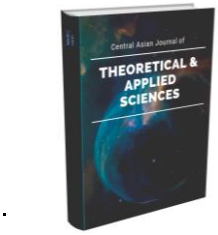

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Article

Preparation and Diagnosis of New Complexes for Hg (II) With 4-Amino Acetanilide And (Dppp) As A Ligand And Study Of The Bacterial Efficacy And Molecular Docking Of The Prepared Complexes

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Abstract: Mercury complexes are increasingly important for antibacterial action, hence novel Hg complexes were created using 3-aminoacetanilide (L) and dppp. The mercury complex has the formula [HgL2]Cl2, whereas phosphine complexes have the formula [HgL2(dppp)]Cl2. The properties of the produced compounds were determined using FTIR, 31P-NMR, and 1H-NMR. Furthermore, this study concludes the evaluation of the biological activity of prepared complexes against two bacterial species, Pseudomonas aeruginosa (gram-positive) and Citrobacer Freundii (gram-negative), using the Agar well method. The prepared complex [HgL2(dppp)]Cl2 showed greater activity against Pseudomonas aeruginosa than Escherichia coli".

Keywords: 3-aminoacetanilide, Hg complexes, molecular docking, Biological activity

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1. Introduction

Acetanilide is an odorless, solid substance that resembles a leaf or flake. It is also known as N-phenylacetamide, acetanil, or acetanilid, and was previously marketed under the brand name Antifebrin[1]. Acetanilide can be synthesized by reacting acetic anhydride with aniline[2]".

$$C_6H_5NH_2 + (CH_3CO)_2O \longrightarrow C_6H_5NHCOCH_3 + CH_3COOH$$

"The preparation was once a standard experiment in introductory organic chemistry lab classes[3], but it has since been widely replaced by the preparation of paracetamol or aspirin[4], both of which teach the same practical techniques (particularly recrystallization of the product) but avoid the use of aniline[5], a suspected carcinogen. Acetanilide is mildly soluble in water and remains stable under most conditions. Pure crystals have a plate-like shape and appear colorless, white, or somewhere in between. Acetanilide prevents hydrogen peroxide breakdown and stabilizes cellulose ester varnishes. It has also been used for intermediation in the manufacture of rubber accelerators, colors, dye intermediates, and camphor [6]. Acetanilide is used to synthesize 4-acetamido benzene sulfonyl chloride, a critical step in the production of sulfa drugs[7]".

"**N-(4-aminophenyl) acetamide** is a synthetic semi-product having the molecular formula C8H10N2O and a mass of 150.1 g/mol. The melting point ranges from 164 to 165

0 C. [8]CAS number is 122-80-5, and pK is 14.75.N-(4-aminophenyl) acetamide crystals range in hue from pink to brown [9,10], and are needle-shaped. It is melted in cold and hot water, alcohol, and ether. Image 1 shows the molecular structure of N-(4-aminophenyl) acetamide. The aromatic molecule has a benzene core with acetamide (-NH-CO-CH3) and amino (-NH2) groups at positions (1,4)[11]".

2. Materials and Methods

All of the ingredients, reagents, and solvents needed to synthesize compounds were given and used without further purification. The melting point of the synthesized compounds was determined using an Automatic (SMP30) melting point equipment. The IR spectra of the produced compounds as KBr pellets were measured with a Shimadzu FTIR 8400S spectrophotometer (400-4000 cm-1). NMR spectra were obtained using a Bruker 400 MHz spectrometer with DMSO-d6 as the solvent. The pathogenic bacteria isolates utilized in the study were collected from the Department of Life Sciences laboratories in the College of Education for Pure Sciences at the University of Tikrit".

Preparation of [HgL2] C12 complex[12] MH1

L=3-aminoacetanilide

"A solution of HgCl2 (0.1g, 0.368mmol) in absolute ethanol (10 ml) was mixed with a solution of one-mole equivalent L in absolute ethanol (10 ml). The mixture was refluxed for three hours, resulting in a red solution suspension that was let to slowly evaporate, followed by the dark red ppt. The product was filtered and dried using a vacuum. The dark red product was recrystallized from DMSO, yielding a white powder {Yield = 0.17 g,%, m.p (C) =126-128 oC}".

Preparation of [HgL2 (dppp)] C13 complex[13] MH2

"A solution of HgCl2 (0.1g, 0.368mmol) in absolute ethanol (10 ml) was mixed with a solution of one-mole equivalent L in absolute ethanol (10 ml). The mixture was refluxed for three hours before adding a hot solution of dppp (0.141g, 0.368 mmol) in absolute ethanol (10 ml) to the red solution, which was then refluxed for three hours at 70°C. The mixture was filtered, washed with hot ethanol, and dried in desiccators over calcium chloride for four days, yield = 0.2g,%, m.p (C) = 156-158 oC, as shown in Scheme (1)".

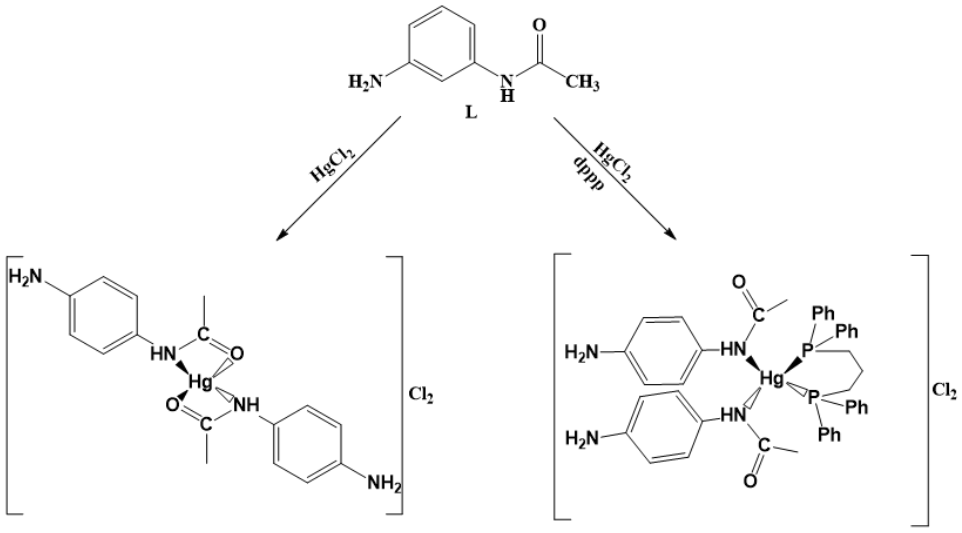
Biological Activity Study

Gram-positive Pseudomonas aeruginosa and gram-negative This study used two harmful bacterial species: Escherichia coli. The College of Pure Science Education and the Department of Life Sciences both use Molter Hinton agar as a bacterial growth medium. Chemical solutions of MH2 were produced with dimethyl sulfoxide (DMSO) at concentrations of (0.1, 0.01, 0.01) mg/mL. This technique calculates and monitors the minimal inhibitory concentration (MIC) [14, 15]. Mueller-Hinton agar served as a nutrient medium, and the diffusion technique was employed to determine the susceptibility of the bacterial isolates used in the study. Once the culture media is ready [16,17], it is sanitized, divided into plates, and solidified. Next, punch four small holes in each panel. They were then incubated at 37°C for an entire day. Derivatives were utilized [18, 19]. To clarify the sensitivity of the derivatives employed. As the diameter grows, these derivatives are determined by the damping diameter of the plate surrounding the hole employed. When a substance produces an inhibitory effect, its biological activity increases, similar to the inhibitory diameter of an antibiotic. [20, 21].

Molecular Docking Study {22}

"The MOE (2009) program was used to conduct molecular docking studies of the complex (MH2) against a common bacterial species, Pseudomonas aeruginosa. The goal was to reduce the complexity of the complex in question in order to achieve the lowest energy barrier, or the most stable configuration. The protein composition of Pseudomonas aeruginosa was derived from the International Protein bank. The high-performance PC610

was used because these programs have a high demand and require multiple, complex and large molecules to be able to calculate efficiently and with a high degree of detail, especially when dealing with large molecules and complex atomic configurations".



3. Results and Discussion

3.1 Characterization of [HgL2] Cl2 Complex [23]

FT-IR(KBr): (3267) ν(N-H), (2929)(2846) ν(C-H), (2064) ν(Ar-H), (1650) ν(C=O), (3419)(3485) ν(NH_2), (1596,1481) ν(C=C), (1234) ν(C-N), (997) ν(N-N),as shown in the figure (1). 1H-NMR (DMSO-d_6) δ(PPm): (6.06) (s, NH_2), (8.50) (s, NH), (3.37) (s, CH_3), (7.24,7.25)(7.35,7.36) (dd, Ar-CH). as shown in figure (2).

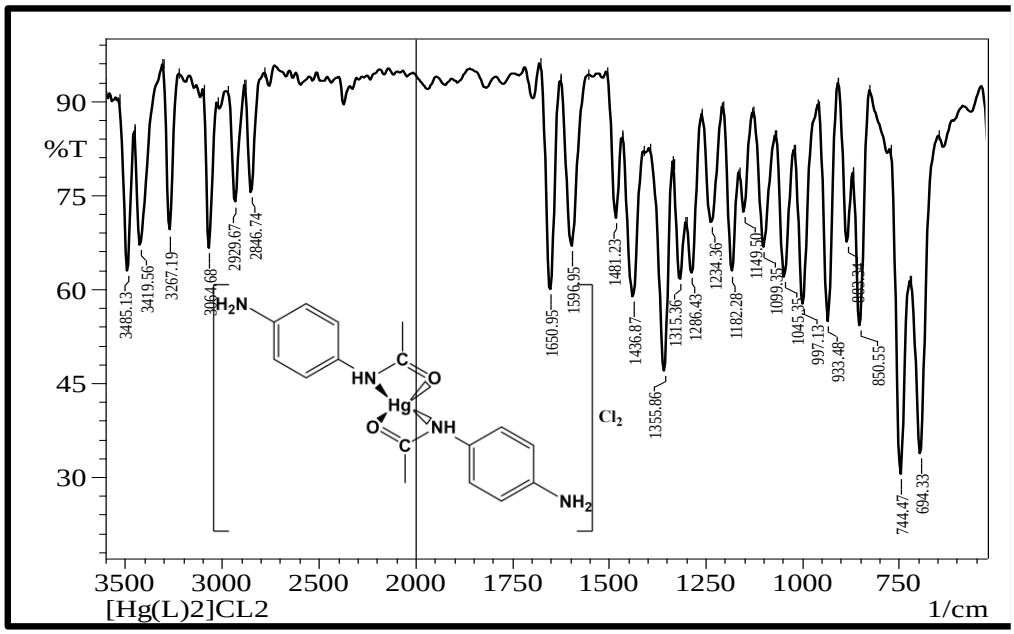


Figure (1): The infrared spectrum of the compound (MH1)

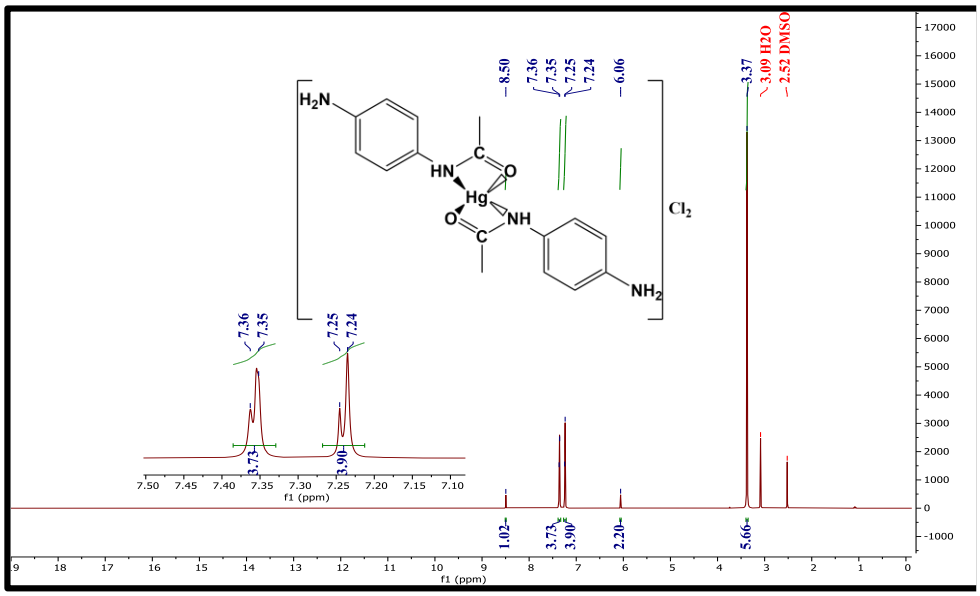


Figure (2): The 1H-NMR spectrum of the compound (MH1)

3.2 Characterization of [HgL2(dppp)] Cl2 complex [24]

FT-IR(KBr): (3222) ν(N-H), (2964)(2896) ν(C-H), (3051) ν(Ar-H), (1639) ν(C=O), (3328)(3413) ν(NH_2), (1591,1485) ν(C=C), (1238) ν(C-N), (997) ν(N-N), (P-Ph) ν(1440), (P-C) ν(1097), as shown in the figure (3). 1H-NMR (DMSO-d_6) δ(PPm): (5.66) (s, NH_2), (9.67) (s, NH), (3.87) (s, CH_3), (2.91-3.00) (b, CH_2), (3.11-3.15) (t, CH_2), (7.07,7.08)(7.49,7.51) (dd, Ar-CH), (7.22-7.38) (m, P-Ph). as shown in figure (4). $^{13}P\{^1H\}$NMR(DMSO-d_6): δ29.95 ppm. as shown in figure (5).

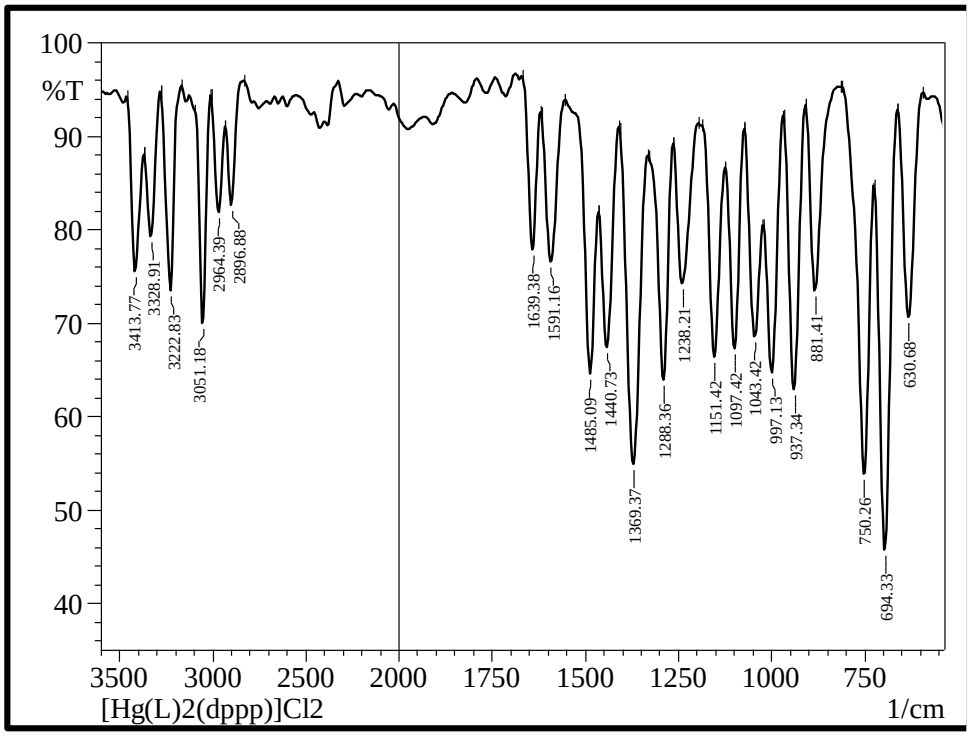


Figure (3): The infrared spectrum of the compound (MH2)

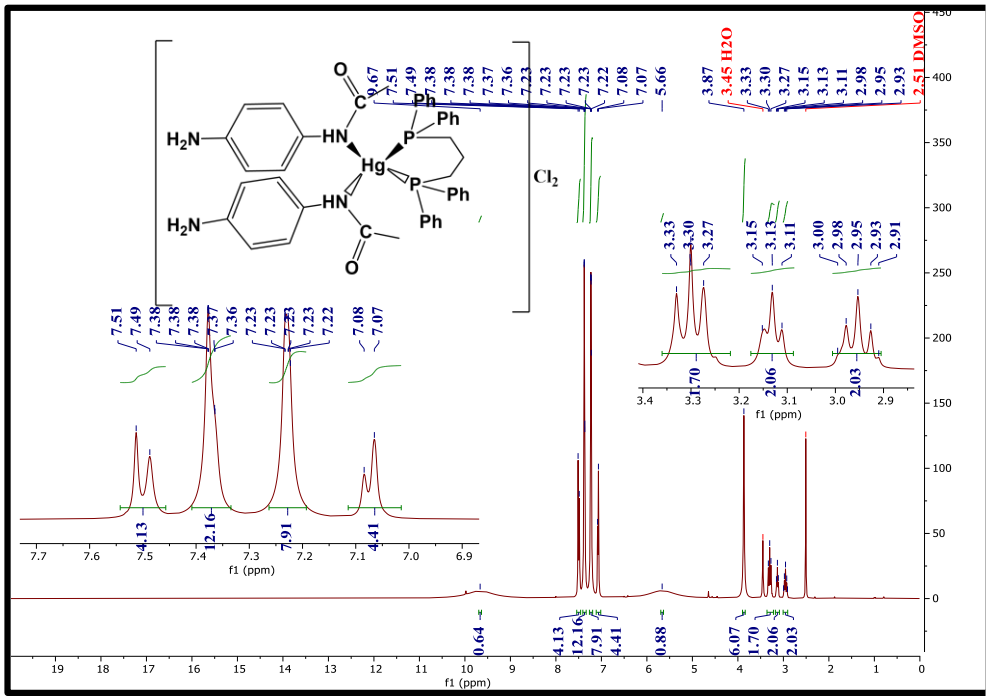


Figure (4): The 1H-NMR spectrum of the compound (MH2)

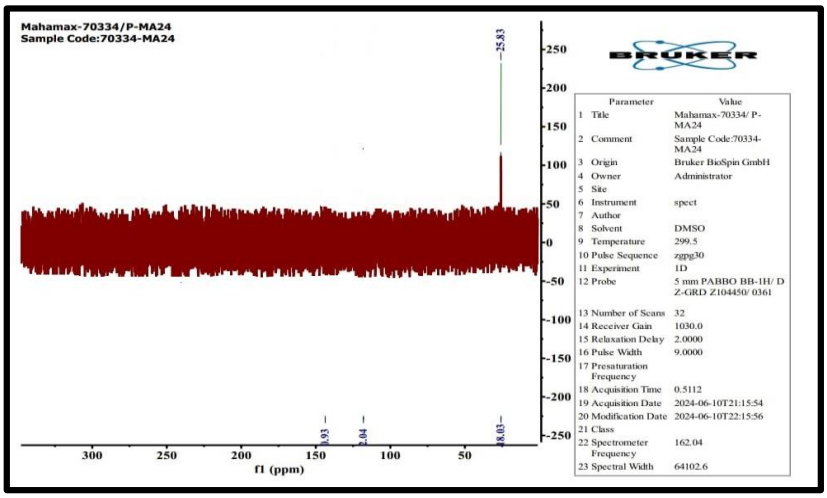


Figure (5): The 13P{1H}NMR spectrum of the compound (MH2)

3.3 Characterization of SEM from [HgL2(dppp)] Cl2 complex[25]

The SEM investigation of the complex [HgL2(dppp)]Cl2 depicted in Figure (6) revealed a regular nanostructure in the form of irregular clustered Nano-balls with a nanoscale thickness ranging from 24.19 to 72.57 Nm, as well as the existence of other nanosheets of varying sizes.

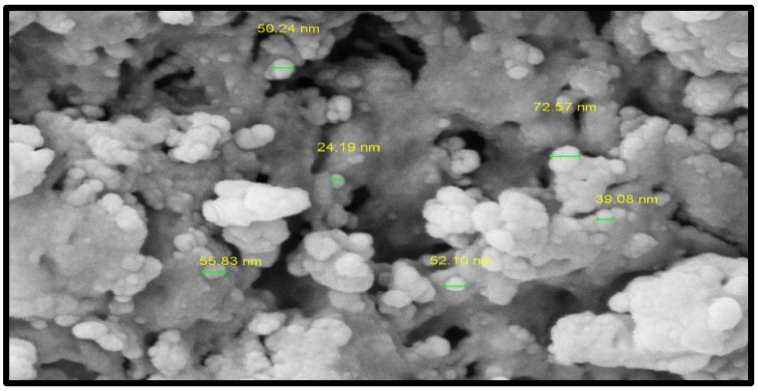


Figure (6): scanning electron imaging of the MH2 complex

3.4 Characterization of XRD [40] from [HgL29dppp]] Cl3 complex [26]

The XRD analysis of the complex (MH2) measured within the range 10-80 showed the presence of a crystal structure of the prepared complex because it gives many beams in the spectrum, as shown in Figure (7); the spectrum also showed the presence of beams of high intensity in the range 10-40 days, as the values of the FWHM signals indicate the presence of a geometric structure with pores and petite crystal sizes, and based on the previously mentioned Debye-Schiro equation,

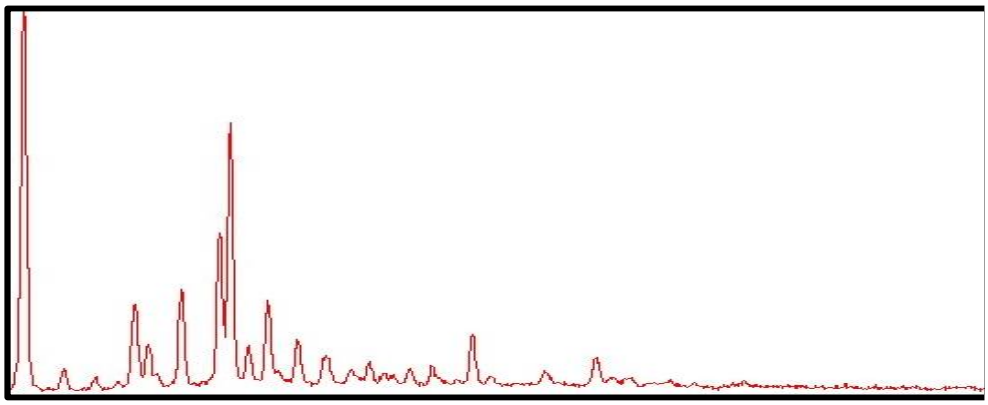


Figure (7): diffraction spectra of the complex (MH2)

Table (1): data of diffraction spectra of the complex (MH2) as well as the rate of minute volumes according to the Scherrer equation

Complex	Pos. (°2Th.)	Height (cts)	FWHM (°2Th.)	d-spacing [Å]	D (nm)	D. Av. (nm)
	12.8085	12561.25	0.3936	6.91156	20.33	24.29
[HgL2(dppe)]	23.5791	3474.32	0.3936	3.77323	28.30	23.5791
	25.9788	4405.72	0.3936	3.42988	22.13	25.9788

3.2 Characterization of Antibacterial activities from [HgL2(dppp)] Cl2 complex

The biological activity of the generated chemicals is investigated in this study using the bacteria Escherichia coli and Pseudomonas aeruginosa. Heterocyclic compounds have a variety of biological activities on both Gram-positive and Gram-negative bacteria[27]. These bacteria were selected because they are known to cause a variety of ailments. Furthermore, these microbes have diverse antibiotic resistance patterns [28,29]. The vital activity of the resultant compounds was determined by measuring the diameter of the inhibitory zone and applying the well-Agar diffusion method [30, 31]. The results revealed that the synthesized compounds can suppress the development of both Gram-positive and Gram-negative bacteria to variable degrees. This compound has strong inhibitory activity

against Escherichia coli and unique inhibitory effects on Pseudomonas aeruginosa [32, 33, 34]. The compound (MH2) inhibited dangerous bacteria (1.2)(1.4)(2.3) cm at various concentrations[35,36], whereas it inhibited positive bacteria (4.0)(3.8)(1.5) cm. As seen in Figure 8.

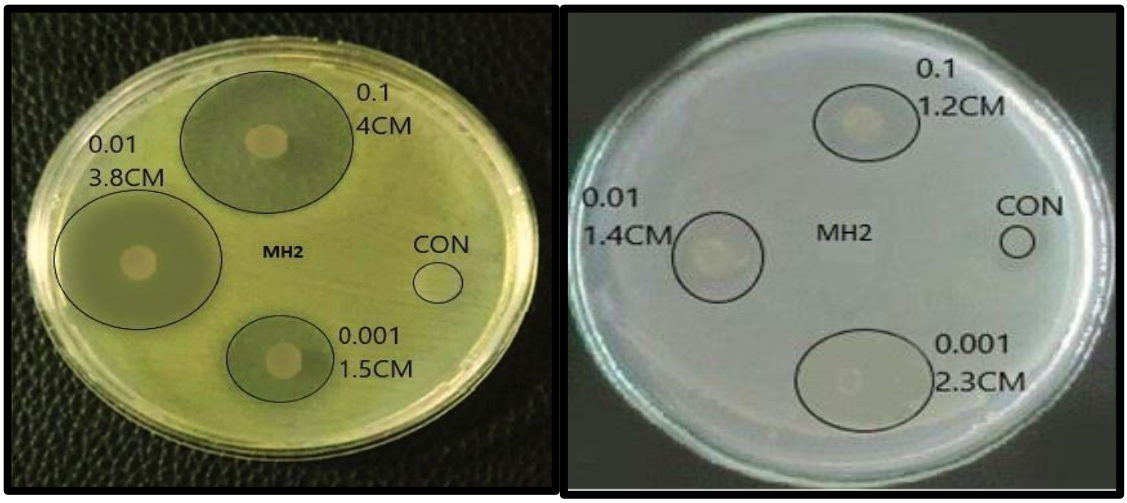


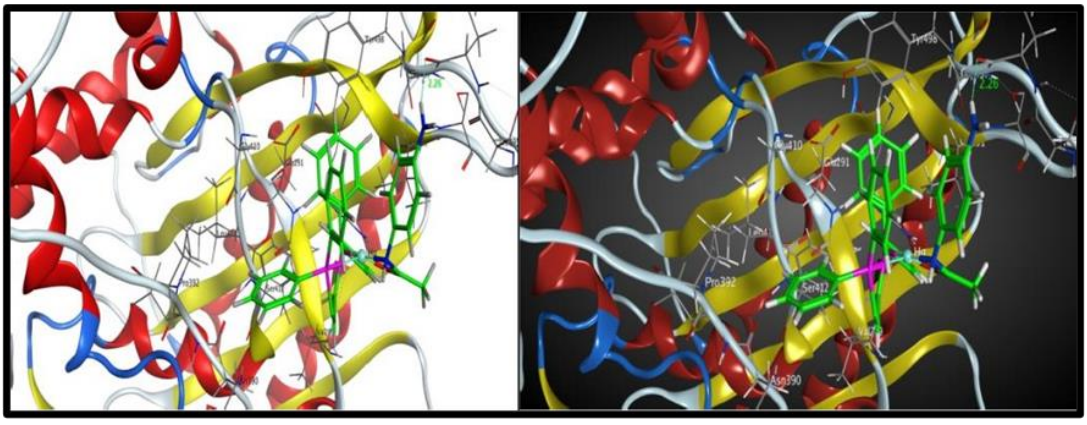
Figure (8):Antibacterial activity of compound [MH2] against P.aeruginosa and E.coli .

3.3 Characterization of Molecular docking from [HgL2(dppp)] Cl2 complex [37]

The molecular anchoring of the complex (MH2) was studied on one line, the bacteria aeruginosa Pseudomonas, using the (MOE 2014) software, in which the energy reduction process of the compound under research was performed to obtain the most stable vacuum body (the least blocking energy). The structure of Pseudomonas aeruginosa bacteria was downloaded from the world protein bank's website (receptor (6r3x)), and a personal calculator was used to compute the binding energies of the compounds", as shown in Table 2.

Comp.	Docking Score	RMDS
MH2	-5.58	4.08

"The study revealed that the complex (MH2) interacts with the amino acid residues present in the active site by forming two types of bonds, as shown in Figure (9), hydrogen bonds connecting the amino acid residues Las.496 the active site is located with the electron pairs of the nitrogen atom of the amine group with a length of A 2.25 and the number of amino acids affected by vandervalls forces and the binding energies are determined" as in Table (2).



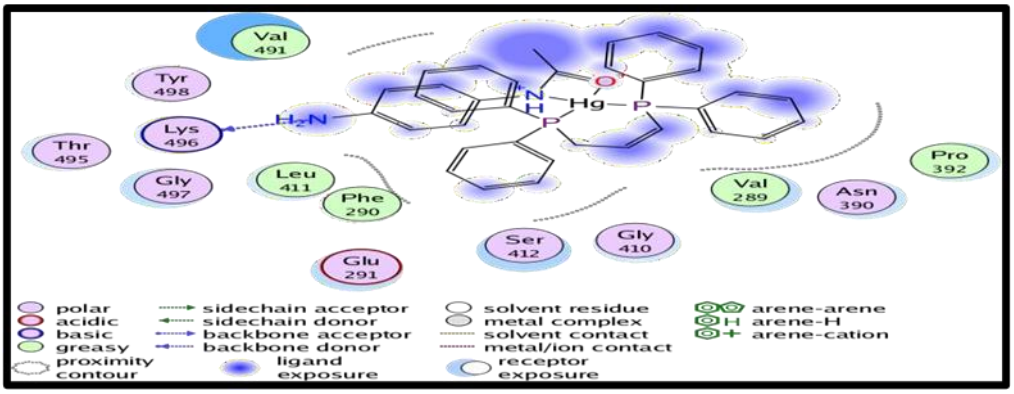


Figure (9) shows a two-dimensional and three-dimensional representation of the results of molecular docking and the binding between the compound (MH2)and the receptor (Pseudomonas aeruginosa)

4. Conclusion

Color and temperature changes were used to confirm the prepared compounds, and distinct bands in the FT-IR spectrum, as well as the expected signals for the prepared compounds in the 13P H1 NMR spectrum, SEM, and XRD, were used for final confirmation. Furthermore, the chemicals showed excellent inhibitory activity against microorganisms. In molecular docking simulations, complexes formed good interactions with amino acids.

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