θ =11.60-55.6523° and is depicted in (Figure 5-b) XRD data indicate that the complex system has a highly poly crystalline nature. The most prominent peak was located at $2\ \theta$ =20-35° and it has 100% intensity than other diffraction peaks [26,27]. All the ligand peaks (Figure5-a) were observed in the XRD data of metal complexes with decreased intensities. In addition to this metal complexes also show some new peaks around 20.0434, 24.4639, 30.3032, 32.1467, 44.3233, 45.6276,45.6276, 47.5331, 48.7115, 51.5774 the crystallite sizes were calculated using Debye Scherer's formula as given in equation $D=0.9\lambda/\beta Cos\theta$, where is Bragg diffraction angle at peak position in degrees; is full width at half maximum of the peak position in radian; λ is the wave length of Cu-K used [30,31] Table 4: complex[Co(K_4-ABin-Gly)$_2$] used of tare X-perthigh score software package.

Table 4: Powder XRD date of [Co (K_4-ABin-Gly) $_2$] complex.

Complex- [Co (K_4-ABin-Gly) $_2$]	
Molecular Formula	$C_{54}H_{46}CoN_8O_6$
Molecular weight	961.29g/mol
Crystal system	Hexagonal
Space group	P.322
Unit cell dimensions (A°)	a=4.9134A° α = 90 (10°) b= 4.91341A° ß = 90 (10°) c= 5.4052A° γ = 120 (10°)
Radiation	Cu α rotating anode
Cell Volume (A^{o3})	113.0X10^{-3} °A
Z	3
Crystallite Size	39.08 nm-27.8
Littice Strain	0.0051 – 0.0066
Theta Range	11.6081- 55.6523θ
Index ranges	1≤ h ≤5, 1≤ k ≤ 3, 0≤ L ≤6

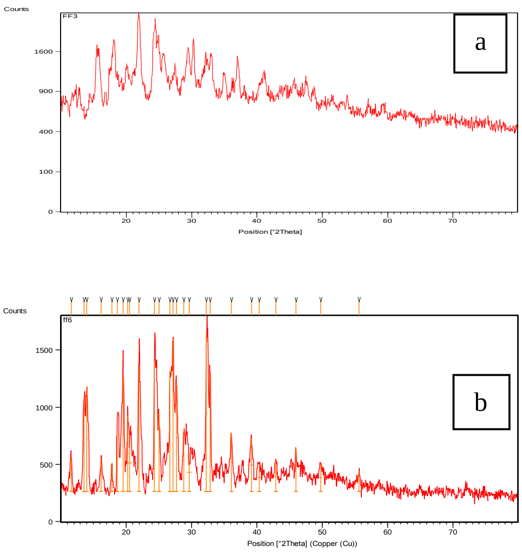


Fig.5. Powder XRD date of ligand(a) and complex. [Co (K_4-ABin-Gly) $_2$](b).

3.7. Thermogravimetric analysis

Complex[Cu(K_4-ABin-Gly)$_2$] the decomposition occurs in at least five major detectable steps (Figure 6), each step does not refer in generally to a single process but rather is reflects of two data obtained support the proposed structure and indicate that Cu- complex [21,22]. The compound suffers a mass loss of 10% at about 300C, this loss may be an evolution of CO_2 moisture again and the azomithine group of coordinated water the compound loses mass 30 % between 300-350 ^{0}Cdue loss azomithine group a mass loss of 50 % coordinated water andloss CH_3 group of amino acid and some of the pyrazole group between 400 -550 ^{0}C, the compound suffers a loss of 70% due to loss phenyl ring, some a part of the ligand and between 550-600 ^{0}C loss of 80% all part of the ligand Table 5.

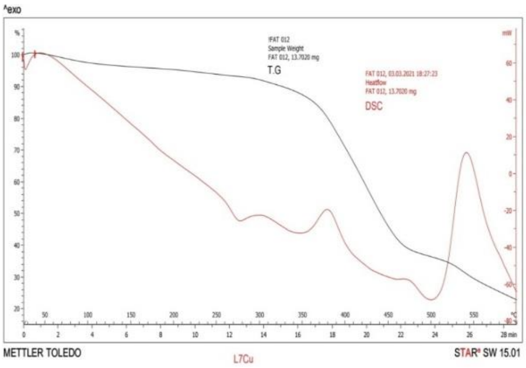


Fig.6. Graphics Date (T.G, DSC) of Cu-Complexes.

Table 5: Date (T.G, DSC) of complex [$Cu(K_4$-ABin-Gly$)_2$].

The quantum parameter	Ligand	[Cd(L)$_2$]
E (a.u.)	−1402.46	−140.88
Dipole moment (Debye)	1.37	18.022
EHOMO (eV)	−6.095	−5.61
ELUMO (eV)	−2.977	−4.096
Δ E (eV)	3.349	1.508
`χ(eV)	4.534	4.853
η (eV)	1.5590	0.7570
σ (eV)$^{-1}$	0.6411	1.3211
Pi (eV)	−4.5340	−4.853
S (eV)$^{-1}$	0.321	0.661
ω (eV)	6.593	15.559
ΔN_{max}	2.900	6.412

3.8. Molecular Parameters

Figures7 and 8 show the molecular orbital representation of the ligand (K_4-ABin-Gly) and its Cd(II) complex along with their HOMO, LUMO energies, and energy band gaps. Both the highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO) were the main orbital's that participate in chemical stability [32, 33] the HOMO represented the ability to donate an electron; LUMO as an electron acceptor represents the ability to obtain an electron. In other words, the energy of the HOMO is directly related to the ionization potential; LUMO energy is directly related to the electron affinity. Hence, these frontier energies play an important role in the electric and optical properties. The energy gap between the HOMO and LUMO energies is a critical parameter in determining molecular electrical transport properties due to providing a measurement of electron conductivity. In addition, this energy gap characterizes the molecular stability and spectroscopic properties of the molecular systems. The smaller energy gap describes a chemically soft molecule which can be easily polarizable. The HOMO-LUMO energy gap has proved to be an important tool in determining the kinetic stability and chemical reactivity of a molecule. The lower energy gap is a suitable condition where a molecule can be exited easily, whereas a higher energy gap leads to higher kinetic stability but lower chemical reactivity of the molecule. The difference between the energy gap for the ligand (K_4-ABin-Gly) reflects the presence of the complexation status. The increase in the global electrophilicity value is attributed to the highest capacity of accepted electrons, so the ligand has a highly powerful donation ability. The calculation of both absolute hardness *(η)* and absolute softness *(σ)* parameters is useful to recognize the molecular stability and reactivity.The calculations of the binding energy indicated that the increase of the value of the calculated binding energy of the complex compared to that of the free ligand (K_4-AMetB-Gly) indicated that the stability of the formed Cd(II) complex was higher than that of the free ligand (K_4-AMetB-Gly). Additional parameters such as chemical potentials *Pi*, global electrophilicityω, global softness *S*, electrophilicity index *(χ)*, and additional electronic charge ΔN_{max} were calculated for the free ligand and the Cd-complex Table 3the high ω value of both free ligand (K_4-ABin-Gly) and Cd(II) complex suggested a great chance and priority for biological activity which is further confirmed by the experimental data.The mentioned quantum chemical parameters were calculated with the help of the following equations [34, 35] and Table6:

$$\chi = \frac{-(E_{HOMO} + E_{LUMO})}{2}$$

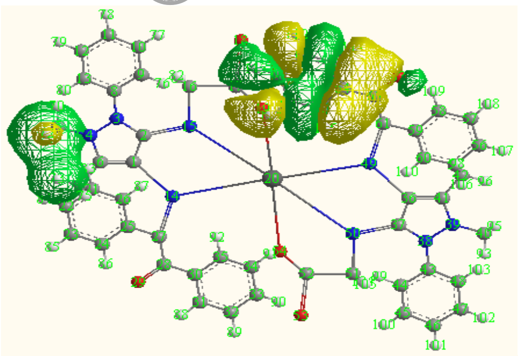
$$\Delta E = E_{LUMO} - E_{HOMO}$$

$$\eta = \frac{E_{LUMO} - E_{HOMO}}{2} \qquad \sigma = \frac{1}{\eta'}$$

$$\rho i = -\chi' \qquad S = \frac{1}{2\eta'}$$

$$\omega = \frac{Pi^2}{2\eta'} \qquad \Delta N_{max} = \frac{Pi}{\eta'}$$

Fig.7. HOMO **[Cd(4-ABin-Gly)$_2$]**



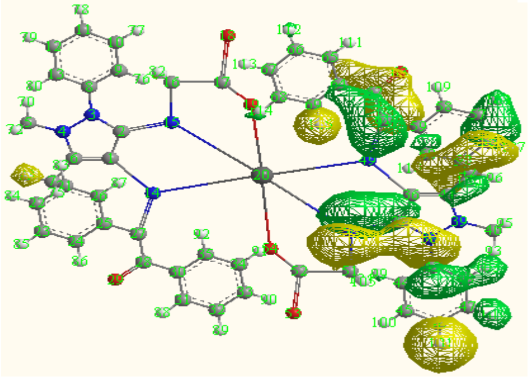


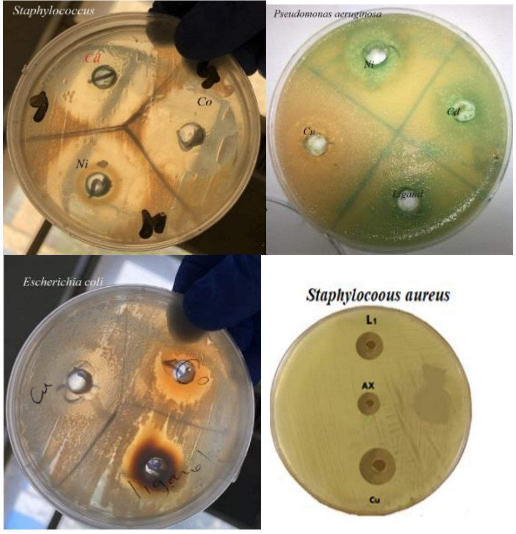
Fig.8.LUMO **[Cd(4-ABin-Gly)$_2$]**

Table 6 : The calculated quantum chemical parameters of ligand (K_4-ABin-Gly) and Cd-complex.

TG Range (°C)	Mass loss%	Assignment	Residue	DSC (°C)
28-300	10	Evolution of CO_2& moisture -Loss Coordinate H_2O-	CuO+2C	50(+) 220(+) 520(+)
300-350	30	-Loss Azomethine group		
350-400	50	-Loss CH_3 group of amino acid -Loss some of pyrazole group		
400-500	70	-Loss phenyl Ring		
500-550		and some a part of the ligand and pyrazole Ring		
550-600	80	-Lose all part of the ligand		

4. Antibacterial activity

The *in-vitro* biological screening effects of the investigated compounds were tested against the bacteria by disc diffusion method using nutrients agar as the medium and the experiment is repeated three times under similar conditions. DMSO is used as negative control and amoxicillin is used as a positive standard for data were summarized in Table 7. It is clear from Table 7 that the zone of inhibition area is much larger for metal chelates than the ligand. Such increased activity of the metalchelates can be explained based on chelation theory. On chelation, the polarity of the metal ion will be reduced to a greater extent due to the overlap of the ligand orbital. Further, it increases the delocalization of π-electrons over the whole chelate ring and enhances the lipophilicity of the complexes [36-44]. This increased lipophilicity leads to a break-down of the permeability barrier of the cell and thus retards the normal cell processes.



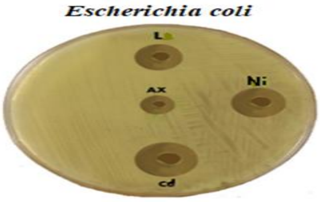


Fig. 9. Results of antibacterial screening for ligand and complexes

5. Conclusions

Five new biologically active 4-aminoantipyrine derived Schiff base ligand, potassium 2-(1,5-dimethyl-4(-2-oxo-1,2-diphenylethylidene)amino) -2-phenyl-1,2-dihydro-3H-pyrazol-3-ylidene) amino) acetate, (K_4-ABin-Gly) was synthesized and treated with different metal salts to give the corresponding metal complexes. The analytical data showed that reactions of the free ligand (K_4-AMetB-Gly) with Co(II), Ni(II), Cu(II), and Cd(II) formed complexes with chemical formulae [M(K_4-ABin-Gly$)_2$] (M=Co(II), Ni(II), Cu(II), and Cd(II)). The possible structures of the ligand and its metal-Schiff base complexes were proposed based on elemental analyses, ^{1}H-NMR, IR, and UV-Vis electronic absorption. It was concluded that the K_4-AMetB-Gly ligand behaved as a neutral tridentate ligand with N,N,O coordination sites leading to the formation of octahedral geometries for all complexes. The thermal studies for the compounds showed higher thermal stability for the complexes than that of the free ligand. This may be due to the chelation of the type and the number of solvents of crystallization in the metal complexes.The ligand and its metal complexes were screened in vitro against microorganisms (bacteria). The results of biological activity showed that the Cd(II) complex had higher antibacterial activity against the (Gram-positive) bacteria and fungi, while Co(II) had higher antibacterial activity against the (Gram-negative) bacteria compared to the free ligand and other metal complexes results of this work can show that the approach of coordinating 4-aminoantipyrine derivatives with pharmacologically interesting metals such ascobalt, copper,and could be a suitable strategy to develop novel therapeutic tools for the medical treatment.

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Table 7: Synthesized compounds against the growth of four bacteria ((MIC) in mg/ml).

Compound	*Escherichia coli*	*Pseudomonas Aeruginosa*	*Staphylococcus Aureus*	*Klebsiella pneumonia*
(K_4-ABin-Gly)	10.8	8.8	14.8	12.8
[Co (K_4-ABin-Gly) $_2$]	20.6	16.8	22.4	14.6
[Ni (K_4-ABin-Gly) $_2$]	26.2	20.4	24.6	24.8
[Cu (K_4-ABin-Gly) $_2$]	22.2	16.6	20.8	18.4
[Cd (K_4-ABin-Gly) $_2$]	26.8	20.2	28.2	24.2
Amoxicillin	10.1	6.6	8.2	9.0

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