Nano-Schiff base Ligand: Synthesis, Characterization, DFT, and Antibacterial Evaluation of Some Complexes Derived From 4-(-4-methoxybenzylidene)amino) -Antipyryl with Glycine amino acid ligand

Fatima Ali. Al wagaa 1, Sahbaa Ali.Ahmed 2
1,2Department of Chemistry, College of Sciences, University of Mosul, Mosul, Iraq.

fatima.scp62@student.uomosul.edu.iq, sahbaa-ali@uomosul.edu.iq

Abstract. Synthesized from a new Neutral tridentate N2O Schiff base 4-(4-methoxybenzylidene)amino)-1,5-dimethyl-2-phenyl-1,2-dihydro-3H-pyrazol-3-one with amino acid ligand. forms stable complexes with transition metal ions such as Co (II), Ni (II), Cu (II), and Cd (II). The complexes were characterized on the basis of their Elemental analysis, molar conductivity, magnetic susceptibility data, IR, 1H-NMR, UV-Vis, XRD, Thermal Analysis (T.G,DTA,DSC), SEM, and Calculation Theoretical studies(DFT). Were used to characterize the complexes. The ligand acts as a tridentate chelating agent, According to physicochemical and spectral results, the ligand acts as a tridentate chelating agent. IR, UV-Vis., and magnetic susceptibility measurements all refer to an octahedral geometry. The general composition of all complexes [M(L)2] is (M= Co(II), Ni(II), Cu(II) and Cd(II), L= (K4-AMetB-Gly) The studies have led to the conclusion that, The coordination sites were established to be oxygen of the carboxyl COO- and two atoms nitrogen of the azomethine (CH= N) group based on the studies. The complexes non-electrolytic nature is verified by the lower conductivity data. The antibacterial activity of the ligand and its complexes was tested against Staphylococcus aureus, Escherichia coli, Klebsiella, and Psedomonas aeruginosa, it was found that these compounds show different activity of inhibition on the growth of the bacteria.

Keywords: Glycine amino acid, 4-methoxybenzylidene, Neutral tridentate N2O complexes, 4-Aminoantipyrylne Schiff base.

1. Introduction

Pyrazole is a five-membered unsaturated heterocyclic ring with nitrogen in 1 and 2 positions. It occupies as an important place in medicinal chemistry and its derivatives are known having a wide range of biological actions namely, antidepressant [1], anticon-vulsant antimicrobial [2,3] anticancer [4], anti-inflammatory [5] and antipyretic [6] some derivatives have inhibitory actions on selected enzymes [7,8]. On computational analysis, it was discernible that pyrazole-based ligands have displayed with complex and coordinating behaviour with transitional metals [9]. activities of 4-aminoantipyryne derivatives are discussed. A part from use for relieving pain, inflammation and fever, it is used for evaluation of therapeutic activities of other drugs, through inhibition of metabolizing enzymes in liver [10]. These heterocyclic compounds are used as precursors for synthesis of novel.
hybrid molecules with critical biological activities [11,12]. Schiff base ligands derivatives from 4-aminoantipyrine derivatives behaviors are discussed. A part from pain management, inflammation, and fever, it's also used to evaluate the therapeutic benefits of other drugs by hindering metabolizing enzymes in the liver [9,10]. These heterocyclic compounds are used as precursor materials for the creation of novel hybrid molecules with essential biological processes, Schiff base ligands, which are derivatives of 4-aminoantipyrine and form stable coordination complexes with transition metal(II) ions, have served an important role in the advancement of coordination chemistry. Metal(II) complexes have also played an important role [11,12]. Metal complexes also played an important role in the history of coordination chemistry, ranging from physicochemical to biochemical studies. Schiff base ligands contain significant anticancer drugs [13]. The anticancer activity of these Schiff base metal (II) complexes reveals significant anticancer activity than the free ligands [14]. Heterocyclic compounds dominated medicinal chemistry due to their broad range of biological activities, Antipyrine and its derivatives have many biological uses [15]. Many researchers were drawn to work on the metal complexes of antipyrine derivatives due to various their intriguing structural features, in addition to their biological activities. Because of their broad range of applications in fields such as biology and chemistry, the transition metal complexes of 4-aminoantipyrine and its complexes have been extensively studied [16,17], antimicrobial, anti-allergic, anti-inflammatory, antitumor, anticancer agents in the pharmacological, scientific, analytical, and industrial areas [18]. The synthesis, characterization, and antibacterial studies of transition metal complexes containing Schiff base derived from condensation 4-methoxybenzaldehyde with 4-aminoantipyrine and glycine amino acid are described in this paper, the compounds that have been synthesized are (NNO).

The form of donor and its ligation activity with various metal ions were investigated, the complexes and ligand were tested in vitro against K. pneumoniae, S. aureus, P. aeruginosa and E. coli strains using the paper disc diffusion method and serial dilutions in liquid broth method.

2. Materials and Methods

provided all of the chemicals,(BHD, Fluke, and Sigma Aldrich) which were used without further purification. The melting point of the ligand and its complexes molar was determined using the electro thermal melting point modern 9300. Using electricity molar electrical conductivity measurements in DMF(10⁻³) conductivity meter (model 4510–jenway) C, H and N analysis was carried out by elemental analyzer PerkinElmer, (USA 2400-II) C, H and N analyzer. Electronic spectra in DMF(10⁻³M) recorded on Shimadzu spectrophotometer double beam model 1700 Uv-Vis spectrophotometer, FTIR spectra were the NMR spectrometer used DMSO-d6 as a solvent and TMS as an internal reference standard and registered reflective on FTIR spectrophotometer (Shimadzu) in wave number (4000-400 cm⁻¹). Shimadzu in Kahan university, Iran, Magnetic susceptibility measurements were carried out on a balance at room temperature, the magnetic susceptibility of the complexes is determined using Guoy's balance with Hg[Co(NCS)₄] as a calibrant, and diamagnetic correction is rendered using Pascal's Constant Absorption, Spectrophotometer (Flame and graphite analysis) in Scientific Research Center. The complexes were studied by thermogravimetry (TG-DSC) in static air atmosphere, with a sample using a DuPont 600 ATG thermobalance. recorded on a TGA-1000, the XRD powder pattern of the Co(II), Ni(II), Cu(II) and Cd(II) complexes its collected using a Philips X'Pert Pro diffract meter, SEM ZEISS Gmb.

2.1. Synthesis of the Schiff base 4-methoxybenzaldehyde-4-aminoantipyrine

A solution of 4-aminoantipyrine in a beaker (4.06g ,0.02 mol) was dissolved in (10mL) ethanolic solution of (50 mL) 4-aminoantipyrine (0.02 mol) was added to an ethanolic solution of 4-methoxybenzaldehyde (0.02 mol). These two mixtures were mixed together and kept for reflex for 3hours with stirring [19,20] the mixture was cooled and pour into crushed ice, dried and recrystallized with ethanol. The resulting yellow precipitate was purified and recrystallized after being dissolved in methanol. Slow evaporation at room temperature yielded fine yellow crystals shown in scheme 1.
2.2. Synthesis of newfangled Schiff base Ligand (K₄-AMetB-Gly)

The potassium salt of the amino acid (Glycine) was made according to a procedure we published in the literature[19]. The amino acid (0.01 mol) was dissolved in a 1:1 water–ethanol solution (40 mL) and then added to a hot ethanolic solution (30 mL) of KOH (0.01 mol), which was then stirred to produce a homogeneous solution. Then, drop by drop, an ethanolic solution was applied to this solution of 4-(4-methoxybenzylidene)amino)-1,5-dimethyl-2-phenyl-1,2-dihydro-3H-pyrazol-3-one (0.01 mol) the resulting mixture was then refluxed for about 3 hours. From ethanol the result was a dark yellow plate-like crystalline substance (Schiff base), which was then purified and recrystallized shown in scheme 2 [19,20].

2.3. Synthesis of Co²⁺, Ni²⁺, Cu²⁺ and Cd²⁺ complexes

The complexes are synthesized An alcoholic solution (20 mL) of Schiff bases (K₄-AMetB-Gly) (2 mmol) Ligand was applied to an aq. alcoholic solution (15 mL) of (1 mmol) CoCl₂.6H₂O/ NiCl₂.6H₂O / CuCl₂.2H₂O / CdCl₂.6H₂O and refluxed on a water bath for 2 hours [19,20]. The separated complex was filtered, washed thoroughly with water, ethanol, ether and finally dried in vacuum over fused CaCl₂ shown in scheme 3.
3. Result and Discussion

General

Schiff base ligand (K₄-AMetB-Gly) is Dark yellow crystal, that is partially soluble in water and soluble in universal biological solvents. Reacting this ligand with the metallic ions has different color crystals. All complexes are reasonably air-stable, insoluble in water, but solvable in most organic solvents as dimethyl sulfoxide, dimethylformamide, chloroform, acetone, methanol and ethanol.

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 (table 1), and The molar conductivities of metal(II) complexes were calculated after they were dissolved in DMF [10⁻³ M] at room temperature, the solution was weighed. The complexes non-electrolytic nature is confirmed by their lower conductance values (11.0–14.7 ohm⁻¹. cm². mol⁻¹), (table 3). The investigative data had been acceptable with planned magnitudes. 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 magnetic susceptibility of metal complexes and molar conductivities. Every [1:2] metal to ligand solid complexes have been separated. demonstrating that the complexes have a [1:2] metal–ligand stoichiometry of the form [1M:2L] with (K₄-AMetB-Gly) acting as a tridentate ligand.

Scheme 3: Preparation of Co(II), Ni(II), Cu(II) and Cd(II) complexes
**Table 1.** Elemental analysis and some physical properties for ligand (K$_4$-AMetB-Gly) and its complex.

| Complexes compound | Color (°C) | M.p (°C) | Yield % | Mol. formula (mol. Wt) | Found (calc)% |
|--------------------|-----------|----------|---------|------------------------|---------------|
| K$_4$-AMetB-Gly    | Dark yellow | 172      | 81      | C$_{42}$H$_{69}$N$_8$O$_6$ (832.04) | 60.56 (5.08) 13.45 -- |
| [Co (4-AMetB-Gly)$_2$] | Dark Green | 195      | 71      | C$_{42}$H$_{69}$CoN$_8$O$_6$ (813.26) | 61.99 (5.20) 13.77 7.24 |
| [Ni (4-AMetB-Gly)$_2$] | Light Green | 190      | 68      | C$_{42}$H$_{69}$NiN$_8$O$_6$ (813.54) | 62.02 (5.20) 13.77 7.21 |
| [Cu (4-AMetB-Gly)$_2$] | Dark brown | 210      | 72      | C$_{42}$H$_{69}$CuN$_8$O$_6$ (818.39) | 61.64 (5.17) 13.69 7.76 |
| [Cd (4-AMetB-Gly)$_2$] | Lemon yellow | 186     | 69      | C$_{42}$H$_{69}$CdN$_8$O$_6$ (868.23) | 58.17 (4.88) 12.92 12.96 |

**IR Spectra**

The IR spectra provide useful information about the ligand's coordinating sites. To assess the changes that may have occurred during complexation, the IR spectra of the complexes were compared to that of the (K$_4$-AMetB-Gly) free ligand. Certain peaks are common in the IR spectra of ligand and its metal complexes (table 2), indicating that they are related only important peaks, which have been either shifted or newly appeared, are discussed. Spectrum of free Schiff base ligand showed a band of the C=N group in the region of 1699 cm$^{-1}$ which was shifted to lower frequencies in the spectra of all the complexes (1654–1642 cm$^{-1}$) indicating the involvement of C=N nitrogen in coordination to the metal ion [21]. The coordination of the Schiff base to the metal through the nitrogen atom was expected to lower the C=N vibration and reduce the electron density in the azomethine link. And it was illustrated $\nu$ asym (COO$^-$) band of (K$_4$-AMetB-Gly) free ligand observed at 1595 cm$^{-1}$ was shifted to lower wave number in the spectra of metal complexes 1585–1591 cm$^{-1}$. The $\nu$ sym (COO$^-$) band of (K$_4$-AMetB-Gly) free ligand observed at 1490 cm$^{-1}$ in the spectra of metal complexes 1453–1496 cm$^{-1}$, was moved to a lower wave number, suggesting carboxylic acid group coordination with metal ion through the oxygen atom [22,23]. The presence of medium bands at the proposed coordination sites added to the assignment of the proposed coordination sites, at 520–480 cm$^{-1}$ and 420–440 cm$^{-1}$ which could be attributed to the $\nu$ (M–O) and $\nu$ (M–N) vibrations respectively. The IR spectrum of (K$_4$-AMetB-Gly) ligand and Co-Complex shown in Figure 1,2.

**Table 2.** Key IR absorption bands (cm$^{-1}$) of the Schiff base ligand and its metal complexes.

| Compounds            | $\nu$(C=N) | $\nu$(C-O) | $\nu$ asym (COO$^-$) | $\nu$ sym (COO$^-$) | $\nu$ (M–N) | $\nu$ (M–O) |
|---------------------|-------------|------------|----------------------|---------------------|-------------|-------------|
| K$_4$-AMetB-Gly     | 1699        | 1157       | 1595                 | 1492                | -----       | -----       |
| [Co (4-AMetB-Gly)$_2$] | 1654        | 1124       | 1585                 | 1458                | 420         | 530         |
| [Ni (4-AMetB-Gly)$_2$] | 1654        | 1138       | 1591                 | 1456                | 432         | 550         |
| [Cu (4-AMetB-Gly)$_2$] | 1642        | 1126       | 1594                 | 1456                | 440         | 552         |
| [Cd (4-AMetB-Gly)$_2$] | 1648        | 1132       | 1590                 | 1453                | 448         | 558         |
1H-NMR spectra
The 1H-NMR spectrum of ligand (K₄-AMetB-Gly) was recorded in (DMSO-d⁶) and Spectrum was shown in figure 3. 1H-NMR The Schiff base ligand has a peak in its spectrum at (7.02 – 7.88 δ ppm, multiplet 9H) aromatic[20,21] the peaks at (9.57 δ ppm H-C=N-) azomethine group [22,23]. The ligand also shows the following signals: (2.10 δppm -CH₃), (3.15 δppm -N-CH₃) (3.40δ ppm - 1H singlet CH-COO-) of Glycine group respectively and all of the protons were discovered to be in the right position. The findings of these studies add to the evidence for the mode of bonding discussed in their IR spectra and elemental C.H.N. the number of protons in the universe.

Figure 1. IR spectrum of ligand
Figure 2. IR spectrum of Co-complex
Figure 3. 1H-NMR of(K₄-AMetB-Gly) Ligand
Magnetic measurements
The Co(II) complex has a magnetic moment of 4.71 B.M. (table 3). This refers to the reported value for octahedral Co(II) complexes [24,25]. The magnetic moment value of the present Ni(II) complex is 3.19 B.M., which is within the range of 2.9–3.3 B.M. [20] indicating an octahedral system. The magnetic moment value of the Cu(II) complex shows a magnetic moment of 2.04 B.M., which is higher than the spin-only value of 1.73 B.M. predicted for one unpaired electron monomeric and consistent with a distorted octahedral geometry [26]. The Cd(II) complex was diamagnetic and had an octahedral geometry, according to empirical formulae.

Electronic spectra
spectrums of ligand (K₄-AMetB-Gly) and its complexes Co(II), Ni(II) and Cu(II) figure.4 in DMF [10⁻³M] have been examined and the spectral details have been depicted in table 3.

Table 3. The electronic spectrums of ligand and its chelate complexes, magnetic susceptibilityand values of molar conductanceof complexes.

| Compounds          | Band position cm⁻¹ | Transition   | Ω⁻¹ cm²mol⁻¹ | Suggested geometry | µeff (B.M.) |
|--------------------|---------------------|--------------|--------------|---------------------|-------------|
| K₄-AMetB-Gly       | 40485               | π → π*       | --           | --                  | --          |
|                    | 23202               | n → π*       | --           | --                  | --          |
| [Co (4-AMetB-Gly)₂] | 39063               | Center ligand|              | octahedral          | 4.71        |
|                    | 33670               | Center ligand|              |                      |             |
|                    | 14556               | ²T₁g → ²A₂g(F)|            |                      |             |
|                    | 16528               | ²T₁g → ²T₁g(P)|            |                      | 14.7        |
| [Ni (4-AMetB-Gly)₂] | 11210               | ³A₂g → ³T₂g(F)|            | octahedral          | 3.19        |
|                    | 13333242            | ³A₂g → ³T₁g(F)|            |                      |             |
|                    | 13                  | ³A₂g → ³T₂g(P)|            |                      |             |
| [Cu (4-AMetB-Gly)₂] | 16528               | ²B₁g → ²Eg   | 12.8         | octahedral          | 2.04        |
| [Cd (4-AMetB-Gly)₂] | 21008               | d π(Cd) → π*(L)| 11.0         | octahedral          | Dimg        |
XRD analysis

Powder X-Ray Diffraction and SEM (figure 5), the XRD patterns indicated crystalline nature for the Shiff base (K₄-AMetB-Gly) ligand and the Cd-complex only. It can be easily seen that the pattern of the Shiff base (K₄-AMetB-Gly) ligand differed from its metal complexes, which may be attributed to the formation of a well-defined distorted crystalline structure. Probably, this behavior was due to the incorporation of water molecules into the coordination sphere. On comparing the XRD spectra of the chelates with the XRD spectra of the free ligand, it was concluded that all chelates under study can be considered to have amorphous structures as they lack sharp peaks except the Cd-complex where it had a crystalline structure. Therefore, the nonsimilarity of the XRD pattern between the metal ions and chelates suggested that these chelates had different phase structures than the free (K₄-AMetB-Gly) ligand. Such facts suggested that Shiff base (K₄-AMetB-Gly) and the Cd(II) complex were crystalline, while its Co(II), Ni(II), Cu(II), and Cd(II) complexes were amorphous. The average crystallite size (ξ) can be calculated from the XRD pattern according to the Debye–Scherrer equation [27, 28]:

$$\xi = \frac{K\lambda}{\beta \cos \theta} \quad ...... \quad (1)$$
the equation uses the reference peak width at angle $\theta$, where $\lambda$ is the wavelength of the X-ray radiation (1.541874 Å), $K$ is a constant taken as 0.95 for organic compounds [29], and $\beta_{1/2}$ is the width at half maximum of the reference diffraction peak measured in radians.

Figure 5. The SEM micrographs of Ligand (K$_4$-AMetB-Gly) (a) and Cd(II) complex (b).

Thermo gravimetric analysis
The (K$_4$-AMetB-Gly) ligand and its complexes [Co(L)$_2$], [Ni(L)$_2$], [Cu(L)$_2$] and [Cd(L)$_2$] were recorded in the ranges 25–700°C TG-DTA values of the metal complexes are given in table 4. In the temperature range of 25–700°C, decomposition steps are obtained. T.G. analysis the ligand and its complexes Co(II), Ni(II), Cu(II) and Cd(II). The compound suffers a mass loss of 2% at about 100°C this loss may be Evolution of CO$_2$ and moisture again [27,28] the compound loses mass 16% between 120-290 and 150°C due loss of coordinated water and loss CH$_3$ group part of ligand and between 290-450°C, the compound suffers a loss of 32% due to loss azomethine group and between 450-520°C, the compound suffers a loss of 58% due to loss pyrazole ring a part of ligand moiety and supported by an exothermic peak at 600At 700°C there exists a residual mass of 88% with the formation of CoO, NiO, CuO and CdO.

Table 4. Date (T.G, DTG, DSC) of Ligand K$_4$-AMetB-Gly and its Complexes.

| Compound      | TG Range (°C) | DTG Mass Loss% (°C) | Assignment                          | Residue DSC (°C) |
|---------------|---------------|---------------------|-------------------------------------|-----------------|
| K$_4$-AMetB-Gly | 28-152        | 296                 | Evolution of CO$_2$ and moisture     | 230(+)          |
|               | 152-270       | 423                 | Loss CH$_3$ group                    |                 |
|               | 270-340       | 26.50               | Loss azomethine group                |                 |
|               | 340-420       | 35.88               | And Loss pyrazole Ring               | 418 (+)         |
|               | 420-547       | 74.1                | A part of the ligand                 |                 |
|               | 547-800       | 81.9                |                                     |                 |
Geometry Optimization

Supplementary (table 5) lists the optimized structures geometric parameters (bond lengths and angles) of the Schiff base Ligand (K4-AMetB-Gly) and its Cd(II) complex (figure 6 ). The following observations were made after analyzing these data:

1-The coordination bonds grew longer after complexation, and there was a lot of variance. As the ligand was complexed, the bond lengths of the ligand changed. C(52)-N(45) Cd-O(43), 39.479 Å, C(52)-N(45)-Cd(53)-N(19) and C(27)-N(45)-Cd(53)-O(17). It grew slightly longer, indicating that azomethine (-C=N-) atoms The coordination included protonated O groups and others.

2-Many of the active groups involved in have bonds that are longer than those of coordination found in the ligand (as an example, N N O).

3-The bond angles surrounding the central cadmium atom in the complex are within the octahedral geometry range [30] whereas the bond angles surrounding the free ligand (K4-AMetB-Gly) moiety were slightly changed upon coordination [30].

4-Intramolecular communication hydrogen bond may be responsible for the decrease in the Hydrogen-Nitrogen angles for azomethine.[30].

Potential Electrostatic in Molecules (MEP)

A plot of electrostatic potential mapped on to the constant electron density surface is referred to as an electrostatic potential plot the MEP. It can also be used to investigate the relationship between molecular structure and physiochemical properties. It can also be used to grasp molecular biology, interactions and predict electrophilic and nucleophilic attack reactive sites chemical reactivity is directly related to the MEP. Negative electrostatic potential was represented by the color red. Electrophilic reactivity is linked to the negative regions. Nonetheless the electron-poor region is colored blue (favor site for nucleophilic attack) [30, 31] while the green-colored region indicates the neutral electrostatic potential region. Figure 6 displays three-dimensional The parent Ligand (K4-AMetB-Gly) and its Cd(II) complex are shown in MEP plots. The oxygen and nitrogen atoms of free Ligand (K4-AMetB-Gly) are surrounded by a more negative charge surface, As a result, these sites may be more vulnerable to electrophilic attack. (Figure 6 (a)), supporting the complexation process, where the metal core was surrounded by a larger negative charge (Figure 6 (b)).
Mulliken Charges

Some basic atoms have Mulliken atomic charges, as explained in Table 5 and Supplementary (Figure 7). In comparison to the predicted value, the measured charge values for N14 and N19 are 0.02 and 0.004, respectively. N45 and N40 are 0.06 and 0.008, respectively. (-1 a.u.), This meant that electrons were being moved from these atoms to the core made of metal. Furthermore, electron migration to the cadmium nucleus is caused by a decrease in oxygen formal charge below predicted values, resulting in the creation of the complex. Finally, this charge transfer from donor atoms to the metal center causes the computed value to decrease, despite the general charge of +2 for the cadmium atom. to 0.750 a.u. [32,33].

Figure 6. The optimized structure of (a) K₄-AMetB-Gly and (b) [Cd (4-AMetB-Gly)₂]⁻

Molecular Parameters

Figure 8 depicts the ligand (K₄-AMetB-Gly) and its Cd(II) complex molecular orbital representations, as well as their HOMO, LUMO and energy band differences. The lowest unoccupied molecular orbital (LUMO) and the highest occupied molecular orbital (HOMO) The key orbitals involved in chemical stability were (LUMO) [33-35]. The ability to donate an electron was represented by the HOMO, while the ability to receive an electron was represented by the LUMO as an electron acceptor. To put it another way, the energy of a HOMO is proportional to its size. The electron affinity is directly proportional to the LUMO energy. As a result the electric and optical properties of these frontier energies are crucial. the disparity in energy between the two HOMO and LUMO since it allows for the calculation of electron conductivity, energies is an important parameter in determining molecular electrical transport properties. Furthermore, the molecular stability and spectroscopic properties of molecular systems are characterized by this energy gap. A chemically soft molecule that is readily polarizable has a smaller energy gap. HOMO-LUMO the energy gap has proven to be a valuable method for evaluating a molecule's kinetic stability and chemical reactivity. The lower the energy gap, the easier it is to exit a molecule, while the higher the energy gap the higher the kinetic stability, the lower the molecule's chemical reactivity. Molecular structure the existence of the complexation
status is indicated by the difference in the energy gap for the ligand (K4-AMetB-Gly). The highest capacity of accepted electrons is due to the increase in global electrophilicity value, indicating that the ligand has a high potential for donation. The molecular stability and reactivity can be calculated using the absolute hardness and absolute softness parameters. By comparing the measured binding energy of the increased complex to that of the free ligand, the binding energy calculations showed that the value of the measured binding energy of the increased complex was higher. (K4-AMetB-Gly) indicated that the stability of the formed Cd(II) complex was higher than that of the free ligand (K4-AMetB-Gly). For the free ligand and the Cd- complex, additional parameters such as chemical potentials, global electrophilicity, global softness, electrophilicity index, and additional electronic charge Nmax were measured (table 3). Both free ligands have a high value (K4-AMetB-Gly) and Cd(II) complex biological activity has a high likelihood and priority, according to the findings which is backed up by experimental evidence. The following equations [32-34] were used to measure the quantum chemical parameters mentioned.

| Compounds            | HOMO | LUMO | HOMO-LUMO energy gap (Hartree) |
|----------------------|------|------|--------------------------------|
| [Cd(L)2]             |      |      | 46500.                         |
| Ligand               |      |      | 0.1230                         |

**Figure 7.** Frontier orbitals' surface process of Ligand (K4-AMetB-Gly) and [Cd(L)2].

\[
\Delta E = E_{\text{LUMO}} - E_{\text{HOMO}} \quad \text{----- (2)}
\]

\[
\chi = \frac{(E_{\text{HOMO}} + E_{\text{LUMO}})}{2} \quad \text{----- (3)}
\]

\[
\eta = \frac{E_{\text{LUMO}} - E_{\text{HOMO}}}{2} \quad \text{----- (4)}
\]
\[ \sigma = \frac{1}{\eta} \quad \text{(5)} \]

\[ \rho \hat{\lambda} = \chi' \quad \text{(6)} \]

\[ S = \frac{1}{2\eta} \quad \text{(7)} \]

\[ \omega = \frac{P_i^2}{2\eta} \quad \text{(8)} \]

\[ \Delta N_{\text{max}} = \frac{P_i}{\eta} \quad \text{(9)} \]

**Figure 8.** (a) (K₄-AMetB-Gly) and (b) [Cd(L)₂] molecular electrostatic potential maps. 0.004a.u is the electron density isosurface.

**Table 5.** The quantum chemical parameters determined of (K₄-AMetB-Gly) and its Cd(II) complex.

| The quantum parameter | Ligand          | [Cd(L)₂]         |
|-----------------------|-----------------|------------------|
| \( E \) (a.u.)        | −1402.33        | −140.66          |
| Dipole moment (Debye) | 1.36            | 18.023           |
| \( EHOMO \) (eV)      | −6.095          | −5.61            |
| \( ELUMO \) (eV)      | −2.977          | −4.096           |
| \( \Delta E \) (eV)   | 3.118           | 1.514            |
| \( \gamma (eV)\)     | 4.5343          | 4.8532           |
| \( \eta (eV)\)       | 1.5590          | 0.7570           |
| \( \sigma (eV)^{-1} \)| 0.6411          | 1.3211           |
| \( Pi (eV)\)         | −4.5340         | −4.8530          |
| \( S (eV)^{-1} \)     | 0.3210          | 0.6610           |
| \( \omega (eV)\)     | 6.5930          | 15.5590          |
Complexes Stability Constant
Where: The spectroscopy method was used to measure the stability constant (K) for each (1:2) (1M:2L) complex using the following equations[36,37].

When:
\[
K = \frac{1 - \alpha}{4 \alpha^3 C^2}
\]

\[\alpha = \frac{A_m - A_s}{A_m}\]

C=the molar concentration of the complex solution
\[\alpha\] = degree of dissociation
\[A_m\] and \[A_s\]=the absorbance of a fully formed chelating complex and a partially formed chelating complex at optimum conditions and (max) of solution, respectively. All \(K\) and log \(K\) data are saved in table 6.

Gibbs free energy (G) thermodynamic parameters were also investigated. As a consequence, the (G) values were extracted from the relationship. \([35,36]\).

\[\Delta G = - R T \ln K\]

Where:
\[R = \text{gas constant} = 8.3 \text{ J.mol}^{-1}.\text{K}\]
\[T = \text{absolute temperature (Kelvin)}\]

All Data of log \(K\) and \(K\) are recorded in The negative value of \(\Delta G\) (table 7) indicates that the interaction between (ligand) and selected transition metal ions are spontaneous.

**Table 6.** The stability constant and Gibb’s free energy for the ligand and its Complexes.

| Compound                  | Log K | \(\Delta G\)   |
|---------------------------|-------|----------------|
| K4-AMetB-Gly              | --    | --             |
| [Co (4-AMetB-Gly)\(_2\)]  | 6.60  | -34435.04      |
| [Ni (4-AMetB-Gly)\(_2\)]  | 6.20  | -32348.07      |
| [Cu (4-AMetB-Gly)\(_2\)]  | 6.08  | -31721.98      |
| [Cd (4-AMetB-Gly)\(_2\)]  | 6.57  | -34278.522     |

4.Antibacterial activity
The investigated compounds *in-vitro* biological screening effects were checked against bacteria using the disc diffusion method with nutrients agar as the medium, and the experiment was replicated three times under similar conditions. The data were summarized in Table 8 using DMSO as a negative control and Amoxicillin as a positive norm.

**Table 7.** The synthesized compounds’ minimum inhibitory against the growth of four bacteria concentrations (MIC in \(\mu\)g/mL).

| Compound                  | Escherichia coli | Pseudomonas aeruginosa | Staphylococcus Aureus | Klebsiella pneumonia |
|---------------------------|------------------|------------------------|-----------------------|----------------------|
| K4-AMetB-Gly              | 15               | 10                     | 12                    | 15                   |
| [Co (4-AMetB-Gly)\(_2\)]  | 18               | 14                     | 18                    | 19                   |
| [Ni (4-AMetB-Gly)\(_2\)]  | 20               | 22                     | 24                    | 26                   |
| [Cu (4-AMetB-Gly)\(_2\)]  | 18               | 19                     | 22                    | 24                   |
| [Cd (4-AMetB-Gly)\(_2\)]  | 26               | 22                     | 27                    | 23                   |
| Amoxicillin               | 8.8              | 6.6                    | 12                    | 10                   |
The zone of inhibition region for metal chelates is much greater than the ligand as shown in Table 8. Chelation theory may describe the increased activity of metal chelates in this way. Due to the overlap of the ligand orbitals, the polarity of the metal ion would be decreased to a greater degree during chelation. It also promotes the delocalization of π-electrons over the entire chelate ring and increases the complexes lipophilicity [38,39]. This increased lipophilicity causes the cell’s permeability barrier to break down slowing down normal cell processes shown in figure 10.

Figure 9. Results of antibacterial screening.

5. Conclusions
From the Schiff base ligand four new biologically active 4-aminoantipyrines were synthesized (K₄-AMetB-Gly), potassium 2-(4-(4-methoxybenzylidene)amino)-1,5-dimethyl-2-phenyl-1,2-dihydro-3H-pyrazol-3-ylidene)amino)acetate was the corresponding metal complexes were synthesized and treated with different metal salts. The new ligand (K₄-AMetB-Gly) had a [1M : 2L] reaction with the metal ions. The results of the study indicated that the free ligand’s reactions (K₄-AMetB-Gly) with Cobalt(II), Nickel(II), Copper(II) and Cadmium(II) formed complexes with formulae in chemistry [M(AMetB-Gly)₂] (M=Co(II), Ni(II), Cu(II) and Cd(II)) and . Based on elemental studies, ¹H-NMR, IR and UV-Vis electronic absorption potential structures of the ligand and its metal Schiff base complexes were suggested. The (K₄-AMetB-Gly) ligand was found to behave like a neutral tridentate ligand with N,N coordination sites and carboxylate. The coordination of oxygen to metal ions results in the creation of octahedral geometries in all complexes. The thermal stability of the complexes was found to be higher than that of the free ligand in the tests. They may be caused by chelation the form of crystallization solvent, as well as the amount of solvents found in metal complexes the ligand and its metal complexes were screened as well against microorganisms in vitro (bacteria). The biological activity results indicated that the Cd(II) and Ni (II) Complexes have better antibacterial activity against Gram-positive bacteria than free ligands and other metal complexes Co(II) has higher antibacterial activity against Gram-negative bacteria. The approach of coordinating 4-aminoantipyrine derivatives with pharmacologically interesting metals such as cobalt, copper and zinc as shown in this study may show that the approach of coordinating 4-aminoantipyrine derivatives with pharmacologically interesting metals such as cobalt, copper and zinc may be successful and may be a good way to come up with new psychological methods for medical care.
Acknowledgement

Financial support from the department of chemistry, Mosul, Iraq, we are thankful to the department of chemistry college of science for providing all necessary facilities to conduct the experiment.

References

[1] T.J. Sullivan, J.J. Truglio, M.E. Boyne, P. Novichenok, X. Zhang, C.F. Stratton, H.J. Li, T. Kaur, A. Amin, F. Johnson, R.A. Stayden, C. Kisker, P.J. Tonge 2006 "High affinity InhA inhibitors with activity against drug-resistant strains of Myco-bacterium tuberculosis", ACS Chem. Biol. 1 43e53.

[2] A.M. Gilbert, A. Failli, J. Shumsky, Y. Yang, A. Severin, G. Singh, W. Hu, D. Keeney, P.J. Petersen, A.H. Katz 2006 "Pyrazolidine-3,5-Diones and 5-Hydroxy- 1H-Pyrazol-3(2H)-Ones, inhibitors of UDP-N-acetylenolpyruvyl glucosamine reductase, J. Med. Chem. 49 6027e6036.

[3] A.M. Isloor, B. Kalluraya, P. Shetty, Regioselective reaction 2009 "synthesis, characterization and pharmacological studies of some new Mannich base derived from 1,2,4-triazoles", Eur. J. Med. Chem. 44 3784e3787.

[4] M.Ghorab, M.El-Gazzar, M.Alsaid 2014 " Synthesis,Characterization and Anti-Breast Cancer Activity of New 4-Aminoantipyrine- Based Heterocycles, Int.J.MolecularSci.15739–7553,doi:10.3390/ijms15057539.

[5] L.S.Athira, S.Balachandran, J.Annaraj, E.AbelNoelson 2019 "Molecular structure ,spectroscopic, solvatochromic, dyeing performance and biological evaluations of heterocyclic azo dye,4-[(E)-(4-hydroxy-2-methylphenyl)diazenyl]-1,5(dimethyl-2-phenyl-1,2-dihydro-3H-pyrazol-3-one" Journal of Molecular Structure 1195,556e569

[6] N. Benaamane, B. Nedjar-Kolli, Y. Bentarzi, L. Hammal, A. Geronikaki, P. Eleftheriou, A. Langunin 2008 " Synthesis and in silico biological activity evaluation of new N-substituted pyrazolo-oxazin-2-one systems, Bioorg. Med. Chem. 16 3059e3066.

[7] Y. Wang, W. Ye, X. Yang, E. Rezaee, H. Shan, S. Yang, S. Cai, J.-H. Pan, J. Xu, Z.-X. Xu 2020 "Hole transport layers based on metal Schiff base complexes in per-ovskite solarcells ", Synth.Met.259,116248.

[8] L.C.Ekowo, S.I.Eze, C.Ezeorah, T.Groutso, S.Atiga, J.R.Lane, S.Okafor, K.G.Akpomie, O.C.Okparaee, 2020, " Synthesis, structure, Hirshfeld surface, DFT and in silico studies of 4-[(E)-(2,5-dimethoxybenzylidene)amino]-1,5(dimethyl-2-phenyl-1,2-dihydro-3H-pyrazol-3-one(DMAP) and its metal complexes", J.Mol.Struct.,127994.

[9] S.Syed Ali Fathima, R.Paulpandiyan, E.R.Nagarajan, 2019 Expatiating biological excellence of amino antipyrine derived novel metal complexes: combined DNA interaction, antimicrobial, free radical scavenging studies and molecular dock-ing simulations, J.Mol.Struct.1178, 179–191,doi:10.1016/j.molstruc.2018.10.021

[10] S.SyedAliFathima, R.Paulpandiyan, E.R.Nagarajan 2019 Expatiating biological excellence of amino antipyrine derived novel metal complexes: combined DNA interaction, antimicrobial, free radical scavenging studies and molecular dock-ing simulations, J.Mol.Struct.1178,179–191,doi:10.1016/j.molstruc.2018.10.021.

[11] A. Iqbal, H.L. Siddiqui, C.M. Ashraf, M.H. Bukhari, C.M. Akram 2007 "Synthesis, spectroscopic and cytotoxic studies of biologically active new Schiff bases derived from p-nitrobenzaldehyde, Chem. Pharm. Bull. 55 , 1070e1072.

[12] P.M.P. Santos, A.M.M. Antunes, J. Noronha, E. Fernandes, A.J.S.C. Vieira, Scavenging 2010 "activity of aminoantipyrines against hydroxyl radical, Eur. J. Med. Chem. 45 2258e2264.

[13] K.Z. Ismail, A. El-Dissouky, A.Z. Shehada 2009 , Polyhedron 16 2909.

[14] L.deMelodaSilva, F.Gozzi,I.Siréz, E.Brilas, S.C.deOliveira, A.Machulek 2018 Degradation of 4-amino antipyrine byelectro-oxidation with a boron-doped diamond anode: optimization by central composite design, oxidation prod-ucts and toxicity,Sci.TotalEnviron.631–632,1079–1088,doi:10.1016/j.scitotenv.2018.03.092.
[15] Í. P. de Souza, B. de P. Machado, A. B. de Carvalho, I. Binatti, K. Krambrock, Z. Molphy, A. Kellett, E. C. Pereira-Maiia, P. P. Silva-Caldeira 2019 "Exploring the DNA binding, oxidative cleavage, and cytotoxic properties of new ternary copper(II) compounds containing 4-amino antipyrene and N,N-heterocyclic co-ligands, J. Mol. Struct. 1178, 18–28, doi: 10.1016/j.molstruc.2018.10.004.

[16] A. Sakthivel a, K. Jeyasubramanian, , Thangagiri , J. Dhaveethu Raja 2020 "Recent advances in Schiff base metal complexes derived from 4-aminoantipyrene derivatives and their potential applications" J. Mol. Struct. 1222, 128885, doi.org/10.1016/j.molstruc.2020.128885.

[17] A.N.M.A. Alaghaz, . S. Alturiqi, R. A. Ammar, M. E. Zayed 2019 "Synthesis, spectral characterization, docking analysis, DNA binding/cleavage, antimicrobial and cytotoxic activity of new dimeric antipyrene−Schiff base metal complexes" Asian J. Chem. 31(199–212), doi: 10.14233/ajchem.2019.21680.

[18] Raman N, Syed Ali Fathima S and Dhaveethuraja 2008 J Serb Chem Soc, 73(11), 1063-1071.

[19] N. Raman, R. Jeyamurugan 2009 "Synthesis, characterization, and DNA interaction of mononuclear copper(II) and zinc(II) complexes having a hard-soft NS donor ligand", J. Coord. Chem. 62, 2375e2387.

[20] N. Raman a, R. Jeyamurugan a, S. Sudharsan a, K. Karuppasamy a, L. Mitu 2013 "Metal based pharmacologically active agents: Synthesis, structural elucidation, DNA interaction, in vitro antimicrobial and in vitro cytotoxic screening of copper(II) and zinc(II) complexes derived from amino acid based pyrazolone derivatives, Arabian Journal of Chemistry, 6: 235–247.

[21] Abdallah F. Al-Burgus , Amerah J. Al-Shaheen 2019 "Metal Based Pharmacologically Active Agents: Mode of Novel Tridentate Amino Acid Based with 4-hydroxy 3-Methoxy 4-Amino antipyrene Complexes " volume 9, Issue 7, 394-410 jour.WJPPS, DOI: 10.20959/wjpps20207-16522.

[22] Abdul Khader Jailani 2020 "Synthesis, Characterisation and Biological Evaluation of Tyramine derived Schiff base Ligand and Its Transition Metal(II) Complexes " Karbala International Journal of Modern Science: Vol. 6 : Iss. 2 , Article 15. doi.org/10.33640/2405-609X.1637

[23] Nakamoto, K. 1978 Infra-Red and Raman Spectra of Inorganic and Coordination Compounds, third ed. John Wiley, New York.

[24] G. H. Elgemeie, M. A. Abu-Zaied, S. A. Loutfy 2017 "4-Amino antipyrene in carbohy-drate research: design, synthesis and anticancer activity of thioglycosides of a novel class of 4-amino antipyrines and their corresponding pyrazolopyrimidine and pyrazolo pyridine thioglycosides", Tetrahedron 73(5853–5861, doi:10.1016/j.tet.2017.08.024.

[25] Kettle, S. F. A. 1969. Coordination Compounds. ELBS, Essex, UK. Kumar, S., Dhar, N.D., Saxena, N.P., 2009, J. Sci. Ind. Res. 68, 181.

[26] Banerjea, D., 1993. Coordination Chemistry. Tata McGraw-Hill. Bauer, A.W., Kirby, W.M.M., Sherries, J.C., Truck, M., 1966. Am. J.

[27] A. Z. El-Sonbati, M. A. Diab, A. A. El-Bindary, G. G. Mohamed, and S. M. Morgan 2015 "ermal, spectroscopic studies and hydrogen bonding in supramolecular assembly of azo rhodanine complexes", Inorganica Chimica Acta, vol. 430, pp. 96–107.

[28] R. Takjoo, S. S. Hayatogheibi, H. AmiriRudbari 2016 "Preparation,X-raystructure, spectralanalysis, DFT calculation and thermal study on palladium(II) coordination compound with Schiff base derived from S-allyl dithiocarba-zate " InorganicaChimicaActa,vol.447,pp.52–58.

[29] W. H. Mahmoud, T. A. Awed, G. G. Mohamed 2019 "Construction and characterization of nano iron complex iono-phore for electrochemical determination of Fe(III) in pure and different real water samples" Applied Organometallic Chemistry, vol. 33, pp. 1–17, Article ID e5206.

[30] Walaa H. Mahmoud Reem G. Deghadi Gehad G. Mohamed 2016 "Preparation, geometric structure, molecular docking thermal and spectroscopic characterization of novel Schiff base ligand and its metal chelates, Screening their anticancer and antimicrobial activities", J Therm Anal Calorim, DOI 10.1007/s10973-016-5826-7.
[31] S. Ramalingam, S. Periandy, S. Mohan 2010 " Vibrational spectroscopy (FTIR and FTRaman) investigation using ab initio (HF)and DFT (B3LYP and B3PW91) analysis on the structure of 2-amino pyridine", Spectrochim. Acta A 77 73–81.

[32] Gehad G. Mohamed , Walaa H. Mahmoud, Ahmed M. Refaat 2020 "Nano-Azo Ligand and Its Superhydrophobic Complexes: Synthesis, Characterization, DFT, Contact Angle, Molecular Docking, and Antimicrobial Studies" Volume, Article ID 6382037, 19 pages https://doi.org/10.1155/2020/6382037

[33] G.M.Morris, D.S.Goodsell, R.S.Hallidayetal 1998 " Automated docking using a Lamarekian genetic algorithm and an empirical binding free energy function", Journal of Computational Chemistry, vol.19, no.14,pp.1639–1662.

[34] T. A. Yousef, O. K. Alduaij, S. F. Ahmed, G. M. Abu El-Reash, and O. A. El- Gammal 2016" Structural, DFTmand biological studies on Cr(III) complexes of semi and thiosemicarbazide ligands derived from diketo hydrazide, " Journal of Molecular Structure, vol. 1125, pp. 788–799,

[35] PerkinElmer, 2012 " Chem Bio Draw Ultra Version (13.0.0.3015), Cambridge Soft Wal-tham, MA, USA; (b) Chemissian, in: L. Skripnikov (Ed.), A Computer Program to Analyse and Visualise Quantum Chemical Calculations, 2012.

[36] Cotton, F.A., and Wilkinson, G., 1980. Advanced inorganic chemistry. Inerstice 4th Edn., London.

[37] El-Haty, M. 2014 "Spectrophotometric Studies on Some Aryl azo Diamino Pyrimidinol in Organic Solvents and in Buffer Solution. " European Journal of Chemistry, 5(1), pp: 41-42.

[38] E. J. Falde, S. T. Yohe, Y. L. Colson, and M. W. Grinstaff 2016 " Superhydrophobic Materials for Biomedical Applications, " Biomaterials, vol. 104, pp. 87–103.,

[39] M.J.Pelczar, E.C.S.Chan, andN.R.Krieg, 1999 "Host-parasite interaction;non specific host resistance, in Microbiology Concepts and Applications", pp.478-479, McGraw-HillInc., NewYork, NY, USA,.6th edition.

[40] Sami Abd ali , mohammed, Shaker Hussein, A., & mohammed hadi, H. (2020). Study The Current Density-Voltage (J-V) Characteristics of α-Fe2O3 Thin Film Prepared by Spray Pyrolysis Technique. Al-Qadisiyah Journal Of Pure Science, 25 (1), Phys 1-7.

[41] Ali , W., & R.Anon, M. (2020). Biological Effective of organic solvent extracts of Mirabilis jalapa Leaves in the Non-cumulative for mortality of Immature stages Culex quinquefasciatus Say ( Diptera : Culicidae ). Al-Qadisiyah Journal Of Pure Science, 25(1), Bio 1-6.