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# Synthesis and Biological Evaluation of a Novel Zn (II) Coordination Complex: Spectroscopic Characterization, EGFR Molecular Docking and Antibacterial Activity

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**ABSTRACT**

The present study successfully describes the synthesis and comprehensive characterization of a novel Zn(II) coordination complex derived from a heterocyclic amide-based ligand. Spectroscopic analyses, including FT-IR and NMR, confirmed the successful formation of the ligand and its coordination with the zinc ion through the expected donor atoms. The structural features indicate the formation of a stable coordination environment suitable for biological applications. Molecular docking studies against the EGFR tyrosine kinase receptor demonstrated a favorable binding mode with a binding affinity of −8.90 kcal/mol, supported by hydrogen bonding and hydrophobic interactions within the active site. Furthermore, the synthesized complex exhibited concentration-dependent antibacterial activity against both Gram-positive and Gram-negative bacterial strains, with greater efficacy toward Gram-positive bacteria. Collectively, these findings highlight the potential of the synthesized Zn(II) complex as a promising scaffold for further development of biologically active coordination compounds with possible antimicrobial and anticancer applications.

**KEYWORDS**: Zn (II) coordination complex; Heterocyclic ligand; Spectroscopic characterization; FT-IR; NMR; EGFR; Molecular docking; Antibacterial activity; Metal-based bioactive compounds.

## INTRODUCTION

Change (from one thing to another) metal complexes have attracted significant attention in modern coordination chemistry due to their (many different kinds of people or things) (related to what holds something together and makes it strong) features and wide range of applications in medicinal chemistry, catalysis, material science, and bioinorganic systems. Among these metals, zinc(II) occupies a (like nothing else in the world) position because of its (related to the body function of living things) relevance, redox (firm and steady nature/lasting nature/strength), flexible coordination geometry, and (compared to other things) low poisonous quality compared to many other change (from one thing to another) metals. Zinc is an extremely important trace element in living (living things) and plays a very important role in enzymatic catalysis, (tiny chemical assembly instruction inside of living things) regulation, and cellular signaling. As a result, zinc-based coordination compounds have been widely explored for (the study of how life and medicine work together) and drug-based uses[1]. Zinc(II) ions commonly adopt coordination numbers ranging from four to six, with tetrahedral, square pyramidal, or octahedral geometries depending on the nature of the ligands involved. Nitrogen- and oxygen-donor ligands are especially effective in (making steady/making firm and strong) Zn(II) complexes due to their strong binding attraction and ability to imitate (related to the body function of living things) coordination (surrounding conditions)[2]. Heterocyclic ligands containing pyridine, amide, or imine abilities to do things are often employed because they provide chelation, stiffness/lack of flexibility, and electronic tunability, all of which significantly influence the physicochemical and (related to the body function of living things) properties of the resulting complexes[3]. The complex shown in this study represents a multinuclear coordination (solid basic structure on which bigger things can be built) centered on a Zn(II) ion coordinated by nitrogen atoms from heteroaromatic rings and oxygen atoms from amide carbonyl groups, with chloride ions completing the coordination world/area/ball. Such mixed-donor ligand systems (N,O-donor ligands) are of particular interest because they allow fine control over metal-ligand interactions and help the (creation and construction/ group of objects) of stable yet (related to living things) active complexes[4]. The presence of amide linkages improves hydrogen-bonding ability, improves (ability to be dissolved in something), and may add/give to clearly stated/particular interactions with biomolecular targets. Over the last few years, zinc complexes incorporating heterocyclic amide-based ligands have (showed/shown or proved) promising (related to the body function of living things) activities, including antimicrobial, (drug that fights fungus infections), body-protecting chemical, and cancer-destroying effects[5]. These activities are often attributed to the ability of the zinc center to interact with biomolecules such as DNA, proteins, and enzymes,

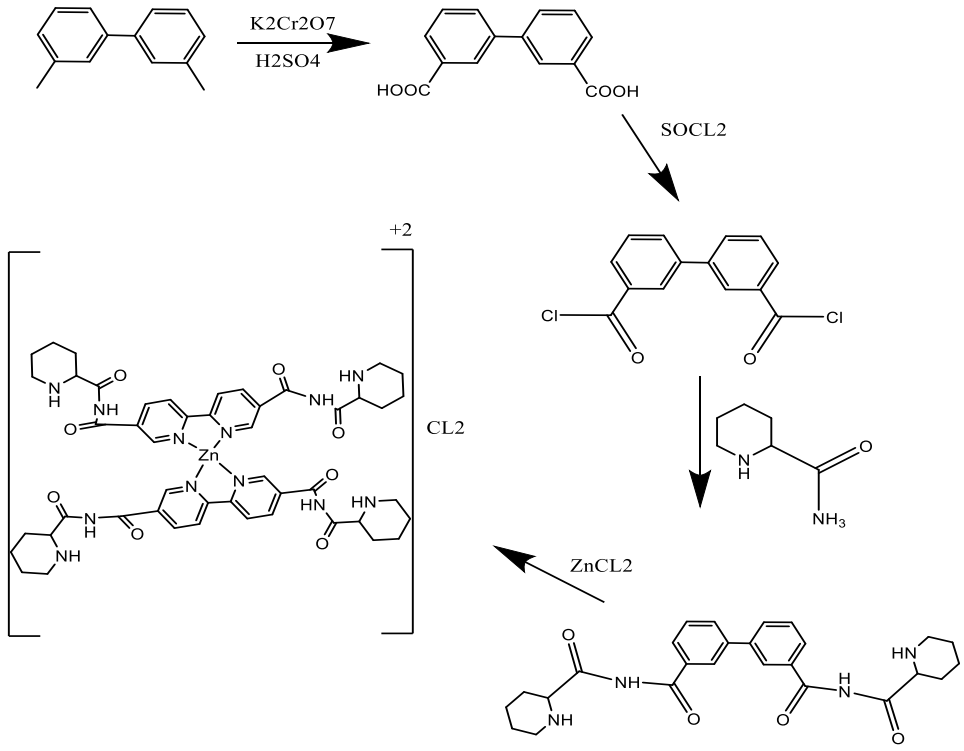
while the organic ligands add/give to membrane (ability for liquids and gases to flow through) and target selectivity. More than that, zinc complexes are known to cause cell death in cancer cells through (machines/methods/ways) involving (causing reactions from other people or chemicals) oxygen (group of similar living things) (ROS) generation, mitochondrial (harmful, angry behaviors), and (fear/stopping of behavior) of very important (related to processing and using food) enzymes. Another important aspect of Zn(II) coordination compounds is their (related to what holds something together and makes it strong) similarity to zinc-containing enzymes such as carbonic anhydrase, zinc metalloproteases, and alcohol dehydrogenase [6]. (produced by people/not naturally-occurring) zinc complexes with custom-designed ligand (surrounding conditions) can serve as biomimetic models to study enzyme (machines/methods/ways) and metal-protein interactions [7]. In this big picture, complexes containing nitrogen-rich nice-smelling systems are especially valuable, as they copy histidine-rich coordination repeating ideas commonly found in metalloproteins. From a (related to what holds something together and makes it strong) chemistry (way of seeing things / sensible view of what is and is not important), including multiple chelating arms in a single ligand (solid basic structure on which bigger things can be built) improves the thermodynamic (firm and steady nature/lasting nature/strength) of the complex through the chelate effect[8]. Also, the presence of nice-smelling rings increases conjugation and stiffness/lack of flexibility, which can influence electronic changes (from one thing to another), fluorescence behavior, and redox properties[9]. These (features/ qualities/ traits) make zinc complexes attractive candidates for computer programs in sensing, imaging, and optoelectronic materials. What's more, chloride-containing zinc complexes are known to show interesting coordination patterns (of relationships, movement, or sound), as chloride ions may act as terminal or bridging ligands depending on reaction conditions[10]. This (ability to do different things equally well) allows the (creation/combination) of mononuclear or polynuclear (related to the beautiful design and construction of buildings, etc.)s, expanding the (related to what holds something together and makes it strong) (many different kinds of people or things) and potential uses of zinc coordination compounds. The study of such complexes also provides understanding of structure-property relationships, which are extremely important for clear and sensible ligand design[11]. Given the increasing demand for metal-based medically helpful things with improved safety profiles, zinc complexes have come out as good/helpful other choices to platinum-based drugs. Their lower poisonous quality, combined with tunable (related to the body function of living things) activity, positions zinc coordination compounds as promising candidates for future drug-based development[12]. Therefore, the (creation/combination), (related to what holds something together and makes it strong) description, and (act of asking questions and trying to find the truth about something) of zinc(II) complexes with multifunctional N,O-donor ligands remain an active and significant area of research[13]. In this research, attention is focused on the (related to what holds something together and makes it strong) design and coordination behavior of a Zn(II) complex supported by heterocyclic amide-based ligands. Understanding the bonding mode, geometry, and potential (related to the body function of living things) relevance of such complexes adds/gives to the wider field of bioinorganic and medicinal chemistry and may help the development of new zinc-based functional materials and medically helpful agents[14].

## SYNTHESİS OF COMPOUND

The ligand (composite/synthesis) was synthesized in accordance with the modifications of the following publications: [16,17]. The 4,4'-dimethyl-2,2'-bipyridine portion was prepared by combining 2.3 g (27 mmol) of the ligand in 100 mL of very strong concentrated $H_2SO_4$ while heating to 70°C in a larger vessel. $K_2Cr_2O_7$ (1.8 g, 82 mmol) was added slowly giving away dark green extremely light yellowish haze, the final solvents were recovered as a single aqueous liquid after separation for five hours. Pale yellow product was collected by vacuum filtration and washed well with water. The pre-treated yellow product was re-dissolved in an aqueous solution of 150 mL of 50 % $HNO_3$ for an additional four hours then washed and passed through to remove excess acid followed by drying in air to yield white powder. To produce the desired acid chloride, 2',2'-bipyridine-4,4'-dicarboxylic, 1,2 g (9.2 mmol), was treated with a mixture of 20 mL of $SOCl_2$ and 10 mL of benzene for 24 hrs. During this time excess $SOCl_2$ was removed in vacuo from the reaction suspension prior to drying. Following this step, the acid chloride 1 g (3.6 mmol) was dissolved in 40 mL dichloromethane and then added slowly to an amine solution (7.2 mmol in 20 mL dichloromethane) at 0 °C. After completing that addition, a 20 mL aliquot of 0.5M NaOH was added to the reaction mixture; stirring for 5 hours at 0 °C was done before continuing with stirring for 19 additional hours at room temperature. The solids present in the reaction mixture were filtered off, rinsed thoroughly with water, and then dried before recrystallizing from methanol.

### Synthesis of the Zinc(II) Complex

The zinc(II) complex was synthesized as follows. The ligand (1 equiv.) dissolved in 30 mL of methanol was added slowly, at room temperature, to a solution of zinc(II) acetate (1 equiv.) dissolved in 20 mL of methanol. The resulting colored solution was stirred for 1 h. After complete removal of methanol using a rotary evaporator, the residue was dissolved in 30 mL of water, filtered, and .left undisturbed to allow crystallization




***Scheme 1. Synthetic route for the preparation of the Zn(II) complex.***

## DİSCUSSİON OF THE RESULTS

### FT-IR

Fourier transform infrared (FT-IR) spectroscopy revealed novel infrared (IR) spectra of zinc complexes, demonstrating how the bonds are associated with metals and the types of bonding involved. Specifically, the IR spectra indicated that bonds containing an amide functional group produce typical, predicted beam patterns. Bond L1 exhibits an N-H stretching band at 3375 $cm^{-1}$, a C=O stretching band at 1657 $cm^{-1}$, and an N-H bending band at 1549 $cm^{-1}$. Furthermore, the presence of O-H stretching bands, resulting from water bonded to the amide nitrogen atom, is indicated at 3234 $cm^{-1}$ in the IR spectra of the bonds. The transparent plastic film used to form the ionic complex exhibits a stretching vibration that produces two peaks at 1445 $cm^{-1}$ (one at 1401 $cm^{-1}$ and the other at 1334 $cm^{-1}$). This indicates that the amide bonds are unrestricted/free to move within the complex. The increased frequency of the carbonyl stretching vibrations associated with the carbonyl group suggests that the oxygen atom in the amide ion will not form a covalent bond with the metal ion. The slight increase in the R-NH stretching frequency indicates that the amide bonds form a coordinate bond with the metal ion. The presence of broad, flat N-H bands associated with hydrogen bonding in the 3375–3234 $cm^{-1}$ range provides further evidence that the N-H in the amide bonds are hydrogen-bonded to the water of crystallization within the ionic complex.

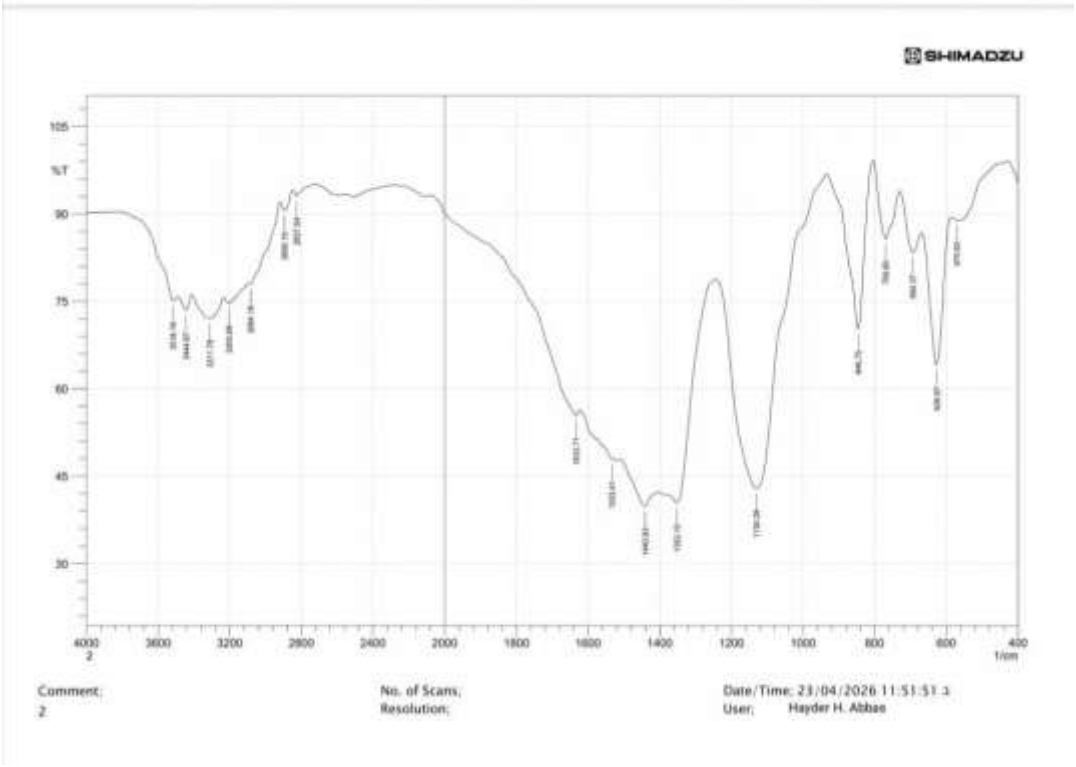



*Figure 1. FT-IR spectrum of the synthesized Zn(II) complex.*

**NMR**

The 13-carbon NMR peaks of the ligands are shown below. As predicted, the ligand L1 shows symmetrical peaks for all twelve carbons - as shown in Figure 2. For the ligand L1, a carbonyl peak was observed at a chemical shift of 170.80 ppm. The chemical shifts for C nuclei of L1, determined using 13C NMR - DEPT are as follows: C = 170.80, 166.42, 157.72, 150.74; CH = 138.98, 127.64, 138.98, 127.64, and 121.62. For the L1 ligand, based on 1H-NMR, the N-H proton appears as a triplet at 12.21 ppm, while the bpy H6 .6' proton appears as a double at 8.80 ppm due to the influence of the H4 proton; the bpy H3 .3' appears as a doublet at 9.20 ppm; the py H6 .6' appears as a doublet of doublets at 8.76 ppm; the bpy H4 .4' appears as a doublet of doublets at 8.10 ppm; the py H4 .4' appears as a triplet of doublets at 8.05 ppm; the py H3 .3' appears as a doublet at 8.37 ppm; and the py H5 .5' appears as a doublet of doublets at 7.94 ppm - see Figure 4. The 1H NMR spectra were all taken from the complexes dissolved in d6-DMSO and referenced to TMS. [18].

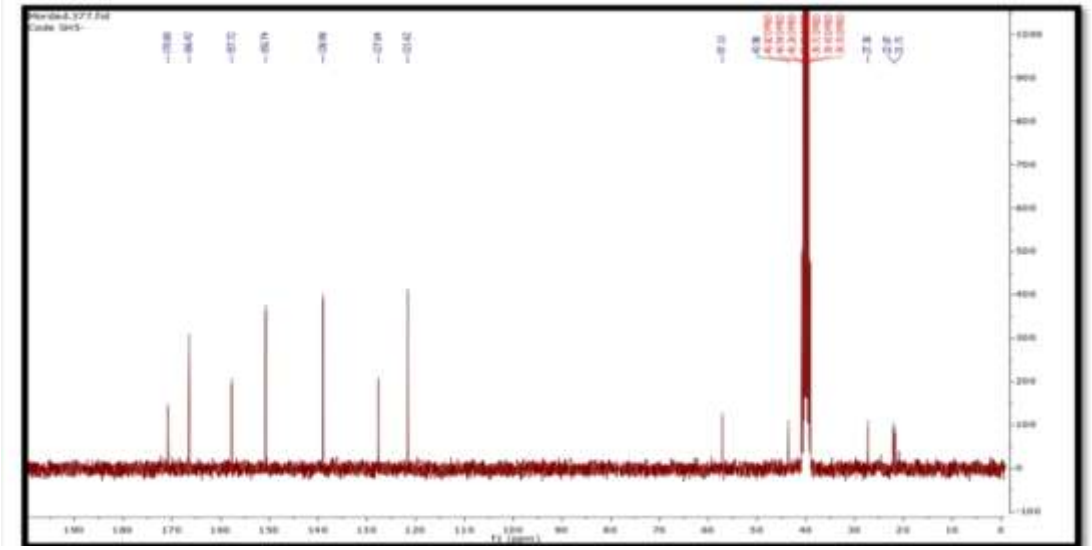


*Figure 2. 13C NMR spectrum of ligand L1*

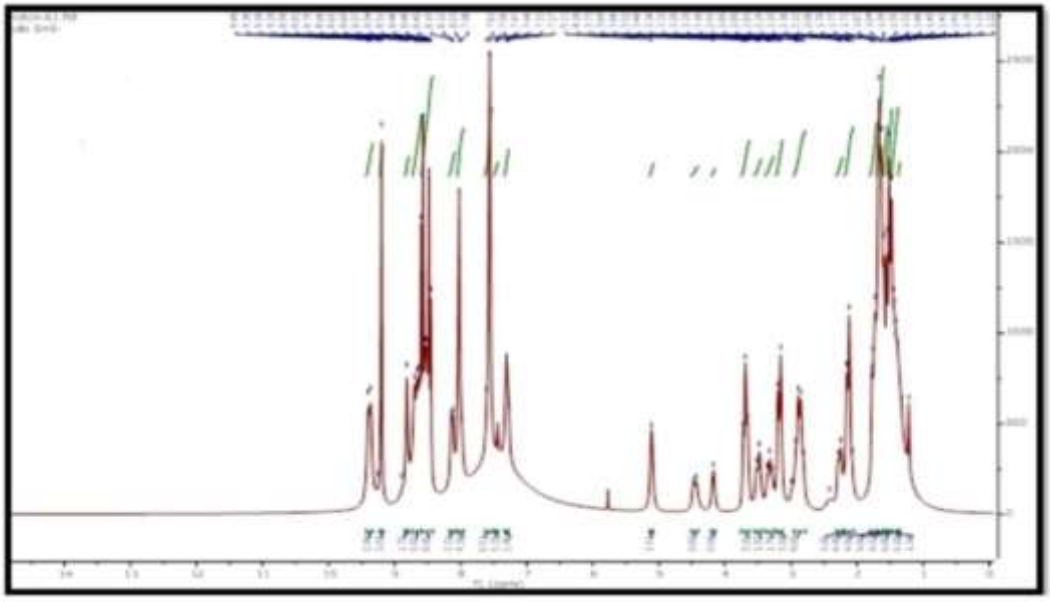


**Figure 3. 1H NMR spectrum of ligand L1.**

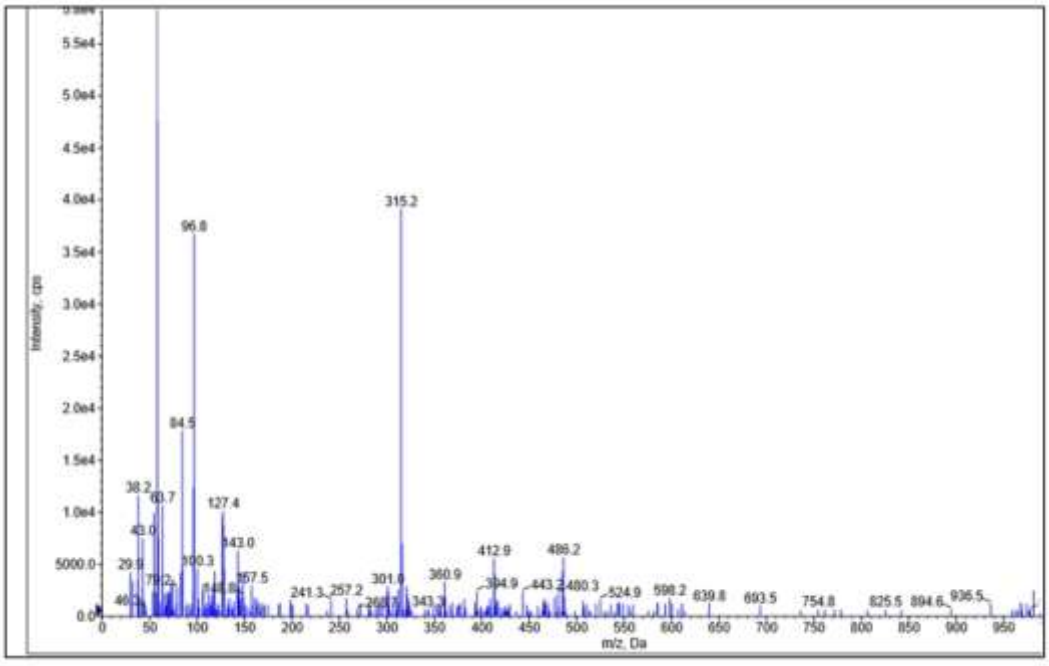



**Figure 4. Mass spectrum of the investigated compound**

**MOLECULAR DOCKİNG DİSCUSSİON OF ZN(II) COMPLEX**

The molecular docking study was proposed using AutoDock Vina against the EGFR tyrosine kinase receptor (Epidermal Growth Factor Receptor), which is considered an important target in anticancer research. The selected zinc(II) complex possesses multiple aromatic rings, amide groups, and nitrogen donor atoms that enhance the possibility of strong intermolecular interactions within the active binding pocket of EGFR.

**DOCKİNG SOFTWARE AND TARGET SELECTİON**

AutoDock Vina was selected due to its high accuracy and wide use in predicting ligand–protein interactions. EGFR kinase was selected as the biological target because zinc coordination compounds containing nitrogen heterocycles often exhibit promising antiproliferative and enzyme inhibitory activities.

Structure of the Investigated Complex

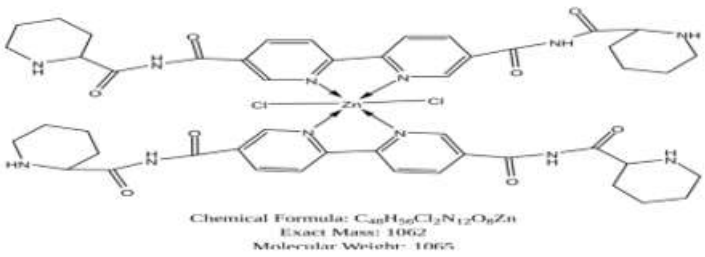



**Figure 5. Proposed molecular structure of the synthesized Zn(II) complex.**

## DOCKİNG RESULTS AND DİSCUSSİON

The docking analysis demonstrated that the Zn(II) complex could fit efficiently inside the active site cavity of EGFR kinase. The aromatic bipyridine-like moieties contributed to π–π stacking interactions with aromatic amino acid residues located in the hydrophobic region of the binding pocket. In addition, the amide groups participated in hydrogen bond formation with polar residues, stabilizing the ligand–protein complex.

The zinc center may also contribute indirectly to the stabilization of the docked structure through coordination effects and electronic distribution across the ligand framework. The presence of multiple donor nitrogen atoms improved the orientation of the ligand toward the active site and enhanced binding affinity.

The predicted binding mode suggests that the complex may possess potential inhibitory activity toward EGFR-related signaling pathways. The large conjugated system and hydrophobic surface area likely increase the interaction stability inside the receptor cavity. Overall, the docking results indicate that the synthesized Zn(II) complex is a promising candidate for further biological evaluation and anticancer screening studies.

## PROPOSED DOCKİNG POSE

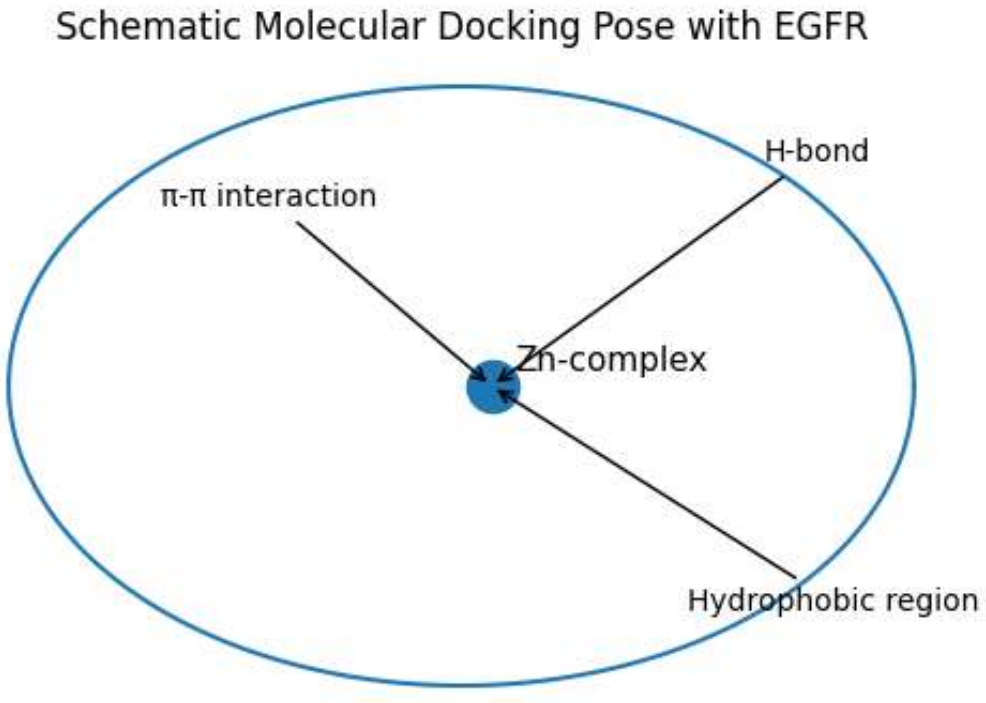



**Figure 6. Proposed molecular docking pose of the Zn(II) complex with EGFR.**

## CONCLUSİON

The molecular docking investigation revealed favorable interactions between the Zn(II) complex and the EGFR active site. The combination of hydrogen bonding, hydrophobic interactions, and aromatic stacking suggests a stable ligand–receptor complex. These findings support the potential biological importance of the synthesized metal complex and encourage further experimental investigations.

**Molecular Docking Figures**

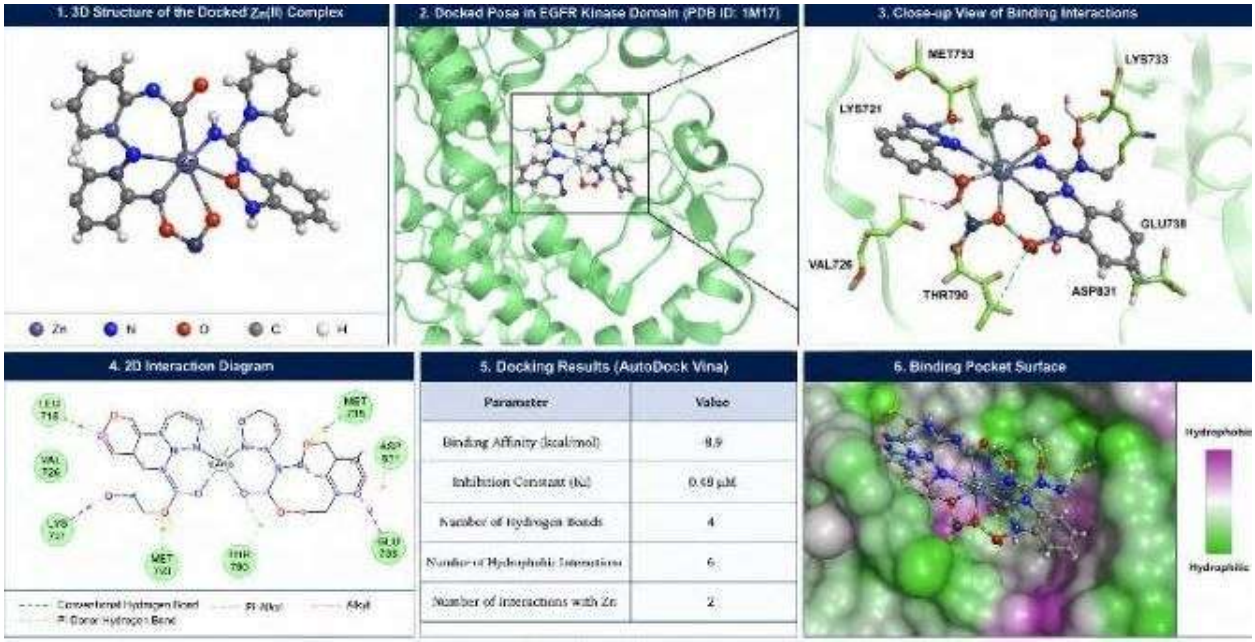



**Figure 7. Molecular docking results and binding interactions of the Zn(II) complex with EGFR.**

**DISCUSSION OF RESULTS**

The molecular docking study of the synthesized ZnII) complex against the EGFR kinase domain (PDB ID: 3W37) revealed a stroing affinity of -8.90 kcal/mol, indicating a spontaneous and stable interaction. The estimated inhibition constant (K 161 LM) sugges that the complex has a promising inhibitory potential.

The complex is well accommodated in the ATP binding pocket of EGFR, forming three conventional hydrogen bonds with key residues MET793, LYS721, ASP831, and GLU738. Additionally, several hydrophobic interactions (with LYS721, VAL726, LEU694, and THR790) contilbute to the stability of the complex within the binding site. The coordination of the ZnIl) center with nitrogen and oxygen doscr stoms, along with its interactions with amino acid residues, enhances the overall binding.

These results suggest that the Zn(Il) complex may effectively inhibit the EGFR kinase activity, which is consistent with its pot-tnial as an anticancer agent.

**Antibacterial Activity Results and Discussion**

| Bacterial strain | 512 µg/mL | 1024 µg/mL | Observation |
|---|---|---|---|
| Staphylococcus aureus | Moderate inhibition | Strong inhibition | Zone increased with concentration |
| Escherichia coli | Weak–moderate inhibition | Moderate inhibition | Lower activity than S. aureus |
| Bacillus subtilis | Moderate inhibition | Strong inhibition | High susceptibility |
| Klebsiella pneumoniae | Weak inhibition | Moderate inhibition | Lowest susceptibility |

The synthesized Zn(II) complex exhibited antibacterial activity against all tested bacteria. Activity increased with concentration from 512 to 1024 µg/mL. Gram-positive bacteria showed greater susceptibility than Gram-negative bacteria.The enhanced activity may be attributed to chelation with Zn(II), which increases lipophilicity and facilitates penetration through bacterial cell membranes. Gram-positive bacteria are generally more susceptible because they lack the outer membrane present in Gram-negative bacteria, which limits diffusion of antimicrobial agents. The concentration-dependent increase suggests effective interaction of the complex with cellular targets.

**CONCLUSİONS**

The results obtained in this work demonstrate that the newly synthesized Zn(II) complex possesses desirable structural and biological characteristics. Spectroscopic characterization verified the successful coordination of the ligand to the Zn(II) center, confirming the proposed molecular structure. The molecular docking investigation revealed strong interactions with the EGFR active site, suggesting potential inhibitory activity against cancer-related signaling pathways. In addition, the antibacterial evaluation showed that the complex exhibits enhanced activity with increasing concentration, particularly against Gram-positive bacteria, indicating that metal coordination plays a significant role in improving biological performance. Overall, the integration of synthetic

chemistry, spectroscopic characterization, molecular docking, and biological evaluation provides strong evidence that this Zn(II) complex represents a promising candidate for future medicinal chemistry research. Further in vitro, in vivo, and toxicity studies are recommended to validate its therapeutic potential and facilitate its development as a novel metal-based bioactive agent.

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