New Materials, Compounds and Applications
Vol.9, No.1, 2025, pp.109-122
https://doi.org/10.62476/nmca.91109

SYNTHESIS, CHARACTERIZATION, *IN SILICO* SCREENING FOR MOLECULAR DOCKING AND COMPUTATIONAL EXPLORATION OF SOME NOVEL METAL COMPLEXES DERIVED FROM AMPICILLIN - ISATINE SCHIFF BASES

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Abstract. The ampicillin - Isatine Schiff base ligand was prepared from the Isatine and ampicillin which is an antibiotic belonging to the aminopenicillin class of the penicillin family. The drug is used to prevent and treat several bacterial infections and its novel Ni, Co, Mn, Zn and Cu complexes have been synthesized. The characterization of these new complexes has been made by physical properties in addition to microanalysis and FT-IR spectroscopic technique of FT-IR and the electronic spectra, molar conductivity of complexes which indicated the validity of two doner atoms and therefore that this coordination occurred via a bidentate ligand with the two chloride atoms which was proved by the non-electrolyte complexes and the ligand donor atoms were the oxygen atom of the exocyclic carbonyl of cyclic (β-lactam ring) and the acyclic amide oxygen atom of the ampicillin, the magnetic susceptibility pointed and proved that the bivalent Mn and Co complexes (IIb-c) showed high spin octahedral geometry, while the bivalent Ni complex (IIa) shows low spin distorted octahedral geometry, but bivalent Cu complex (IId) and Zn complex (IIe) show low magnetic moment indicate low spin distorted octahedral geometry. The docking study revealed that the newly synthesized nickel complex (IIa) demonstrates significant potential in inhibiting the enzymes KacT, CinB and Tryptophanase. The strong interactions observed between the compound and the target enzymes suggest its viability as a promising therapeutic candidate.

Keywords: *Ampicillin-Isatine Schiff base, Ni, Co, Mn, Zn and Cu complexes, In silco Screening, molecular docking, computational exploration.*

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Received: *14 January 2025;* ***Accepted:*** *19 March 2025;* ***Published:*** *9 April 2025.*

1. Introduction

Scientists have carried the concerns of microbes since the late seventeenth century and since then, they have aspired to manufacture or discover anti-drugs that treat diseases

How to cite (APA):
Albotani, A.S.A., Mohammed, E.R., Al-Dulaimi, M.S., Saied, S.M. & Saleh, M.Y. (2025). Synthesis, characterization, *in silico* screening for molecular docking and computational exploration of some novel metal complexes derived from ampicillin - Isatine Schiff bases. *New Materials, Compounds and Applications*, *9*(1), 109-122 https://doi.org/10.62476/nmca.91109

caused by these microbes, since the early days of the use of anti-infective agents especially after the World War, the so-called resistance to these antibiotics began (Banoon *et al*., 2021; Muteeb *et al*., 2023), which created clinical problems that became more important to be interested in solving. In addition, researchers around the world have begun to seek to solve this problem either by synthesizing new drugs or modifying existing drugs and studying the structure-activity relationships (Al-Jubori *et al*., 2024; Banoon *et al*., 2025), which guided many scientists to solve the resistance problems of the anti-infective medicines such as beta-lactams or anticancer (AlHasan *et al*., 2013; Ramos-Martín & D'amelio, 2023; ul Qamar *et al*., 2025). One of these approaches is the development of coordinating chemistry, i.e. the use of complex protocols that use important drugs with resistance problems as organic ligands especially those of multidentate ligands of (bi- or tridentate). Some of these complexes work to load the drug and decompose it slowly, as it does to the jawbone in rabbits (Yaseen *et al*., 2025).

Metal complexes have been used in the preparation of a large number of modern nanocatalysts, such as Palladium salts fabricated on Fe_3O_4 (Saleh *et al*., 2025), as an organic-inorganic hybrid nanocatalyst, Sulfonated Multi-Walled Carbon Nanotubes (Saied *et al*., 2022), as Heterogeneous Nanocatalysts and $TiFe_2O_4$@ SiO_2-SO_3H (Saleh *et al*., 2024) which was used for esterification. Many of these complexes have succeeded in acting as antimicrobials and resistance blockers, this provided chances for the field of these complexes to increase the bacteriostatic or bacteriotoxic effects (Hussein *et al*., 2022; Ahmad *et al*., 2024) and thus the recent works highlighted divergent strategies on the field of metal-based antibacterial agents (Ali *et al*., 2022; Al-Saady *et al*., 2022; Pandey & Boros, 2022).

In addition to the problem of drug resistance, the problem of serious side effects (allergies to some of them, such as antibiotics, have reached a dangerous level or even death), besides the spread of new and deadly types of diseases such as immunodeficiency (HIV/AIDS) and Covid 2019. New resistant cancer cells (Al-Rashidi *et al*., 2024; Ali *et al*., 2025), have accelerated the need to develop these complex protocols. Furthermore, metal complexes have demonstrated significant antioxidant properties, which play crucial roles in various human diseases. These compounds can act as free radical scavengers, helping to combat oxidative stress and contributing to bacterial resistance and disease progression (Falih *et al*., 2021; Lawi *et al*., 2021). Since that time, research has tended towards benefiting from coordination chemistry based on considering the chemical forms of the drugs are organic ligands (Lewis bases) that can bind to the many transition metals (Lewis acids) and studying the characters of the novel complexes formed and their pharmaceutical effects within the coordinating spheres on the pharmacodynamic (Azez *et al*., 2021), pharmacokinetic and thermal properties, as well as knowing the degree of increase in biological activities and the mode of actions of these complexes and their new ways to attack the receptors or enzymes thus their mode of actions (Al-Sultan *et al*., 2022).

The preparation these types of complexes as new from a mixture of aspirin (acetylsalicylic acid), paracetamol and methyldopa with divalent manganese, iron, cobalt, nickel and copper, with a study of their physical and chemical properties, preparation of new complexes of bivalent manganese, iron, cobalt and nickel with mixed ligands achieved by (Saleh *et al*., 2022; Raoof *et al*., 2022a; Al-Abboodi *et al*., 2024), of ciprofloxacin (Cip) and metronidazole (Met) or 4-amino antipyrine (4AAP) with the study of their chemical, physical properties and antibacterial activity and synthesis, characterization and biological evaluation study of cephalexin (Ceph) and Isatine Schiff

base and its complexation with some divalent metal ions (Aziz *et al*., 2021; Raoof *et al*., 2022b; Mohammed *at al*., 2022). In addition to this work of enhancing ampicillin's therapeutic function by modification of its molecular to Schiff base and coordinating it with binary metals of (Ni, Co, Mn, Zn or Cu metals): synthesis, characterization and in Silico screening for molecular docking and computational exploration.

2. Experimental Methods

Material and Measurements

The chemical reagents such as the transition bivalent element salts of (manganese, cobalt, nickel, zinc and copper) and divalent were used as provided. Fourier-transform infrared spectra were recorded as cesium iodide discs on an 8300 Shimadzu spectrophotometer. Ultraviolet light - visible spectra were measured in ethyl alcohol using Shimadzu light - visible 160 A spectrophotometer in the range (200-1000) nm. Magnetic susceptibility balance model MSB-MKI and flame atomic absorption of the elemental analyzer, Shimadzu AA-670, was used for metal determination. CHNS elemental analyzer model 5500-Carlo Erba instrument. Gallen Kamp M.F.B.600.010 F was used for elemental analysis.

Synthesis of Ampicillin - Isatine Schiff Base Ligand (AI)

The title Schiff base was synthesized by mixing an equimolar quantity (5 mmoles) of ampicillin (2.097 gm) and Isatine (0.736 gm) in 35 ml of methanol containing 0.5gm of Reline (deep eutectic solvent) in 100 ml boiling flask. Then this boiling flask mixture was refluxed for 3 hours and the precipitated product of the nticipated Schiff base was washed with the anticipatedter, dried and recrystallized from ethanol (Al-Mudhafar, 2022; Mahmood *et al*., 2024). All the physical properties of "% yields, melting point and elemental analysis" are shown in Table 1.

General synthesis of the Schiff base ligand – Bivalent metal complexes of 1: 2 ratio II (a-e)

A mixture of Schiff base (5 mmoles) and appropriate metallic salt (2.5 mmoles) with the ratio of 2:1 refluxed in ethanol (20 ml.) for 10hrs. The precipitated product was cooled, filtered and dried (Mohammed *et al*., 2022). All the physical properties of "% yields, melting point and elemental analyses" are shown in Table 1.

3. Results and Discussion

The designated Ampicillin - Isatine Schiff base ligand, (AI) (I) was synthesized by the nucleophilic addition reaction of the ampicillin primary amine group to the isatine electron-deficient carbonyl carbon under suitable conditions of Reline ionic solvent (deep eutectic solvent) as a catalyst to produce this important organic bond, namely the azomethine (imine) or ketimine because it made from ketone group of carbon-nitrogen double bonds (-CH=N-), Figure 1 (Khandelwal *et al*., 2016).

The using of the green catalyst (Reline), the deep eutectic solvent (the ionic solvent), which is usually used as a magic catalyst for many organic synthesis reactions in this laboratory helped to enhance the percentage yields of over 90%, this catalyst is prepared from the heating a mixture of (1:2) of urea and choline chloride till their fusion and then obtain the Reline which is liquid of little freezing points (deep eutectic) related to the starting constituents (eutectic mixtures), (Abdullah *et al*., 2021).

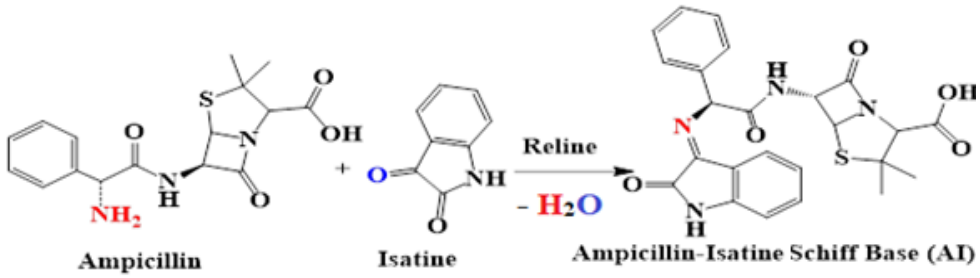

Figure 1. Synthesis of Ampicillin-Isatine Schiff Base (AI)

The pink colour of this Schiff base is due to the characteristic of all Schiff bases, which are always developed of UV light-controlled molecular logic gates (Bar *et al*., 2021).

The ^{1}H-NMR for the Schiff base ligand (AI):

The ^{1}H-NMR ppm for the ligand which was recorded in deuterated dimethylformamide solution ($(CD_3)_2NCOD$) are: 2.13-2.18 6H dimethyl groups, 2.73 and 3.11 and 3.14 for the 3H cyclic protons for the ß -lactam and thiophen fused rings (carbons 2,5 and 6 respectively of Penam subgroup) of the antibiotic ampicillin, 7.30-7.37 9H aromatic protons, also, 10.89-10.91 for the 2H for aliphatic and cyclic amides respectively and all these 1H-NMR spectra of this synthesized Schiff base is agreed with (Silverstein *et al*., 2005).

The FT-IR spectra of the Schiff base ligand I (AI):

The infrared spectrum of the ligand showed the following absorption bands at frequencies 1733 cm^{-1}, 1614 cm^{-1}, 754 cm^{-1}, 3550 cm^{-1} and 3394 cm^{-1}, which correspond to the vibrational frequencies of the functional groups υ (C=O) of carboxylic acids, υ (C=O) of amides, υ (C=N), υ(C-S), υ(H-O) and υ (N-H), respectively (Silverstein *et al*., 2005; Canisares *et al*., 2020). This Schiff base is commonly used to synthesize the target complexes compounds II(a-e), by acting as ligands, i.e. they are Lewis bases “they donate the two oxygen atoms of amides (cyclic and acyclic) to the central metal atom” via the refluxing of the mixture of the Schiff base ligand (AI) and appropriate metallic salt (Ni, Co, Mn, Zn or Cu) with the ratio of 2:1 in ethanol, as shown in Figure 2 (Al-Mudhafar 2022; Mahmood *et al*., 2024), Table 1 shows the melting points, colours, metal %, CHNS and physical properties of the ligand and all complexes. From the many active donor atoms are the oxygen atom of the exocyclic carbonyl of cyclic (β-lactam ring) and the acyclic amide oxygen atom of the ampicillin, Figure 2.

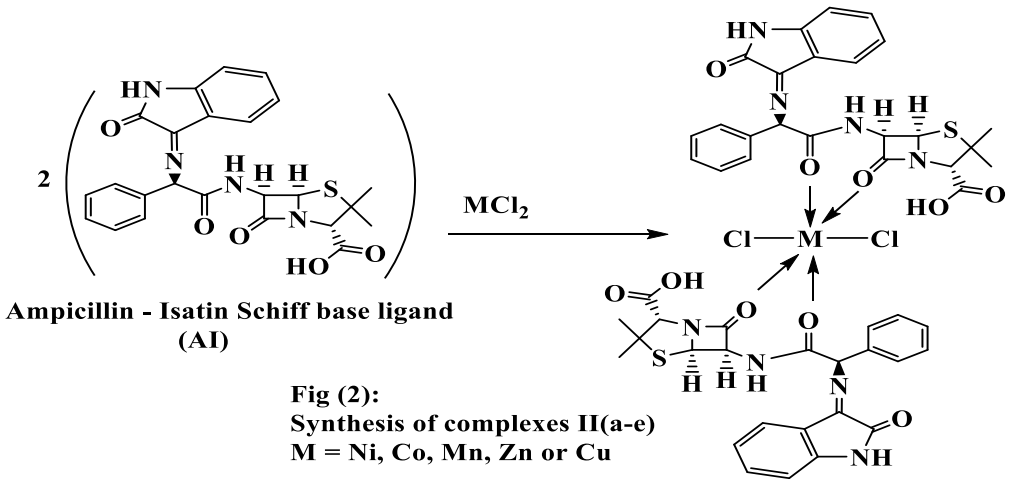

Figure 2. Synthesis of complexes II(a-e) M= Ni, Co, Mn, Zn or Cu

All the analyses that were made conclusively indicated the validity of two donor atoms and therefore, that this coordination occurred via a bidentate ligand with the two chloride atoms, which was proved by the non-electrolyte complexes by the molar conductivity analysis, as we will see later. This is in addition to the elemental microanalysis, which gives respectable agreement with the calculated values and accepted limits, Table 1.

Table 1. The % of metal and CHNS with the physical properties of ligand AI (I) and complexes II(a-e)

Ligand and complexes numbers and formula	colour	Melting point °C	CHNS (calculate/found)				
			C%	H%	N%	S%	M%
AI	pink	235	60.17/59	4.8/4.5	11.7/11.3	6.67/6.53	----
IIa[Ni(AI)$_2$Cl$_2$]	Light brown	>200	54.77/54.33	4.37/4.3	10.6/10.3	6.08/6.1	5.5/5
IIb[Co(AI)$_2$Cl$_2$]	Dark brown	>200	54.73/54.7	4.3/4.2	10.64/10.8	6.08/6.2	5.59/5.5
IIc[Mn(AI)$_2$Cl$_2$]	Dark brown	>200	54.9/54.5	4.38/4.3	10.68/10.3	6.1/6.2	5.2/4.7
IId[Cu(AI)$_2$Cl$_2$]	Green	>200	54.4/55.1	4.35/4.3	10.59/10.3	6.05/6.4	6/5.8
IIe[Zn(AI)$_2$Cl$_2$]	Brown	>200	54.4/54.5	4.34/4.27	10.57/10.52	6.04/6.1	6.16/6.4

The FT-IR spectra of the complexes II(a-e):

The prepared ligand coordinates with the metal salts MCl_2 (where M = Mn, Co, Ni, Cu, Zn) through the amide carbonyl groups of ampicillin. This coordination results in a decrease in the frequency of the $(C=O)^{\upsilon}$ amide band, which shifts to the range of 1652-1674 cm^{-1}. Additionally, a new band appears, corresponding to (M-O), which is observed in the range of 530–611 cm^{-1} in the infrared spectrum of the complexes. This indicates that the ligand behaves as a bidentate ligand, all these absorption bands are shown in Table 2 which agrees with the literature data (Hamdoon *et al*., 2022).

Table 2. The IR spectra of the ligand (AI) and the complexes I(a-e)

Ligand and complexes numbers and formula	carboxylic C=O	amidic C=O	C=N	C-S	O-H	N-H	M-O
AI	1733	1687	1614	754	3550	3394	
IIa [Ni $(AI)_2Cl_2$]	1718	1658	1618	752	3421	3305	530
IIb [Co $(AI)_2Cl_2$]	1735	1660	1625	754	5529	3296	527
IIc [Mn $(AI)_2Cl_2$]	1730	1657	1627	752	3431	3317	531
IId [Cu $(AI)_2Cl_2$]	1733	1652	1623	754	3394	3342	611
IIe [Zn $(AI)_2Cl_2$]	1728	1674	1622	754	3485	3201	592

The electronic spectra of the ligand (AI) and the complexes II (a-e):

The geometry of complexes II(a-e) and hence its request essentially needs the electronic spectra which are appreciated information and these spectra occur, when electrons within the complexes molecules or ions transfer from one energy level to another. Therefore, absorption spectra tell which are the energy levels of the ground state, which are excited and the possibilities for several possible absorptions to happen (Rajnikant, 2000).

These novel complexes II(a-e) electronic spectral assignments were concise in Table 3. The following bands of nickel (IIa) were observed: 11680 cm^{-1}, 13800 cm^{-1} and 26315 cm^{-1} which correspond to the transitions:

$^3A_2g(F) \rightarrow {}^3T_2g(F)\ \upsilon_1$

$^3A_2g(F) \rightarrow {}^3T_1g(F)\ \upsilon_2$

$^3A_2g(F) \rightarrow {}^3T_1g(P)\ \upsilon_3$ respectively.

These values align with a distorted octahedral geometry, (Khalaf *et al.*, 2024).

The absorption spectrum manganese complex (IIc) exhibits no d→d transitions observed in the visible region due to Laporte's rule which forbids both spin and orbital transitions (Chandra & Gupta, 2005). Instead, a broad band was observed at 27777 cm^{-1} attributed primarily to charge-transfer transitions involving the ligand (AI) spectrum with charge-transfer spectra. The electronic spectra cannot be used to determine the spatial geometry of the manganese complex. However, based on magnetic moment data, IR spectroscopy and analytical results it was inferred to have an octahedral geometry (Rodrigues & Galzerani, 2013). Regarding the cobalt complex spectrum (IIb), three bands were expected and they can be assigned as follows:

Table 3. The electronic spectra of the ligand (AI) and the complexes I(a-e)

No	Compounds	Absorption bands (cm^{-1})	Assignment electron transition	Geometry
AI	$C_{24}H_{22}N_4O_5S$	30303 39840	$n \rightarrow \pi^*$ $\pi \rightarrow \pi^*$	
IIa	[Ni $(AI)_2Cl_2$]	11680 13800 26315	$^3A_2g(f) \rightarrow {}^3T_2g(f)$ $^3A_2g(f) \rightarrow {}^3T_1g(f)$ $^3A_2g(f) \rightarrow {}^3T_1g(P)$	oct
IIb	[Co $(AI)_2Cl_2$]	11771 15447 20570 31645	$^4T_1g(f) \rightarrow {}^4T_2g(f)$ $^4T_1g(f) \rightarrow {}^4A_2g(f)$ $^4T_1g(f) \rightarrow {}^4T_1g(p)$ Charge transfer	oct

IIc	[Mn (AI)$_2$Cl$_2$]	27777	Charge transfer	oct
IId	[Cu (AI)$_2$Cl$_2$]	15573 27548 29850 31545	$^2B_1g \rightarrow {}^2A_1g$ $^2B_1g \rightarrow {}^2B_2g$ $^2B_1g \rightarrow {}^2Eg$ Charge transfer n $\rightarrow$ π* π $\rightarrow$ π*	oct
IIe	[Zn (AI)$_2$Cl$_2$]	27397 29498 31152	Charge transfer n $\rightarrow$ π* π $\rightarrow$ π	oct

An absorption band at 11771 cm^{-1} corresponding to the transition $^4T_1g(F)\rightarrow{}^4T_2g(F)$ and an absorption band at 15447 cm^{-1} corresponding to $^4T_1g(F)\rightarrow{}^4A_2g(F)$. Also, an absorption band at 20570 cm^{-1} corresponding to $^4T_1g(F)\rightarrow{}^4T_1g(P)$, these observations are consistent with an octahedral geometry, along with an additional band at 31645 cm^{-1}, attributed to charge-transfer transitions (Sotiles *et al*., 2019). In the copper complex spectrum (IId), which has an octahedral geometry, a single broadband was observed at 15573 cm^{-1} resulting from a combination of two or three transitions: $^2B_1g\rightarrow{}^2A_1g(\upsilon_1)$, $B_1g\rightarrow{}^2B_2g(\upsilon_2)$ and $^2B_1g\rightarrow{}^2Eg(\upsilon_3)$, in addition to the following bands were observed: 27548 cm^{-1}, 29850 cm^{-1} and 31545 cm^{-1} which were attributed to charge-transfer and the n $\rightarrow\pi*$ and $\pi\rightarrow\pi*$ transitions respectively (Hazra *et al*., 2014).

Finally, the zinc complex (IIe), with no d→d transitions occurs due to the filled d-orbitals which makes zinc not show the typical possessions of the transition metals such as forming ions with incomplete d-orbitals. It is not considered a typical transition metal (Cotton *et al*., 1999). However, the following bands were observed: 27397 cm^{-1}, 29498 cm^{-1} and 31152 cm^{-1} which attributed to charge transfer and n $\rightarrow\pi*$ and $\pi\rightarrow\pi*$ transitions, respectively, Table 3 (El-ghamry *et al*., 2022).

Molar conductivity of complexes (IIa-e):

Table 4. Molar conductance of AI ligand and their metal complexes (IIa-e)

No.	Formula	Molar conductance (ohm^{-1} cm^{2}mol^{-1})
Ligand (AI)	L= $C_{24}H_{22}N_4O_5S$	28
Complex (IIa)	[Ni (L)$_2$ Cl$_2$]	50
Complex (IIb)	[Co(L)$_2$Cl$_2$]	49
Complex (IIc)	[Mn(L)$_2$Cl$_2$]	46
Complex (IIe)	[Cu(L)$_2$Cl$_2$]	59
Complex (IId)	[Zn(L)$_2$Cl$_2$]	39

The observed values of the molar conductivity of these novel five complexes (II a - e) were in the range 49 - 59 ohm^{-1}cm^{2}mol^{-1}, which were displayed in Table 4 given below, these values suggest that those complexes are non-electrolytes (El-ghamry *et al*., 2022).

Magnetic susceptibility of complexes (IIa-e):

The magnetic susceptibility value of these novel metal complexes (IIa-e) is given in Table 5, the magnetic moment of bivalent Mn and Co (II) complexes (IIb-c) show high spin octahedral geometry. The bivalent Ni complex (IIa) shows low spin distorted octahedral geometry. But bivalent Cu complex (IId) shows low magnetic moment

indicating low spin distorted octahedral geometry. The zinc complex Zn (IIe) was diamagnetic because it was filled by electrons and thus octahedral geometry (El-ghamry *et al*., 2022).

Table 5. Magnetic susceptibility measurements of complexes (IIa-e)

No.	Chemical formula	μeff (B.M)
IIa	$[Ni (L)_2 Cl_2]$	3.6
IIb	$[Co(L)_2Cl_2]$	4.8
IIc	$[Mn(L)_2Cl_2]$	5.8
IId	$[Cu(L)_2Cl_2]$	3.2
IIe	$[Zn(L)_2Cl_2]$	-------

Background of in Silico Screening for Molecular Docking and Computational Exploration:

A molecular docking study was also carried out using the Auto Dock 4.2 program to predict the best-fit orientation of the complex molecule which was the Schiff base - nickel complex (IIa) which was chosen as representative for these novel complexes (II a-e). It binds to a specified protein target of interest to find out the activity and affinity of the complex molecule. This will enable to establish the mechanism by which the complex prevents bacterial growth.

The 5XUN protein:

The 5XUN protein represents the Y145F mutant of the KacT enzyme, which is part of the type II Toxin-Antitoxin (TA) system in *Klebsiella pneumoniae* (Wei *et al*., 2016). KacT, a Gcn5-related N-acetyltransferase (GNAT), inhibits bacterial cell growth by acetylating aminoacyl-tRNA, effectively blocking protein translation. Its primary function is to induce a "dormant" state or form highly resistant persister cells in response to stress or antibiotic exposure, making infections harder to eradicate (Majorek *et al*., 2013).

Inhibiting KacT could prevent persistent cell formation and enhance antibiotic treatment, but careful evaluation is necessary to avoid unintended bacterial overgrowth, Figure 3 (Vetting *et al*., 2005).

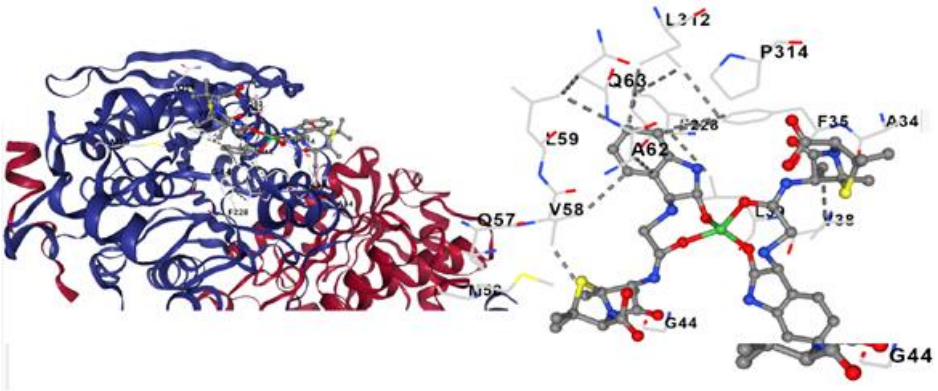

Figure 3. The 2D and 3D, molecular docking contacting compound with amino acid of (KacT enzyme)

The CinB enzyme (PDB code: 6KMO):

Commonly known as the "lipase/esterase superfamily", the CinB enzyme (PDB code: 6KMO) from *Enterobacter asburiae* belongs to the α/β-hydrolase family. Essential for bacterial metabolism depending on ester breakdown into simpler components for energy and biosynthesis, it accelerates the hydrolysis of ester bonds. Crucially in their adaptation and survival, CinB helps bacteria to use complicated fatty molecules in nutrient-starved conditions. Inhibition of CinB would throw off this process, therefore restricting the availability of fatty acids as an energy source and so impeding the growth and adaptability of the bacterium. This implies that, particularly in situations where bacterial life depends on CinB, CinB could perhaps be targeted for antibacterial treatments. Given its particular catalytic triad (Ser180-His307) and limited substrate binding sites, which could enable exact inhibitor design, Figure 4, further research is needed to fully understand its impact and potential as a therapeutic target.

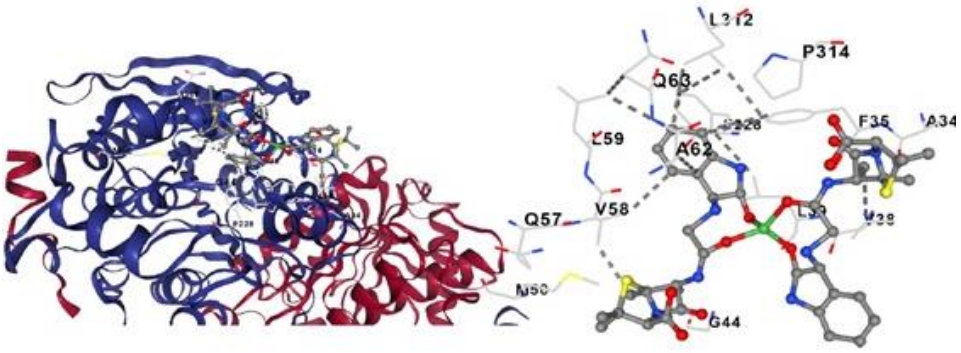

Figure 4. The 2D and 3D molecular docking contacting compound with amino acids of (CinB enzyme)

Tryptophanase (PDB code: 1AX4):

Tryptophanase (PDB code: 1AX4) from *Proteus vulgaris* is a key enzyme that catalysis the breakdown of the amino acid L-tryptophan into indole, 2-aminoprop-2-enoate and ammonia. This reaction is crucial for the metabolism of aromatic amino acids and is facilitated by the cofactor pyridoxal 5'-phosphate (PLP), which binds directly to the enzyme's active site, making it essential for its catalytic function, Figure 5 (Christen & Mehta, 2001; Amadasi *et al*., 2007).

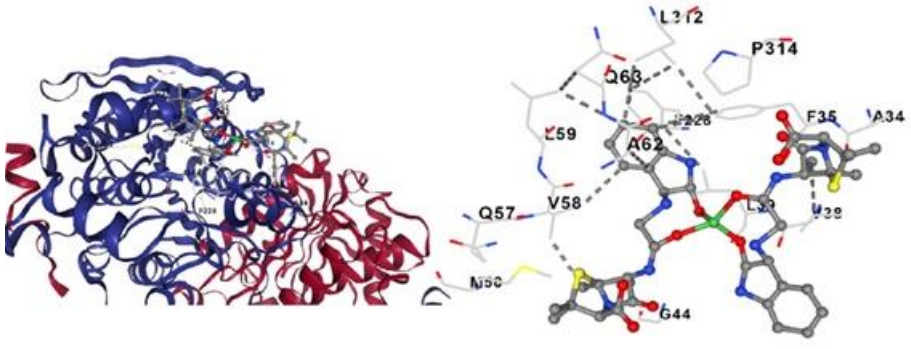

Figure 5. The 3D molecular docking contacting compound with amino acids of (Tryptophanase)

By converting tryptophan into indole, a signaling molecule affecting gene expression, biofilm development and antibiotic resistance, the enzyme is crucially

involved in bacterial physiology. By preventing tryptophanase, indole generation would be blocked, possibly upsetting biofilm development and lowering the bacterial tolerance to environmental stress and antibiotics (Bais *et al*., 2006; Kulikova *et al*., 2006). Consequently, especially under conditions when tryptophan is the main energy source, the bacteria may suffer slower development and disturbed metabolic balance. Thus, especially against bacteria that mostly depend on this metabolic pathway, tryptophanase could be a suitable target for creating new antibacterial drugs.

Docking Discussion:

According to the docking analysis, the recently produced nickel complex (IIa) has great potential in reducing the enzymes KacT, CinB and Tryptophanase (Fukunishi & Nakamura, 2012). Applications of artificial intelligence (AI) and nanotechnology help to improve the production and characterisation of these unique metal complexes even more. Particularly for the nickel complex (IIa), AI systems can maximize the molecular docking process, hence increasing binding affinity predictions and protein-ligand interaction studies. Spectral data interpretation might be improved by machine learning models (Geng *et al*., 2019; Hassan *et al*., 2023).

4. Conclusion

Structural studies support the ligands connected with metal ions by bidentate interactions between the oxygen atoms of the exocyclic carbonyl in the β-lactam ring and the amide oxygen of ampicillin. Electronic spectra and magnetic studies suggest that the generated complexes have octahedral geometries and metal ion-dependent spin states. Furthermore, molecular docking revealed that the nickel complex (IIa) might inhibit bacterial enzymes like Tryptophanase, CinB and KacT. Strong interactions between the complex and these enzymes imply it may cure bacterial illnesses. These results reveal that coordination chemistry allows Schiff base metal complexes to be applied in drug design to solve antibiotic resistance.

In vitro and in vivo research should be done to verify the antibacterial action of these complexes. Furthermore helping to maximize and utility of these compounds in pharmaceutical formulations are computer techniques, artificial intelligence and nanotechnology.

Acknowledgements

Authors are grateful to the Researchers Supporting Project (ANUI/2025/SCI07), Alnoor University, Mosul, Iraq, the researchers also thank the University of Mosul for the support provided in the field of laboratory work.

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